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Palladium-mediated cyclizations

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Palladium-mediated cyclizations

by

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In Charge of Major Work

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For the Major Department

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For the Graduate College

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TABLE OF CONTENTS

DEDICATION

I would like to dedicate this work to my two grandmothers, Mabel Post and the late Eleanore Fried and to my great-grandmother, the late Carrie Wallin. These three women have provided me with the inspiration necessary for pursuing an advanced degree. As each of these women have met the challenges of their lives, I hope to meet the challenges in mine.

GENERAL INTRODUCTION

The development of synthetic methods which utilize palladium has become an important area in organic chemistry. There are two main reasons for the recent growth in organopalladium chemistry. First, palladium-based methodology is able to accommodate a wide variety of important organic functional groups. Secondly, palladium can catalytically affect a number of novel synthetic transformations.

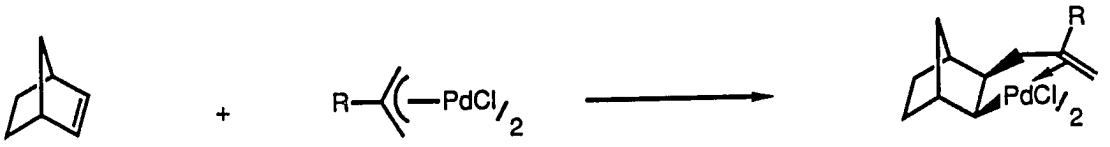
The work in this dissertation involves formation of carbon-carbon bonds utilizing palladium-mediated reactions. Both the versatility and the tolerance of palladium-based methodology is demonstrated in this work. Each section examines a unique question in organopalladium chemistry. The first section discusses the exploration of a single reaction, the reaction between norbornadiene-palladium dichloride and 1-iodomercurio-2-butyne. The second section examines the utility of palladium-catalyzed arylannulation of conjugated dienes. Finally, the third section probes further extensions of the palladium-catalyzed arylannulation discussed in Section Two.

SECTION 1. REACTION OF NORBORNADIENE-PALLADIUM DICHLORIDE AND 1-IODOMERCURIO-2-BUTYNE

INTRODUCTION

Palladium-mediated additions of organic compounds to bridged, bicyclic olefins have been studied extensively. The reaction of norbornene and related compounds with a wide variety of organopalladium compounds proceeds via syn addition to yield the cis-exo product 1 (Scheme I).[1-18] The

Scheme I

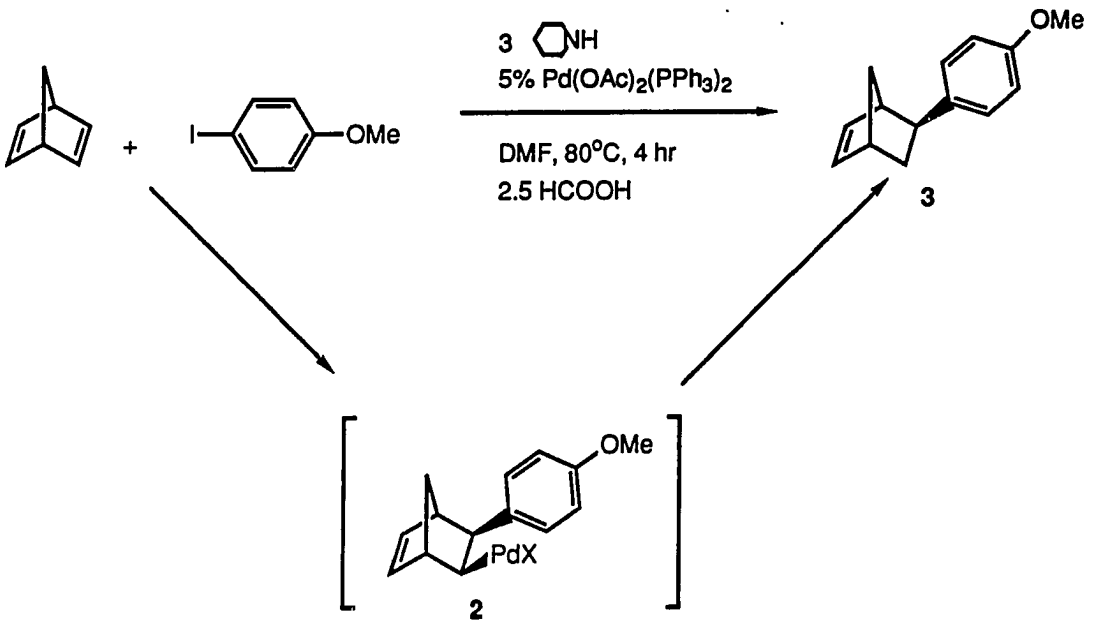


1

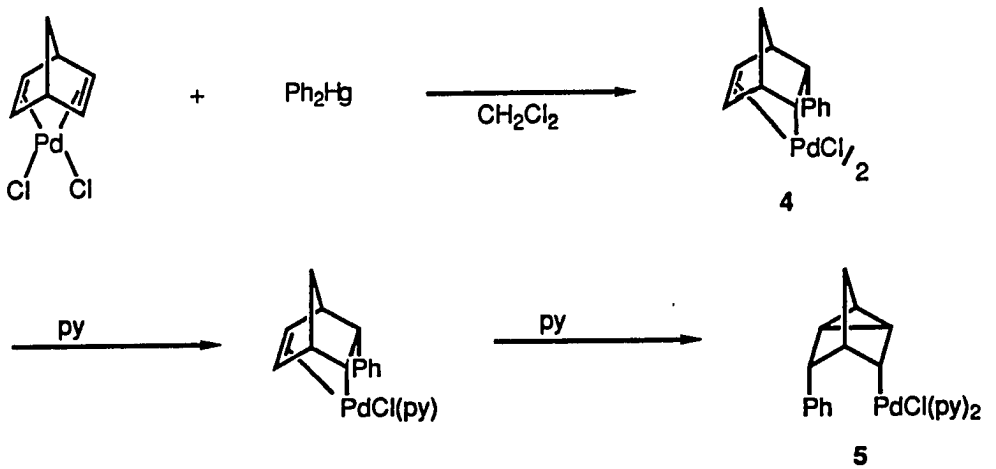
stereochemistry of a number of these products has been confirmed by X-ray studies.[3,4] Arcadi and co-workers recently reported the palladium-catalyzed addition of arenes to norbornadiene (Scheme II).[18] The intermediate σ-alkylpalladium species 2 is reduced in situ to afford 3. Again, the exo product is formed.

Prior coordination of the olefin to the palladium drastically affects the stereochemistry of the product. Addition of diphenylmercury to norbornadiene-palladium dichloride initially yields di-μ-chlorobis(2,5,6-η^3-3-endo-phenylnorbornen-2-yl-endo-palladium) 4 (Scheme III).[8,9] Upon addition of excess pyridine, the palladium σ,π-complex 4 undergoes rearrangement to the σ-nortricyclenyl complex 5.

Scheme II

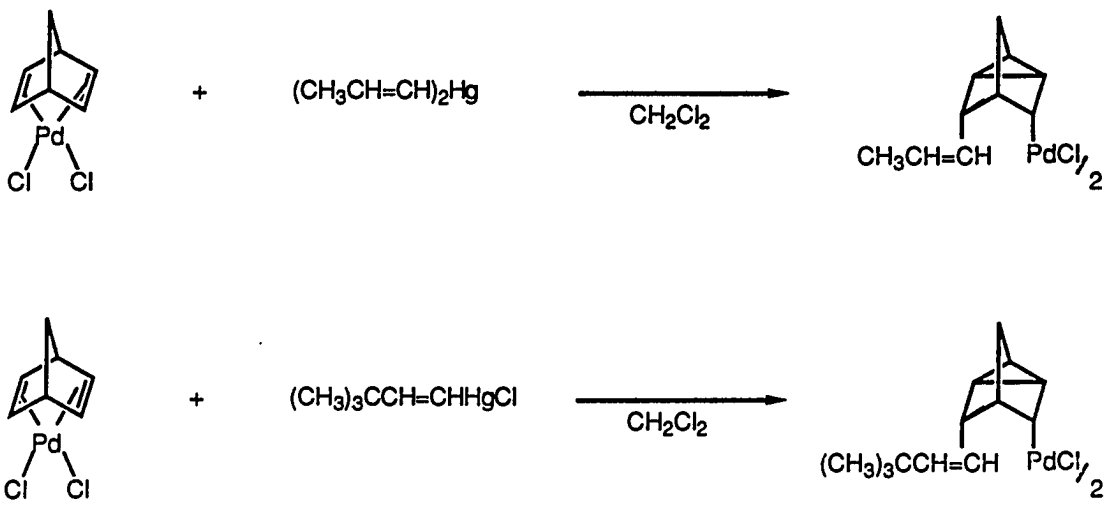


Scheme III



The reaction of vinylmercurials with norbornadiene-palladium dichloride immediately yields the σ-nortricyclenyl complex (Scheme IV).[13,14]

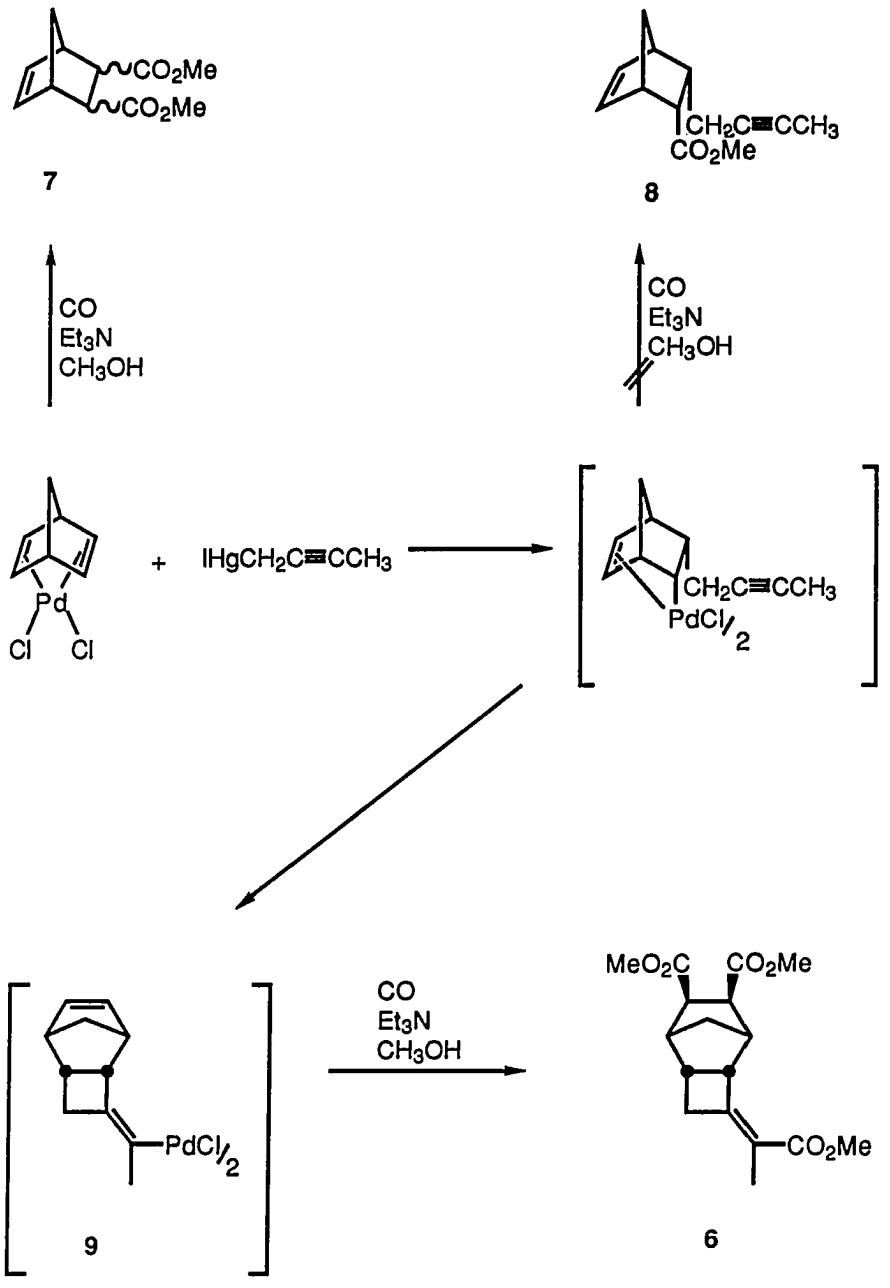
Scheme IV.



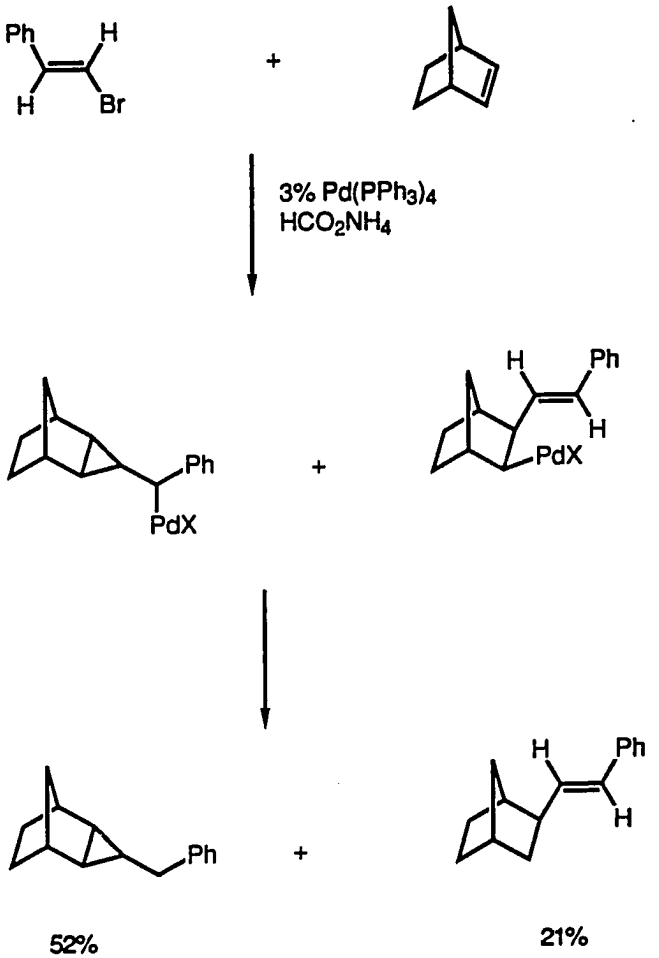
Ward used norbornadiene-palladium dichloride in an attempt to synthesize prostaglandin endoperoxide analogues.[19] Norbornadiene-palladium dichloride was reacted with 1-iodomercurio-2-butyne and carbonylated in situ to yield two unexpected products, 6 and 7. None of the expected product 8 was formed (Scheme V).[19] The product yields were low, and Ward was never able to isolate the proposed intermediate palladium compound 9.[19]

Catellani and co-workers have reported similar cyclizations upon adding vinylic groups to norbornene.[15,16] The intermediate palladium compounds formed during the palladium-mediated reactions of vinylic bromides and norbornene were trapped in situ with ammonium formate (Scheme VI).[15,16]

Scheme V


CO2Me
CO2Me
7
CH2C≡CCH3
CO2Me
8
CO
Et3N
CH3OH
CO
Et3N
CH3OH
Pd
Cl
Cl
+
IHgCH2C≡CCH3
CH2C≡CCH3
PdCl2
PdCl2
9
CO
Et3N
CH3OH
MeO2C
CO2Me
CO2Me
6

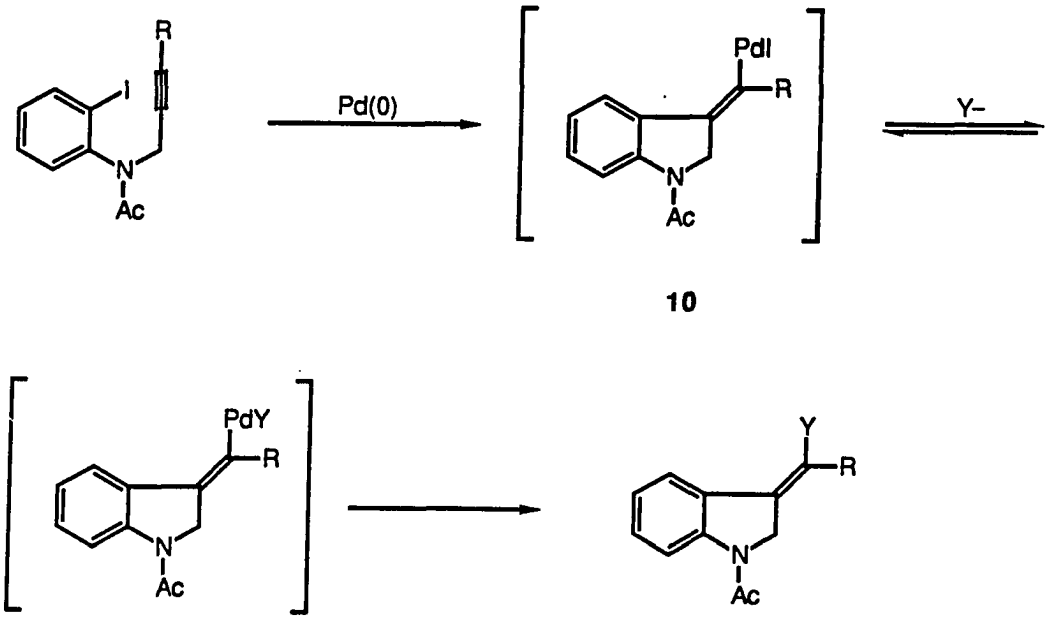
Scheme VI



Recently, Burns et al. have reported palladium-catalyzed 5- and 6-exo-dig cyclizations onto proximate alkynes (Scheme VII).[20-23] The proposed intermediate palladium compound 10 was then trapped in situ with hydride sources,[20,21] organotin reagents,[21] or organozinc or organoboron reagents.[22]

Vinylpalladium compounds have been isolated by a number of research groups.[24-30] The vinylpalladium compounds isolated thus far have all been stabilized by phosphine

Scheme VII



ligands on the palladium, and halides or electron-withdrawing groups on the olefin. Isolation of the σ-vinylpalladium intermediate 9 from the reaction of norbornadiene-palladium dichloride and 1-iodomercurio-2-butyne would provide a unique compound for study.

Prior to initiating our study of the reaction of norbornadiene-palladium dichloride and 1-iodomercurio-2-butyne, there were no reports of intramolecular cyclizations of organopalladium compounds onto alkynes to yield stable σ-vinylpalladium species. The work in this section involves a study of a novel, intramolecular, palladium-mediated cyclization, and characterization of two novel palladium compounds.

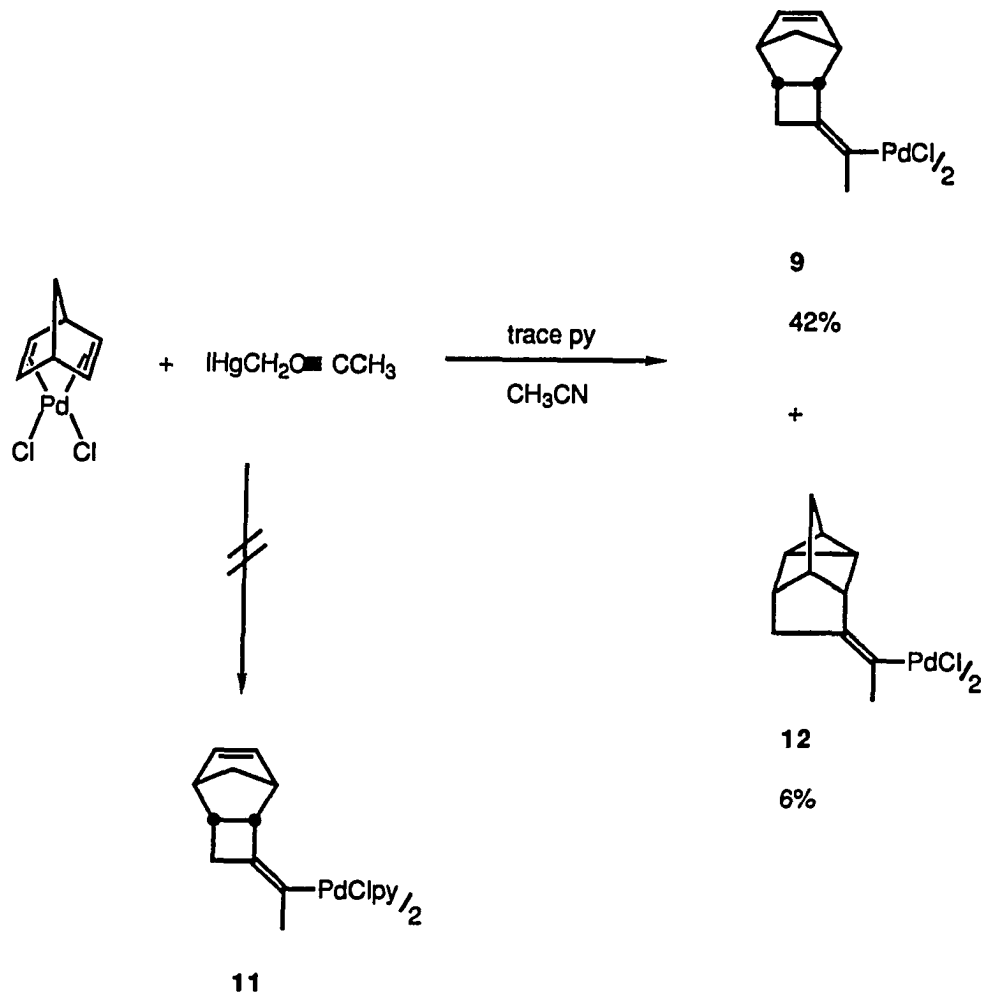
RESULTS AND DISCUSSION

Norbornadiene-palladium dichloride generally reacts with organomercurials to yield endo,endo-norbornenyl palladium compounds.[1,8,9,11-14] However, when Ward reacted norbornadiene-palladium dichloride with 1-iodomercurio-2-butyne, and carbonylated the palladium intermediate in situ, he isolated a tricyclic ester 6.[19] He was never able to isolate the intermediate σ-vinylpalladium compound 9.

Initial attempts at isolating compound 9 met with failure. It was not until addition of pyridine was attempted that a stable palladium compound was isolated (Scheme VIII). The expected pyridine adduct 11 was not isolated, but rather, two σ-vinylpalladium compounds 9 and 12 were found. It was thought that the addition of a base, pyridine, had inhibited decomposition of the organopalladium compounds during work-up. Subsequent reactions, run in the presence of potassium or sodium carbonate afforded the two palladium compounds in high yield.

The work of Segnitz and co-workers suggests that isomerization of palladium σ,π-complex 4 to σ-nortricyclenyl complex 5 is dependent on the addition of outside ligands.[8,9] Since the reaction of norbornadiene-palladium dichloride and 1-iodomercurio-2-butyne yielded two products, and polar solvents, such as acetonitrile, are known to act as ligands

Scheme VIII



for palladium,[31] a solvent study was initiated on this reaction (Table I).

The results of the solvent study indicate that polar solvents favor the formation of nortricyclenyl palladium compound 12, while less polar solvents favor the formation of 9. These results are consistent with the results of Segnitz et al.[8,9] Segnitz and associates found that phenyl-

Table I. Solvent studies in the reaction of norbornadiene-palladium dichloride and 1-iodomercurio-2-butyne

entry	solvent	ratio 9 : 12[a]
1	DMF	1 : 3
2	d^6-DMSO	1 : 2
3	d^3-CH_3CN	1 : 1
4	d-$CHCl_3$	5 : 2
5	d^2-CH_2Cl_2	7 : 2
6	d^6-PhH	1 : 0

[a]Product ratios determined by ^1H NMR spectroscopy.

norbornenyl-palladium chloride 4 isomerized to phenyl-nortricyclenyl-palladium chloride 5 in the presence of added ligands.

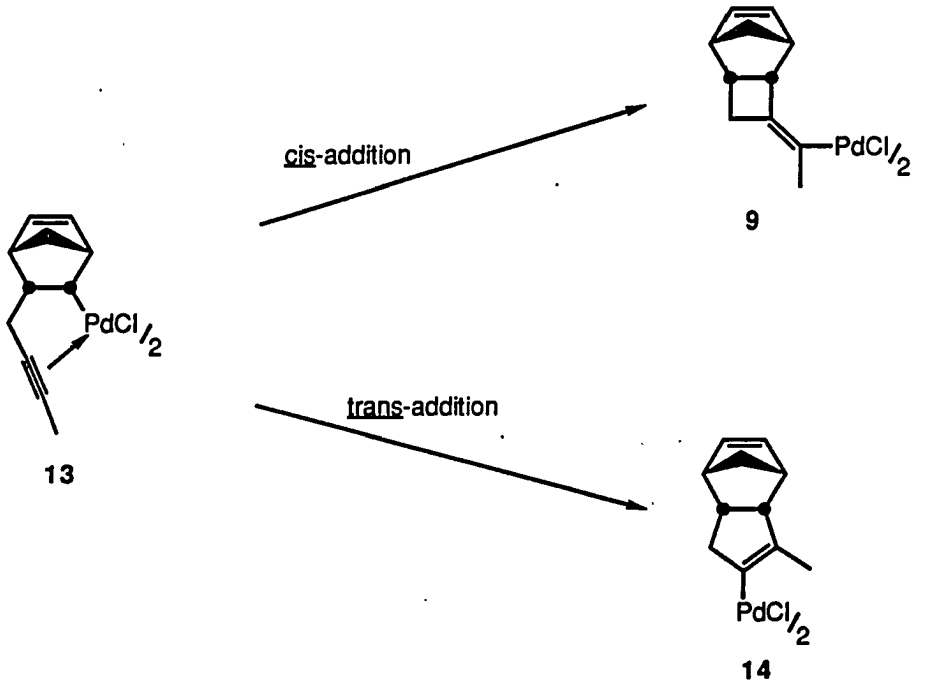
Since benzene led to exclusive formation of 9, it was the solvent of choice for isolation of the norbornenyl compound. While polar solvents tend to give better ratios for the formation of the nortricyclenyl compound, they also give lower overall yields, and the products tend to decompose more readily upon removal of solvent. For this reason, 12 was best isolated from methylene chloride. Compound 12 could be easily separated from compound 9. The solution was concentrated until solid just began to form, then diluted with pentane and cooled in the freezer overnight. Filtration of the suspension yielded 12 cleanly, and the filtrate could be evaporated to give 9.

Having found conditions to furnish the two organo-palladium compounds, we sought to fully characterize compounds 9 and 12. ^{1}H NMR, ^{13}C NMR, IR and mass spectra were obtained on both compounds. Full spectral data are reported in the experimental section, and only the general highlights will be discussed here.

The ^{1}H NMR spectrum of compound 9 shows eleven protons in the aliphatic region from δ 1.0 - 4.0. The other two protons resonate at δ 6.15. The pattern of the ^{1}H NMR is very similar to the ^{1}H NMR spectra of other norbornenyl compounds.[32] The initial σ-alkylpalladium intermediate 13

formed in the reaction of norbornadiene-palladium dichloride and 1-iodomercurio-2-butyne is consistent with the observed ^1H NMR spectrum. Two other possible structures 9 and 14, arising from palladium-carbon addition across the triple bond, are also consistent with the ^1H NMR spectrum (Scheme IX). Structure 13 has two olefinic carbons and two alkynyl

Scheme IX



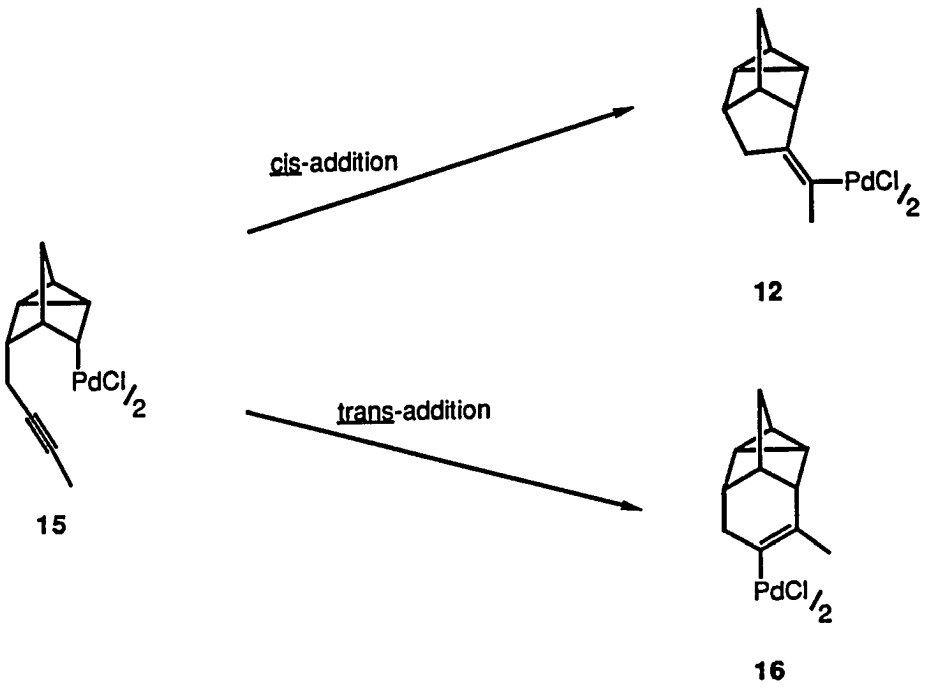
carbons, but the ^{13}C NMR spectrum of 9 shows four olefinic carbons at δ 127.85, 128.34, 136.11 and 137.81 and no alkynyl carbons. Structure 14 has been ruled out mainly for mechanistic reasons. Structure 14 would arise via trans addition of the palladium-carbon bond of 13 to the internal alkyne. The vast majority of organopalladium additions to triple bonds occur in a cis fashion.[33] Furthermore, the ^1H

NMR of 9 does not resemble that of dicyclopentadiene. One would expect the aliphatic region in the ^{1}H NMR spectrum of 14 to be very similar to the ^{1}H NMR spectrum of dicyclopentadiene. Based on the spectral analysis outlined here, structure 9 was chosen as the most likely structure for this compound.

The ^{1}H NMR of compound 12 lacks signals in the olefinic region. All thirteen protons resonate in the aliphatic region between δ 1.0 - 4.0. The pattern seen in the ^{1}H NMR spectrum is similar to the ^{1}H NMR spectra of other nortricyclic compounds.[32] The ^{1}H NMR spectrum of 12 is consistent with the initially formed nortricyclic intermediate 15. However, structure 15 is inconsistent with the ^{13}C NMR spectrum of 12. Structure 15 has two alkynyl carbons and no olefinic carbons. The ^{13}C NMR spectrum of 12 shows two carbon resonances in the olefinic region, and no signals in the acetylenic region. Two σ-vinylpalladium compounds 12 and 16 could presumably arise from 15 (Scheme X). Using arguments analogous to those used for compound 9, structure 12 was chosen as the most likely structure for this compound.

An X-ray single-crystal structure analysis was desired for compounds 9 and 12, since they are novel structures. Upon isolation, compound 9 is an oil whereas compound 12 is a powder. Numerous attempts have been made at obtaining crystals suitable for an X-ray crystal structure analysis.

Scheme X



Numerous solvents and solvent mixtures were tried in crystallization studies of compound 9 (Table II), and compound 12 (Table III). Neither compound 9, nor compound 12, yielded crystals suitable for an X-ray analysis.

Since compounds 9 and 12 could not be crystallized in suitable form for single-crystal X-ray structure analysis, the next step was to isolate and crystallize various adducts of 9 and 12. Compounds 9 and 12 may be stabilized by the addition of ligands to form the tetracoordinate palladium(II) species 17 (Scheme XI).[34,35] Two of the more common ligands employed in palladium chemistry are pyridine and various phosphines.[36]

Table II. Crystallization of 9[a]

entry	solvent	temperature (°C)	results
1	CH_2Cl_2	rt	black powder
2	CH_2Cl_2	10	black powder
3	CH_2Cl_2	-10	black powder
4[b]	CH_2Cl_2	10	black powder
5	$CHCl_3$	rt	black powder
6	$CHCl_3$	10	black powder
7	$CHCl_3$	-10	black powder
8[b]	$CHCl_3$	10	brown powder
9	Et_2O	rt	yellow powder
10[c]	Et_2O	10	yellow powder
11	t-$BuOCH_3$	rt	yellow powder
12	$C_6H_5OCH_3$	rt	black powder
13	$C_6H_5CH_3$	10	yellow oil
14	EtOAc	10	yellow powder
15[c]	EtOH	rt	brown powder
16[c]	EtOH	-78	yellow powder

[a]The oil was dissolved in an excess of solvent, and the solvent was allowed to slowly evaporate.

[b]The solution was washed with saturated ammonium chloride before the solvent was evaporated.

[c]The solid was dissolved in a hot solution, and the solution was slowly cooled to the temperature indicated.

Table II (continued)

entry	solvent	temperature (°C)	results
17[d]	Et_2O/C_6H_6	10	yellow crystals
18	i-PrOH/CH_2Cl_2	10	brown solid
19	C_6H_6/Me_2CO	rt	yellow powder
20	CH_2Cl_2/Me_2CO	rt	brown powder
21	THF/C_6H_{14}	rt	yellow powder
22[e]	$MeOH/C_6H_6$	rt	yellow crystals
23	CH_2Cl_2/C_6H_{14}	rt	brown powder
24	C_6H_6/C_5H_{12}	rt	brown powder
25	CH_2Cl_2/MeOH	rt	brown powder
26	$EtOH/H_2O$	rt	yellow powder
27	$EtOH/H_2O$	10	yellow powder
28	$C_6H_{11}OH/C_6H_6$	rt	yellow powder
29[f]	CH_3CN	-	brown powder
30[f]	C_6H_6/C_6H_{14}	-	yellow powder
31[f]	CH_2Cl_2	-	black powder

[d]Crystals proved to be conglomerates, and were unsuitable for X-ray analysis.

[e]Crystals decomposed during X-ray analysis.

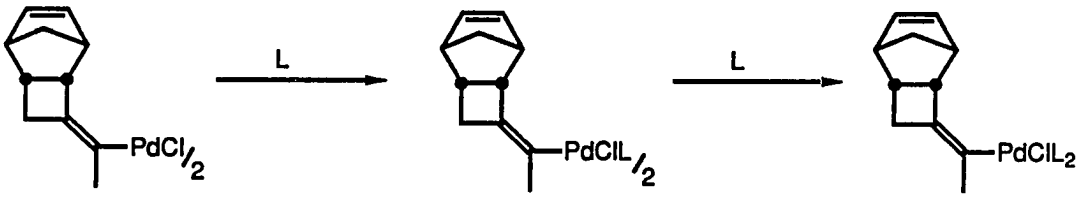
[f]The oil was dissolved in a minimum of solvent, and the resultant solution was slowly cooled to -78°C.

Table III. Crystallization of 12[a]

entry	solvent	temperature (°C)	results
1	CH_2Cl_2	rt	black solid
2	CH_2Cl_2	10	black solid
3	CH_2Cl_2	-10	black solid
4	$CHCl_3$	10	black solid
5	C_5H_{12}	rt-40	insoluble
6	C_6H_{14}	rt-40	insoluble
7	Me_2CO	rt	yellow powder
8	Et_2O	-10	yellow powder
9	CH_2Cl_2/C_5H_{12}	-10	yellow powder
10	$CHCl_3/C_5H_{12}$	-10	brown powder

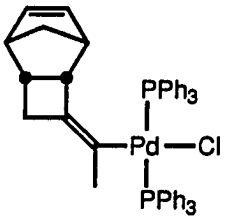
[a]The powder was dissolved in an excess of solvent, and the solvent was allowed to slowly evaporate.

Scheme XI

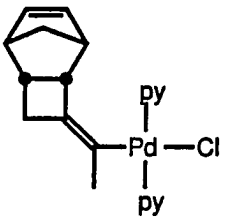


17

The addition of triphenylphosphine, 1,2-bis(diphenylphosphino)ethane or pyridine ligands to vinylpalladium compounds 9 and 12 is readily achieved by simply stirring either compound with the desired ligand. Formation of compounds 18-20, was effected within three hours at room



18



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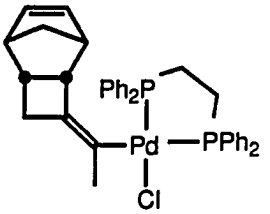


20

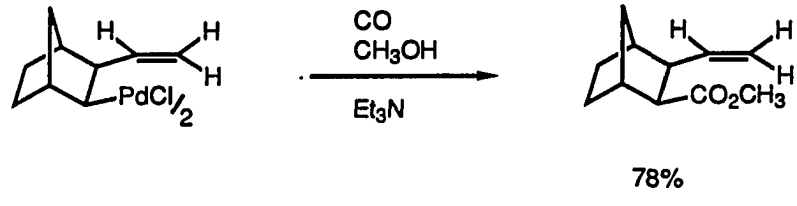
temperature. ^{1}H NMR spectra of adducts 18-20 were remarkably similar to the ^{1}H NMR spectrum of vinylpalladium species 9 except for additional peaks due to the ligand. Compound 18 was the only adduct that formed reasonable crystals after crystallization, but these crystals proved to be unstable to X-ray crystal analysis.

Formation of suitable derivatives would provide added proof of the proposed structures 9 and 12. In order to be useful, the reaction to form the desired derivative must

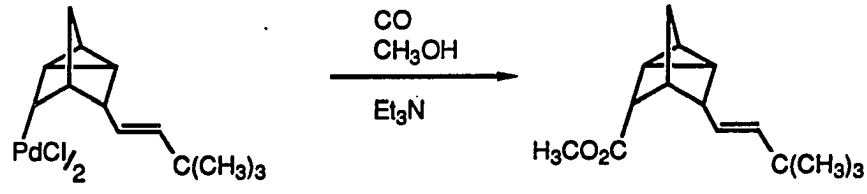
proceed in high yield, and give only one product. A variety of different reactions were tried including carbonylation, reduction and reaction with organolithium reagents. None of these reactions provided a suitable derivative.

The carbonylation of organopalladium compounds has been observed to proceed with retention of configuration[37,38] (Scheme XII).[13] However, Ward observed that in the reaction

Scheme XII

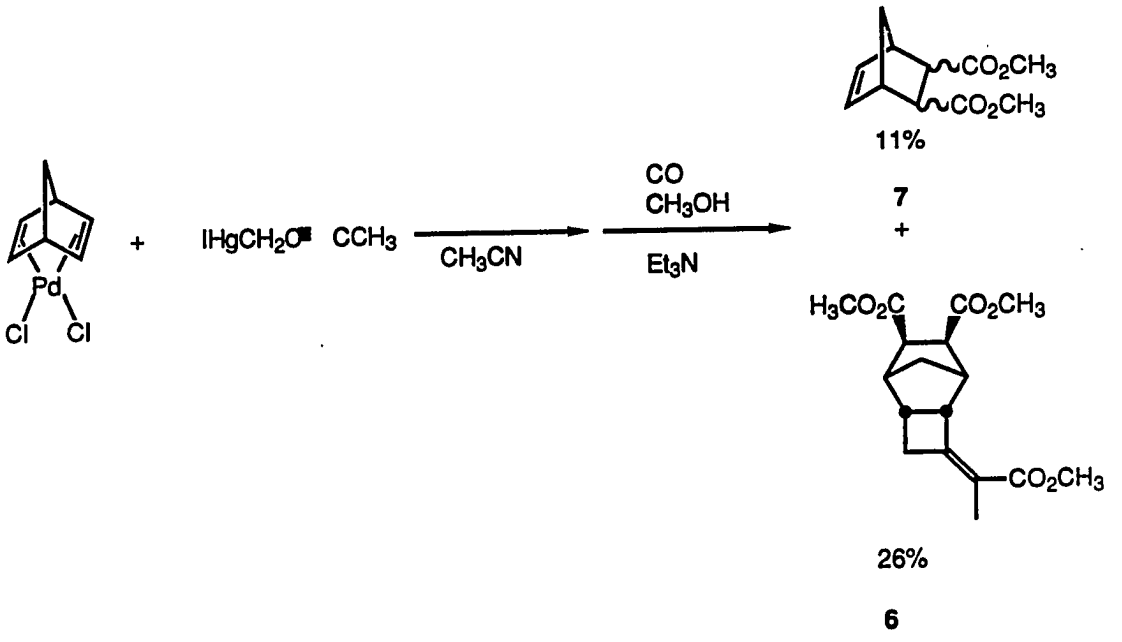


78%



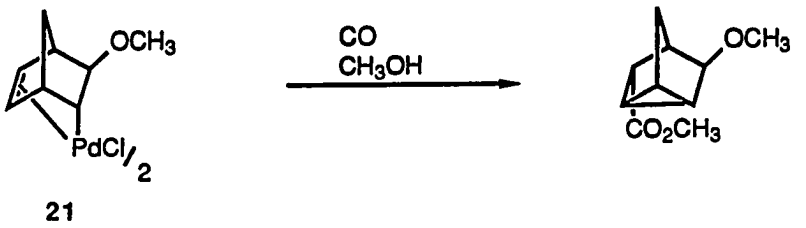
of norbornadiene-palladium dichloride and 1-iodomercurio-2-butyne, two products were formed in low yield upon carbonylation (Scheme XIII).[19] Ward hypothesized that compound 7 arose from carbonylation of unreacted norbornadiene-palladium dichloride. It was felt that isolation of the intermediate vinylpalladium compounds 9 and 12 might make carbonylation a suitable reaction providing support for the proposed structures. When 9 was dissolved

Scheme XIII

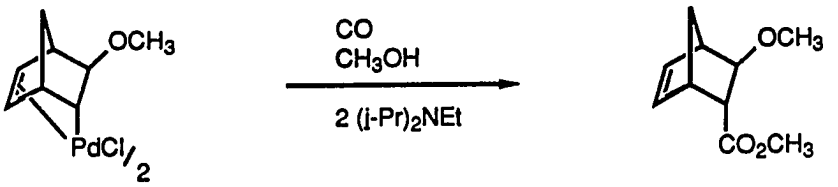


in methylene chloride and subjected to a carbon monoxide atmosphere in the presence of methanol at -78°C, then warmed to room temperature overnight, 78% of the vinylpalladium compound 9 was recovered. Larock and Leach found that addition of diisopropylethylamine altered the carbonylation of di-μ-chlorobis(2,5,6-η^3-3-exo-methoxynorbornen-2-yl-endo-palladium (11) (Scheme XIV).[39] It was felt that the addition of an amine to the carbonylation-reaction mixture of 9 would help this reaction proceed smoothly and cleanly. However, the presence of triethylamine in the carbonylation of 9 promoted formation of a number of different products,

Scheme XIV



21

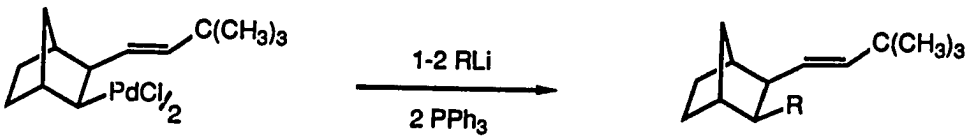


21

each of which contained a carbomethoxy group as evidenced by ^{1}H NMR spectroscopy. Since this reaction produced so many compounds, it was not useful in providing structural proof of 9.

Organolithium reagents are known to react with σ-alkylpalladium compounds, with retention of configuration, to yield carbon-substituted products (Scheme XV).[11-13,40,41] Larock and co-workers found that the reaction of organopalladium compound 22 with organolithium reagents proceeded best with methyl lithium.[13] Reaction of 9 with methyl lithium afforded one compound, which appeared to be 23 by ^{1}H NMR spectroscopy, but it proved to be unisolable from the solvent (Scheme XVI).

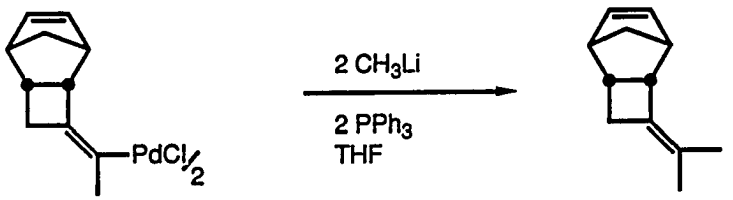
Scheme XV



22

$R = CH_3$	83%
$CH=CH_2$	34%
C_6H_5	24%
C≡CH	54%

Scheme XVI

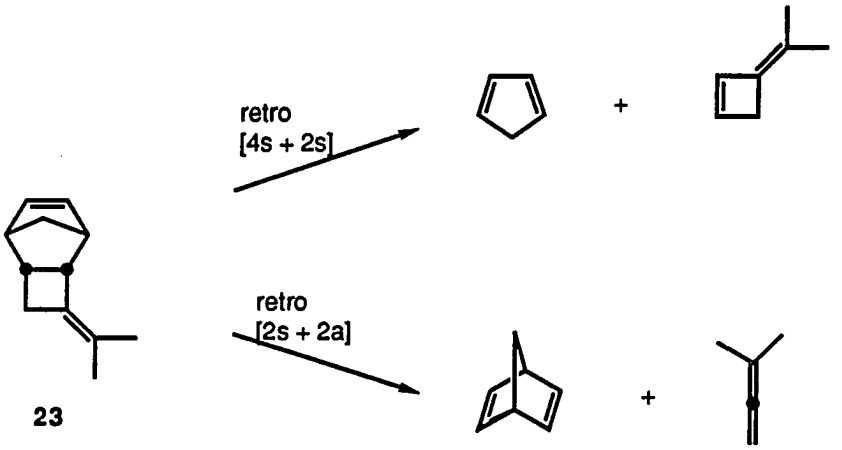


23

The reaction of an organopalladium compound with an organolithium reagent is typically carried out in THF. The product 23 could never be fully separated from THF or the solvents used in flash column chromatography. When the product could not be separated from lower boiling solvents, the reaction was run in the high boiling ether, 2-methoxyethyl ether and Kugelrohr distillation was attempted as a means of isolating the product. Nothing was isolated.

Preparative gas chromatography also failed as the product appeared to decompose in the GC. The product 23 may decompose through thermally-allowed, pericyclic reactions (Scheme XVII).[42]

Scheme XVII

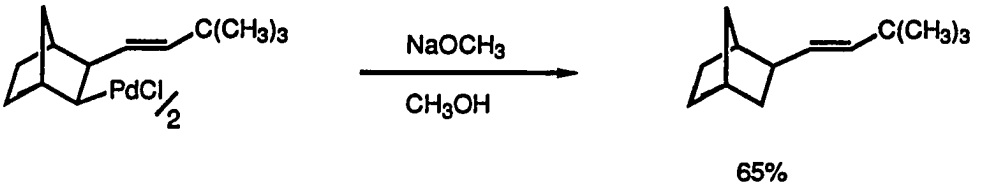


Reaction of 9 with phenyl lithium was also tried in the hopes of obtaining a more stable, less volatile product. The only product isolated from the reaction of 9 and phenyl lithium was biphenyl.

Another common reaction of organopalladium compounds is reduction to yield the hydrogen-substitution product.[13,15-18,27,28,43-49] Larock and co-workers found sodium methoxide to be an efficient agent for the reduction of organopalladium compounds (Scheme XVIII).[13] Reaction of 9 with either sodium methoxide or sodium formate afforded what appeared to be the reduced compound 24 by ^{1}H NMR spectroscopy

(Scheme XIX). However, like 23, 24 proved to be difficult to isolate.

Scheme XVIII



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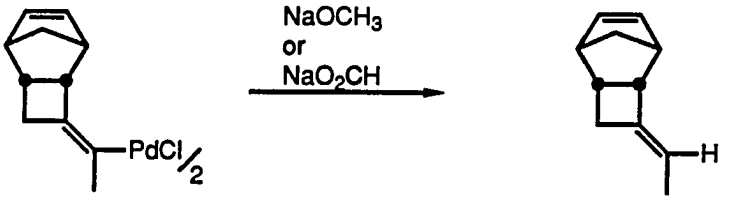
Scheme XIX



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CONCLUSION

The study of the unprecedented reaction between norbornadiene-palladium dichloride and 1-iodomercurio-2-butyne has yielded many interesting results. This reaction yields two novel σ-vinylpalladium compounds 6 and 9. While the two proposed structures fit the spectral analysis, all attempts at forming derivatives of these compounds have failed. Since these two compounds constitute novel organopalladium compounds, further studies of their reactivities are warranted.

EXPERIMENTAL SECTION

Equipment

NMR spectra were recorded on a Nicolet NT-300 spectrometer (^{1}H NMR, 300 MHz: ^{13}C NMR, 75 MHz), and chemical shifts are reported in ppm relative to TMS (δ 0.00) as an internal standard. IR spectra were obtained on an IBM IR98. High-resolution mass spectra were recorded on a Kratos MS-30 spectrometer.

Reagents

All chemicals were used directly as obtained commercially unless otherwise noted. Methylene chloride was distilled over phosphorous pentoxide and stored over 4 Å molecular sieves. Acetonitrile and benzene were distilled over calcium hydride and stored over 4 Å molecular sieves. Tetrahydrofuran was distilled over sodium benzophenone ketal and used immediately. Methanol was distilled over sodium methoxide and stored over 4 Å molecular sieves. Triphenylphosphine was recrystallized from absolute ethanol. Sodium methoxide was obtained from Aldrich or prepared from sodium and methanol.

Preparation of norbornadiene-palladium dichloride

Norbornadiene-palladium dichloride was prepared by the method of Corey and Beames.[50] Palladium(II) chloride (2.3 g,

13 mmole) was dissolved in hot, concentrated hydrochloric acid (5 ml). Absolute ethanol (150 ml) was carefully added to the hydrochloric acid solution, and the resulting mixture was filtered. Norbornadiene (2.0 ml, 20 mmole) was added to the filtrate. A bright yellow solid precipitated out immediately, and was isolated by filtration. Recrystallization from boiling methylene chloride afforded norbornadiene-palladium dichloride (3.28 g, 94% yield) as a bright yellow solid.

Preparation of 1-iodomercurio-2-butyne

1-Iodomercurio-2-butyne was prepared in two steps from 2-butyn-1-ol by the method of Larock and Chow.[51]. 2-Butyn-1-ol (7.5 ml, 0.10 mmole) was added to a crude mixture of triphenylphosphite-methyl iodide complex (0.10 mmole), prepared from methyl iodide and triphenylphosphite, in methylene chloride (75 ml). The reaction mixture was stirred at 0°C for 8 hr, then warmed to room temperature and stirred an additional 36 hr. Distillation under reduced pressure (33°C, 2 mmHg) afforded 1-iodo-2-butyne (97%) as a pale yellow liquid. ^{1}H NMR δ 1.843 (t, J = 2.4 Hz, 3H, CH_3), 3.682 (q, J = 2.4 Hz, 2H, CH_2). Mercury (4.01g, 20 mmole) was weighed into a reaction tube sealed at one end with a septum. The reaction tube was sealed, flushed with nitrogen, and 1-iodo-2-butyne (1.80 g, 10 mmole) was added via syringe. Following vigorous shaking, the reaction tube was placed in

direct sunlight for 2 hr, and shaken intermittently. After refrigerating the reaction mixture for 12 hr, the solid was dissolved in tetrahydrofuran, and the excess mercury filtered off. Removal of tetrahydrofuran in vacuo afforded a pale tan solid which was recrystallized from hot ethanol to yield 1-iodomercurio-2-butyne (84%). ^{1}H NMR δ 1.802 (t, J = 2.7 Hz, 3H, CH_3), 2.576 (q, J = 2.7 Hz, 2H, CH_2).

Preparation of norbornenyl-palladium compound 9

Norbornadiene-palladium dichloride (0.2696 g, 1 mmole) and potassium carbonate (0.1382 g, 1 mmole) were weighed into a flame-dried round-bottom flask equipped with a septum inlet and a magnetic stirring bar. After flushing with nitrogen, benzene (5 ml) was added via syringe and the solution was cooled to 10°C. 1-Iodomercurio-2-butyne (0.3804 g, 1 mmole) was added all at once while backflushing with nitrogen. The reaction mixture was stirred for 2 hr while warming to room temperature. Ether (75 ml) and Celite (0.5 g) were then added to the reaction mixture, and the resulting slurry was filtered through a fritted-glass funnel. The pale yellow solution was washed with saturated ammonium chloride (3 x 25 ml) and dried over magnesium sulfate. Removal of the solvent in vacuo afforded a bright yellow solid which was passed through a silica gel column using methylene chloride to yield norbornenyl compound 6 (71 %) as a yellow oil. ^{1}H NMR δ 1.490 (s, 3H), 1.632 (m, 2H), 2.576 (s, 1H), 2.605 (s, 1H),

2.739 (s, 1H), 2.824 (s, 1H), 3.204 (s, 1H), 3.980 (d, J=1.8 Hz, 1H), 6.145 (m, 2H). ^{13}C NMR δ 15.742, 39.395, 39.919, 43.242, 47.890, 52.874, 53.916, 127.850, 128.339, 136.107, 137.811. IR: 2943 (C-H), 1734 (C=C), 1244 (C-C) cm^{-1}. Elemental analysis was not obtained because the compound readily decomposed upon removal of solvent.

Preparation of nortricyclenyl-palladium compound 12

Norbornadiene-palladium dichloride (0.2696 g, 1 mmole) and potassium carbonate (0.1382 g, 1 mmole) were weighed into a flame-dried, round-bottom flask equipped with a septum inlet and a magnetic stirring bar. After flushing with nitrogen, methylene chloride (5 ml) was added via syringe and the solution was cooled to -30°C. 1-Iodomercurio-2-butyne (0.3804 g, 1 mmole) was added all at once while backflushing with nitrogen. The reaction mixture was stirred for 2 hr while warming to room temperature. Ether (75 ml) and Celite (0.5 g) were then added to the reaction mixture, and the resulting slurry was filtered through a fritted-glass funnel. The pale yellow solution was washed with saturated ammonium chloride (3 x 25 ml) and dried over magnesium sulfate. The solution was concentrated to ca. 10 ml, and pentane (10 ml) was added. The resulting pale yellow precipitate was isolated via filtration to yield the nortricyclic compound (10 %). ^{1}H NMR δ 1.254 (m, 1H), 1.460 (s, 3H), 1.706 (m, 1H), 1.842 (m, 2H), 2.198 (m, 1H), 2.290 (m, 1H), 2.562 (m,

2H), 3.165 (m, 1H), 4.068 (m, 1H). ^{13}C NMR δ 16.367, 23.102, 32.797, 39.713, 49.645, 50.504, 55.194, 44.387, 55.799, 108.954, 109.821. IR: 2957, 2926, 1728, 1283, 1123, 1072 cm^{-1}. Anal. Calculated for $C_{11}H_{13}PdCl$: C, 46.02; H, 4.56. Found: C, 45.87; H, 4.48.

General procedure for solvent studies

Norbornadiene-palladium dichloride (0.0269 g, 0.1 mmole), 1-iodomercurio-2-butyne (0.0381 g, 0.1 mmole) and potassium carbonate (0.0138 g, 0.1 mmole) were weighed into a flame-dried 10-ml round-bottom flask equipped with a septum inlet and a magnetic stirring bar. The flask was flushed with nitrogen, and placed in a -78°C bath. Solvent (2 ml) was added via syringe, and the mixture was stirred for 3 hr while warming to room temperature. The resulting solution was filtered through Celite to afford a clear yellow solution. Isomer ratios were determined from integration of the ^{1}H NMR spectrum by comparing the region between 6.1 and 6.25 ppm (two protons from the norbornenyl compound) to the region from 4.0 to 4.1 ppm (one proton from the nortricyclic compound). When d^2-methylene chloride was used, the solvent had disappeared after three hours. In this case, d^2-methylene chloride (2 ml) was added to the reaction flask before filtering over Celite. When d^6-DMSO was used as the solvent, the black color could not be removed even after repeated filtering through Celite. With DMF as the solvent,

the reaction mixture was worked up as described in the preparation of the norbornenyl compound, the solvent was removed, and the reaction mixture was dissolved in d-chloroform to obtain the isomer ratio.

Preparation of pyridine and phosphine adducts of the vinyl-palladium compounds

The vinylpalladium compound (0.1152 g, 0.4 mmole) was weighed into a round-bottom flask equipped with a septum inlet, gas dispersion tube and magnetic stirring bar. The flask was flushed with nitrogen, and the ligand (0.8 mmole) was added all at once while backflushing with nitrogen. The resultant solution was stirred for 3 hours, filtered over Celite, washed with brine (2 x 25 ml) and dried over magnesium sulfate.

Carbonylation of the vinylpalladium compounds, procedure 1

The vinylpalladium compound (0.0220 g, 0.8 mmole) was placed in a 3-necked, 50-ml round-bottom flask equipped with septum inlets, a gas dispersion tube and a magnetic stirring bar. The flask was flushed with nitrogen and methanol (5 ml) was added via syringe. The solution was placed in a dry ice-acetone bath. Carbon monoxide was introduced to the stirring solution, and the reaction mixture was allowed to warm to room temperature overnight. The black solution was filtered through Celite, diluted with ether (25 ml), washed with water

(1 x 25 ml) and saturated ammonium chloride (2 x 25 ml), then dried over magnesium sulfate.

Carbonylation of the vinylpalladium compounds, procedure 2

The vinylpalladium compound (0.0220 g, 0.8 mmole) was placed in a 3-necked, 50-ml round-bottom flask equipped with septum inlets, a gas dispersion tube and a magnetic stirring bar. The flask was flushed with nitrogen, and methanol (5 ml) was added via syringe. The solution was placed in an ice bath. Carbon monoxide was introduced, followed by triethylamine (2.0 ml), and the stirring reaction mixture was allowed to warm to room temperature overnight. The black solution was filtered through Celite, diluted with ether (25 ml), washed with water (1 x 25 ml) and saturated ammonium chloride (2 x 25 ml) and then dried over magnesium sulfate.

Reaction of the vinylpalladium compounds with methyl lithium

The vinylpalladium compound (0.1435 g, 0.5 mmole) and triphenylphosphine (0.2627 g, 1 mmole) were weighed into a round-bottom flask equipped with a septum inlet, magnetic stirring bar and gas dispersion tube. After flushing with nitrogen, tetrahydrofuran (10 ml) was added via syringe. The reaction mixture was cooled in an ice bath, then methyl lithium (1.0 mmole) was added via syringe. The resultant solution was slowly warmed to room temperature and stirred overnight. The excess methyl lithium was quenched with

methanol. Ether (50 ml) and Celite were added to the reaction mixture before filtering. The filtrate was washed with 2N hydrochloric acid (1 x 25 ml) and aqueous sodium chloride (2 x 25 ml), then dried over magnesium sulfate.

Reaction of the vinylpalladium compounds with phenyl lithium

The vinylpalladium compound (0.2081 g, 0.7 mmole) and triphenylphosphine (0.5695 g, 2.2 mmole) were weighed into a round-bottom flask equipped with a septum inlet, magnetic stirring bar and gas dispersion tube. After flushing with nitrogen, tetrahydrofuran (10 ml) was added via syringe. The reaction mixture was cooled in an ice bath then phenyl lithium (1.8 mmole) was added via syringe. The resultant solution was slowly warmed to room temperature and stirred overnight. The excess phenyl lithium was quenched with methanol. Ether (50 ml) and Celite were added to the reaction mixture which was then filtered. The filtrate was washed with 2N hydrochloric acid (1 x 25 ml) and aqueous sodium chloride (2 x 25 ml), then dried over magnesium sulfate.

Reduction of the vinylpalladium compounds with sodium methoxide

Sodium methoxide (0.0253 g, 0.46 mmole) was weighed into a 25-ml round-bottom flask equipped with a septum inlet, a gas dispersion tube and a magnetic stirring bar. The flask

was flushed with nitrogen, and methanol was added via syringe (10 ml). The mixture was placed in an ice bath, and the vinylpalladium compound (0.0718 g, 0.25 mmole) dissolved in benzene (5 ml) and methanol (2 ml) was added via cannula. The resultant mixture was stirred under nitrogen while warming to room temperature overnight.

In situ reaction of the vinylpalladium compounds with sodium formate

Norbornadiene-palladium dichloride (0.1347 g, 0.50 mmole), 1-iodomercurio-2-butyne (0.1909 g, 0.50 mmole) and potassium carbonate (0.3317g, 2.5 mmole) were weighed into a 25-ml round-bottom flask equipped with a septum inlet and magnetic stirring bar. The flask was flushed with nitrogen and placed in an ice bath. Benzene (5 ml) was added via syringe and the reaction mixture was warmed to room temperature over 2 hr. Sodium formate (0.1656 g, 2.4 mmole), dissolved in N,N-dimethylformamide (10 ml) was added via cannula. The reaction flask was sealed with parafilm and placed in an 80°C bath. Stirring continued for 3 days, then the reaction mixture was diluted with ether, filtered through Celite, washed with saturated ammonium chloride (2 x 25 ml) and dried over magnesium sulfate.

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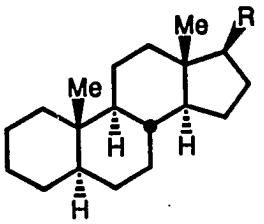
SECTION 2. ARYLANNULATION OF CONJUGATED DIENES

INTRODUCTION

Formation of carbocycles fused to other rings through regioselective annulation is an area of current interest in organic chemistry. A wide variety of biologically active compounds are polycycles including steroids (1), gibberellins (2), some terpenes (3 and 4) and some alkaloids such as morphine (5). The development of new general methods for



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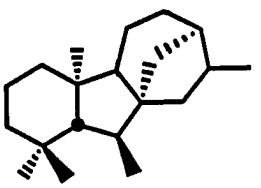

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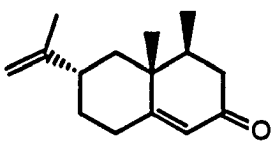

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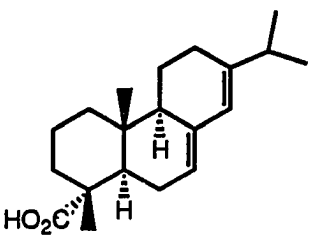

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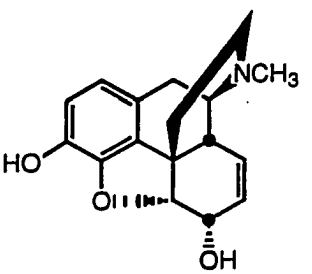

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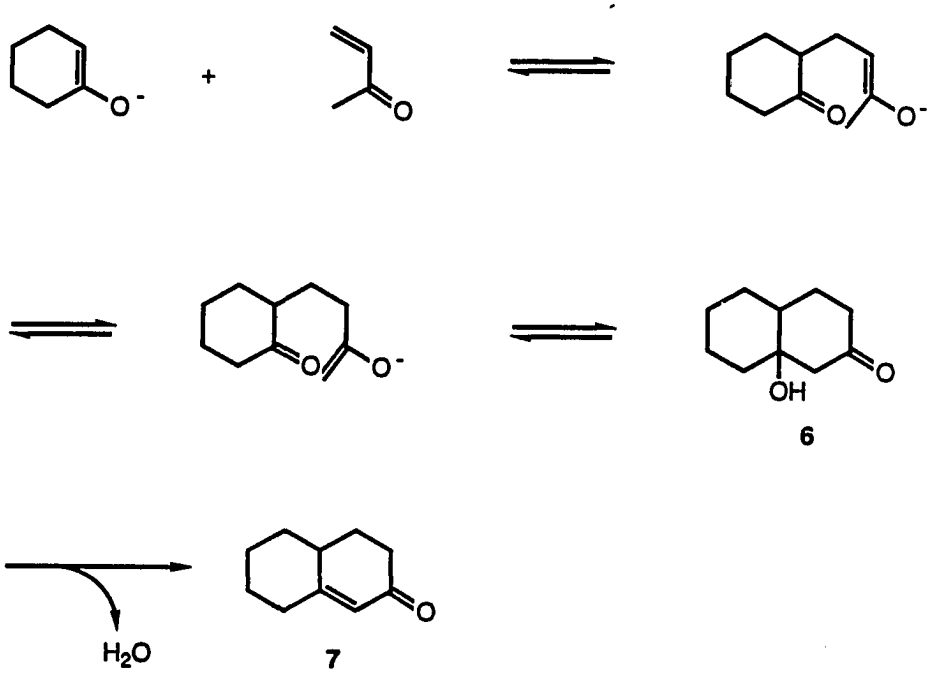
the synthesis of complex polycycles such as these, has been a research area of much recent growth.[1] Of particular interest within this field are annulation processes which form more than one carbon-carbon bond in a single step.

Annulations related to the Robinson annulation reaction[2] have been some of the most widely used synthetic methods in

organic chemistry[3]. Many syntheses of complex natural products such as steroids, terpenes and alkaloids rely on this reaction. The original procedure involved nucleophilic attack of an enolate on an enone, followed by aldol type ring closure to form the keto alcohol **6**. Dehydration of **6** yielded the annulation product **7** (Scheme I). Although the Robinson

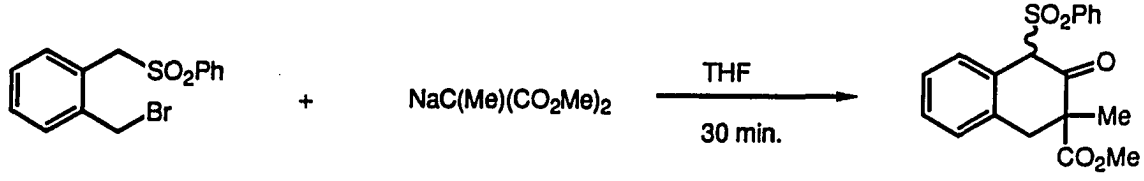
Scheme I



annulation reaction is very valuable, it is unsuited for ordinary carbonyl compounds, since these polymerize under the reaction conditions. A variety of modifications to overcome this restriction have been reported.[4] Current interests in annulation chemistry have focused on using bifunctional reactants to mimic the Robinson annulation procedure.[5-8]

Members of Ghera's lab have utilized bifunctional arenes to rapidly construct naphthalenes (Scheme II),[5] anthracenes

Scheme II



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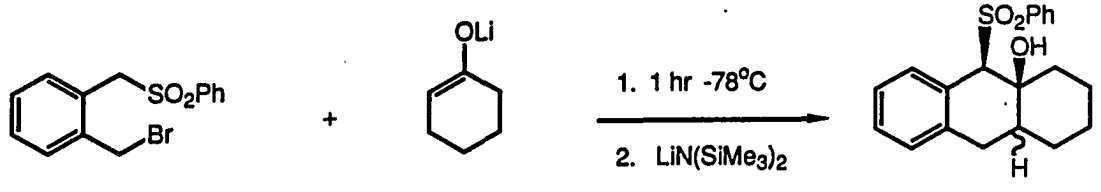
(Scheme III),[6] and phenanthrenes (Scheme IV).[7] The

Scheme III



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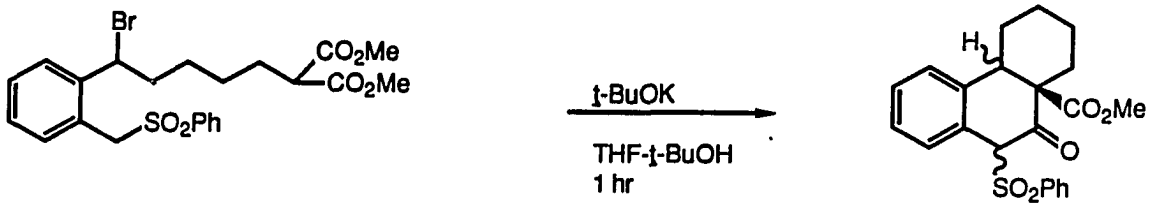
Scheme IV



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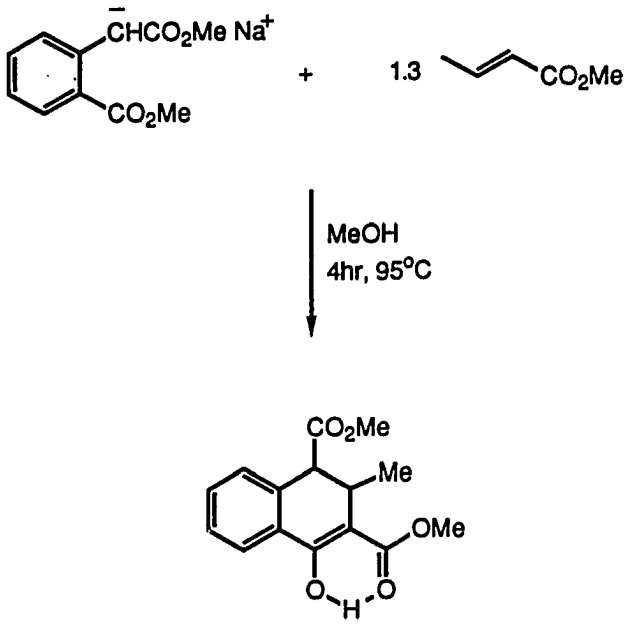
diastereoselectivity of these reactions is relatively poor.

As such, the Ghera annulation procedure has limited use in the synthesis of complex natural products.

Others have used Michael-induced ring closure (MIRC) reactions to annulate activated olefins.[8] Like the Ghera reaction, the MIRC reaction requires both a nucleophilic center and an electrophilic center on the reactant. A representative example of the MIRC reaction was reported by Eisenhuth and co-workers.[8a] They used the preformed anion of methyl o-methoxycarbonylphenylacetate as the annulating agent for methyl crotonate (Scheme V). In general, MIRC reactions

Scheme V



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proceed under fairly mild conditions to afford the annulated product in a moderate yield. However, the MIRC reaction is intolerant of a wide variety of functionality on either the

arene or the alkene. This limitation often necessitates the use of numerous functional group manipulations following the annulation reaction.

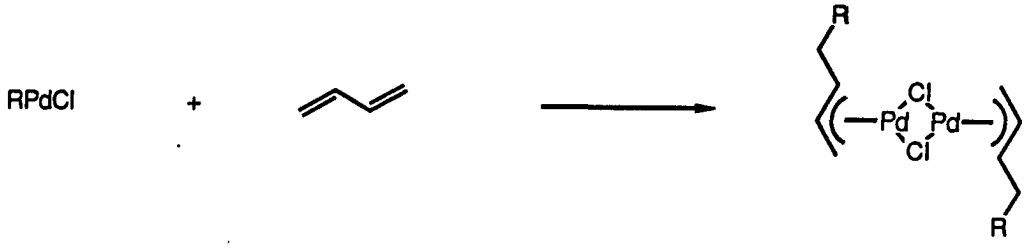
What we sought to accomplish was to develop an annulation method which would proceed under mild conditions, be tolerant of a wide variety of functional groups, start from readily available starting materials and be applicable to the formation of a number of ring sizes.

Palladium can mediate a number of carbon-carbon bond forming processes under relatively mild conditions. One of the more common palladium-catalyzed carbon-carbon bond forming processes is the Heck reaction (Scheme VI).[9] The

Scheme VI

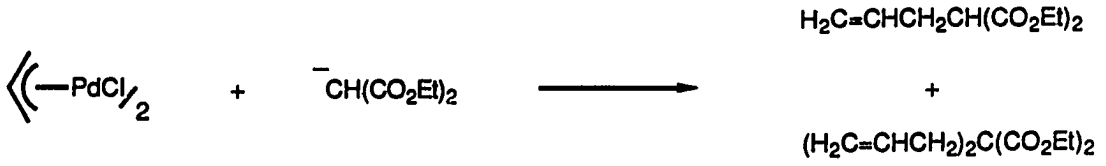
reaction proceeds via cis addition of an organopalladium compound onto an alkene and subsequent cis beta hydride elimination to afford vinyl hydrogen substitution products. When the Heck reaction is run with a 1,3-diene, instead of an simple alkene, π-allylpalladium compounds are formed (Scheme VII).[10] Once formed, the π-allylpalladium compound

Scheme VII



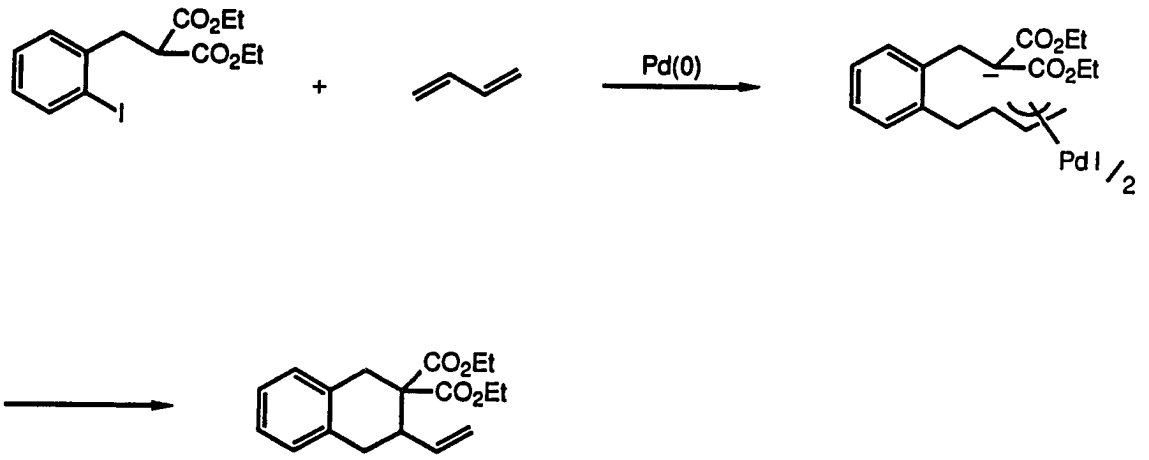
can be attacked by stabilized carbanions to form a new carbon-carbon bond under very mild conditions (Scheme VIII).[11] We thought that addition of an aryl iodide to a

Scheme VIII



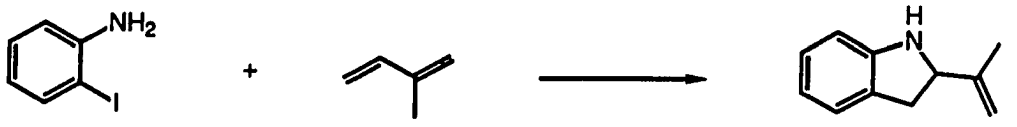
diene, and trapping of the intermediate π-allylpalladium compound with a stabilized carbanion could be combined into a one-step arylannulation procedure (Scheme IX).

Scheme IX



Other groups have used similar palladium-assisted annulations to form heterocycles.[12-15] O'Connor and associates were able to couple 2-iodoaniline with isoprene to afford 2-isopropenyl-2,3-dihydroindole in 72% yield (Scheme X).[12] The reaction proceeds in good yield, but the reaction conditions are rather harsh. Horino and Inoue used

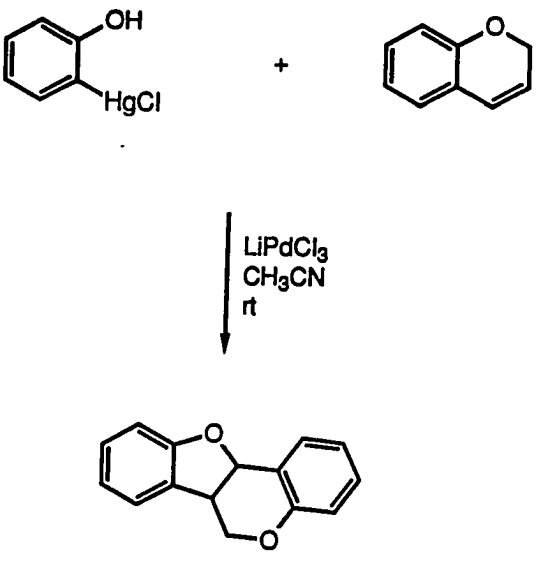
Scheme X



72%

2-chloromercuriophenol under palladium(II)-catalysis to annulate dihydrochromens (Scheme XI).[13] In this reaction,

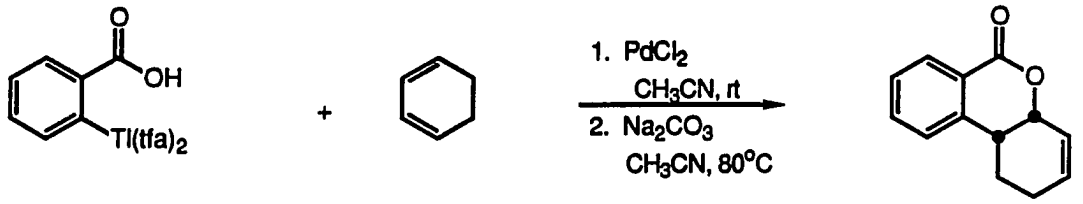
Scheme XI



85%

conditions are fairly mild, but use of an arylmercurial is required. Larock and co-workers used o-thallated benzoic acid to annulate various 1,3-dienes (Scheme XII).[15] The reaction conditions are again fairly mild, but the starting material, an arylthallium compound, is highly toxic.

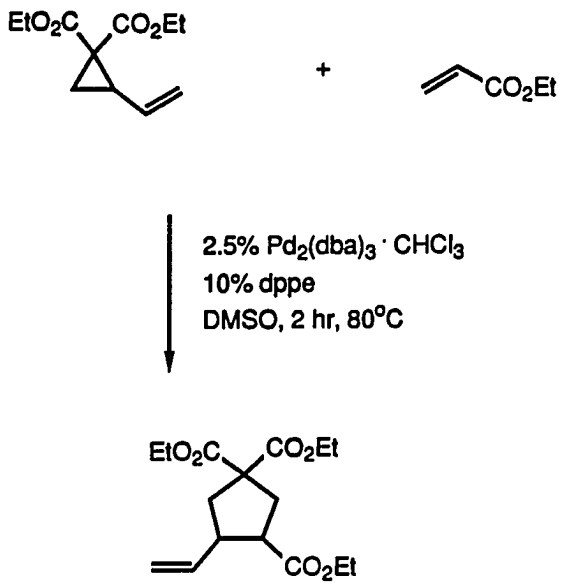
Scheme XII



45%

Various groups have performed carboannulations where a key step in the reaction is attack of a stabilized carbanion onto a presumed intermediate π-allylpalladium species.[16-18] Shimizu and co-workers used vinylcyclopropane diesters to form five-membered rings (Scheme XIII).[16] This reaction is

Scheme XIII

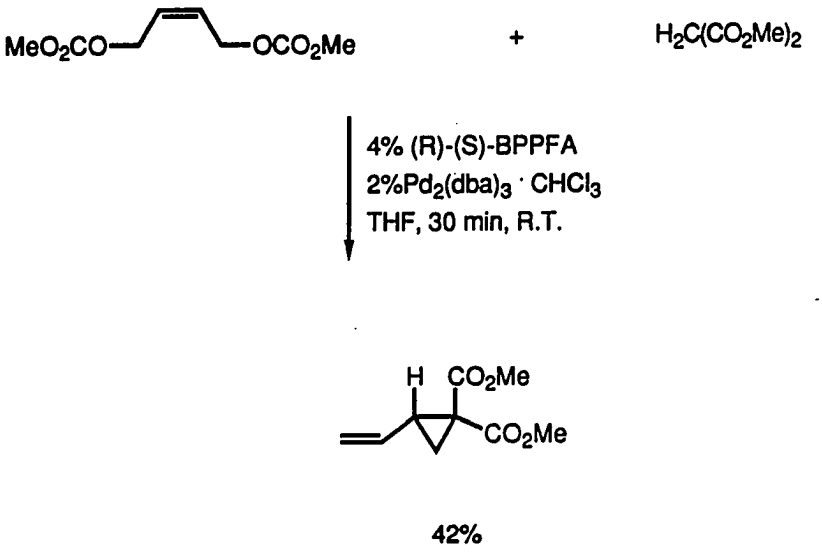


84%

tolerant of a number of organic functional groups. However, it has only been extended to the formation of five-membered rings.

In another example of carboannulation, Hayashi et al. were able to generate optically active vinylcyclopropanes (Scheme XIV).[17] Although a number of other palladium-

Scheme XIV



42%

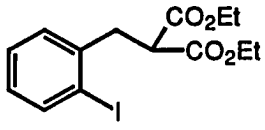
mediated carboannulations have been studied,[18] the above two examples are representative of the rest of the work.

The work in this section involves a study of palladium-catalyzed arylannulation of conjugated dienes. Prior to initiating our study of arylannulation onto 1,3-dienes there was only one report of a palladium-catalyzed annulation involving an aryl iodide and a conjugated diene.[12] In this reaction, O'Connor et al. formed dihydroindoles from 2-iodoaniline and either isoprene or 1,3-cyclohexadiene. Since

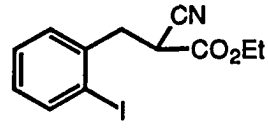
O'Connor's report in 1983, no other similar reactions have appeared in the literature. Our research involves the formation of carbocycles under mild, catalytic palladium conditions which is tolerant of a wide variety of functional groups.

RESULTS AND DISCUSSION

The following aryl iodides **8-23** were considered for the carboannulation procedure. Compounds **8-12** were prepared from



8



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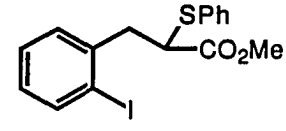

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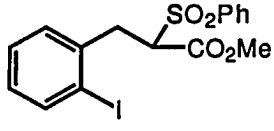

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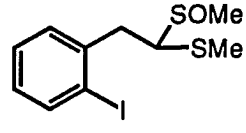

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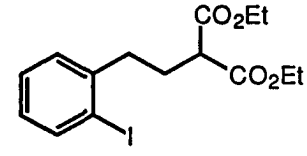
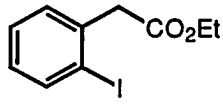


13



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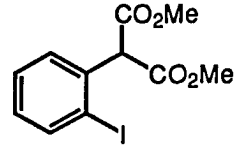

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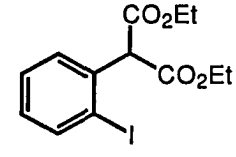

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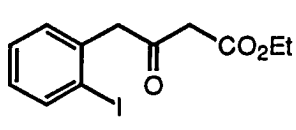
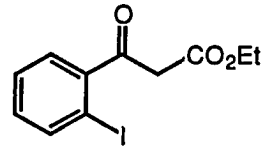


17



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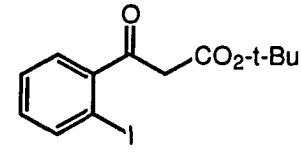

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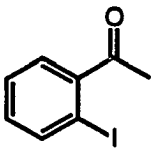

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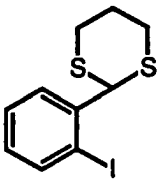

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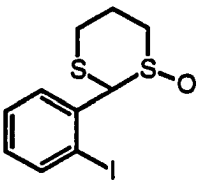
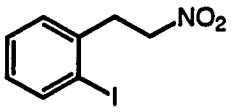


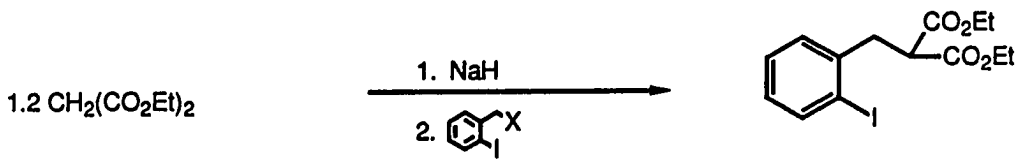
22



23

2-iodobenzyl mesylate or 2-iodobenzyl bromide and the corresponding stabilized carbanion. The preparation of 8 is representative (Scheme XV). Compound 13 was prepared in a

Scheme XV

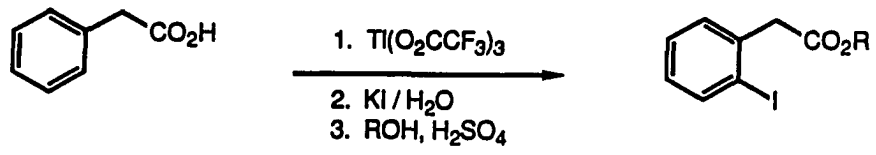


8

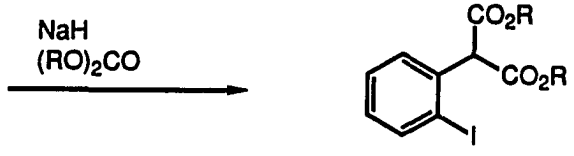
X = Br 78%

similar fashion from o-iodophenethyl mesylate and diethyl malonate. Phenylacetic acid was used to prepare compound 14 in three steps, and compounds 15 and 16 in four steps (Scheme XVI). Compounds 17-19 were prepared by the method of Ohta

Scheme XVI



R = Et (14)

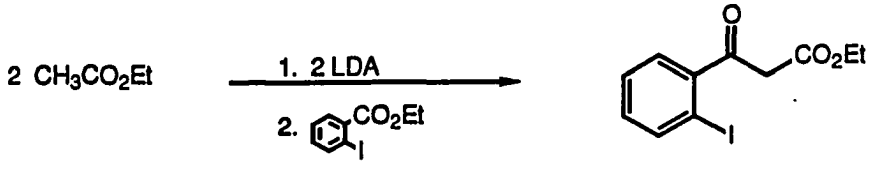


R = Me 40% (15)

R = Et 41% (16)

and associates.[19] The preparation of ethyl 3-(2'-iodophenyl)-3-oxopropanoate 18 is representative (Scheme XVII). Ethyl 3-(2'-iodophenyl)-3-oxopropanoate was then used

Scheme XVII

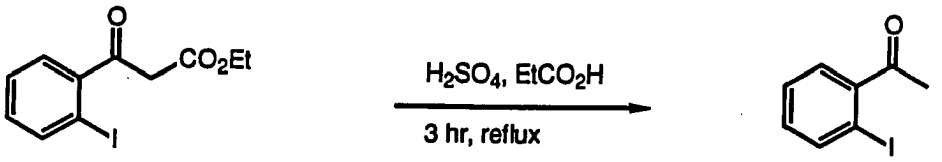


18

98%

to prepare 2-iodoacetophenone (Scheme XVIII). Compound 21, 2-(2'-iodophenyl)-1,3-dithiane was prepared from 2-

Scheme XVIII

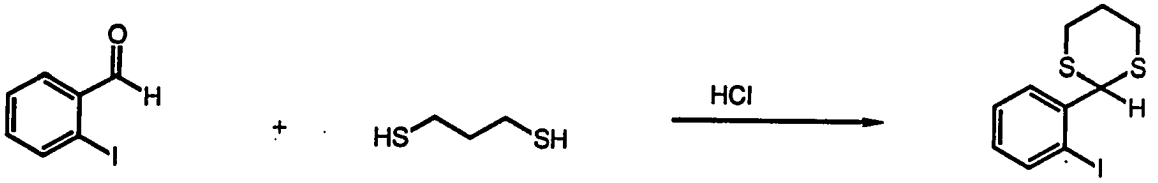


18 20

91%

iodobenzaldehyde by the method of Stütz and Stadler (Scheme XIX).[20] Oxidation of 21 by the method of Johnson and Keiser

Scheme XIX

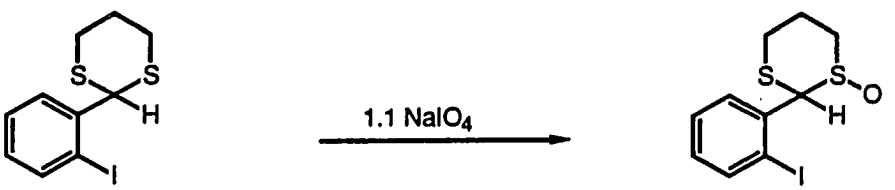


21

100%

afforded 2-(2'-iodophenyl)-1-oxo-1,3-dithiane (22) as a mixture of diastereomers (Scheme XX).[21] Finally,

Scheme XX

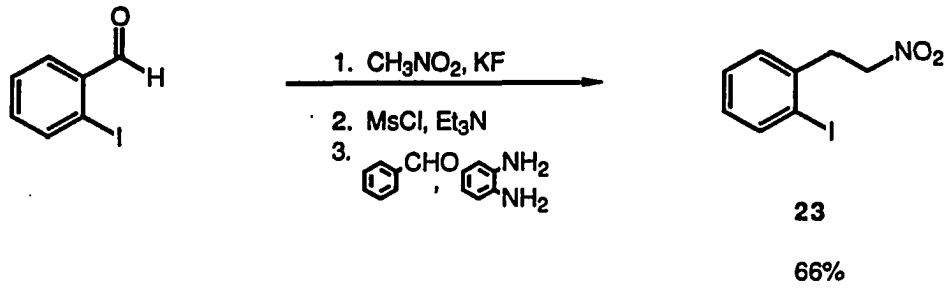


21 22

42%

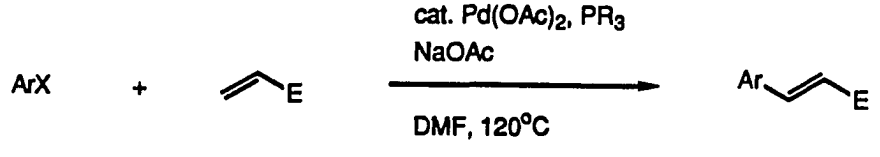
2-(2'-iodophenyl)-1-nitroethane (23) was synthesized in three steps from o-iodobenzaldehyde (Scheme XXI).

Scheme XXI



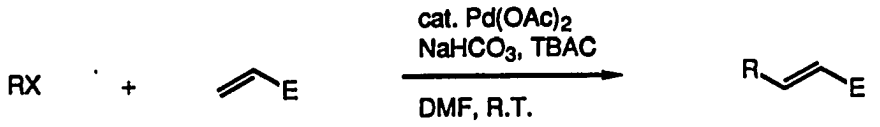
In 1983, Spencer reported that use of a base, sodium acetate, and a polar solvent, N,N-dimethylformamide, in palladium-catalyzed vinylation of arenes greatly increased the turnover of the palladium making the reaction more economical (Scheme XXII).[22] Jeffery then expanded on these

Scheme XXII



results and found that addition of a phase transfer catalyst, tetra-n-butylammonium chloride, to the reaction mixture allowed the palladium-catalyzed vinylation of aryl,[23] vinylic[24] and alkynyl[25] halides to proceed at room temperature (Scheme XXIII). Members of our research group have extended Jeffery's phase transfer conditions to the

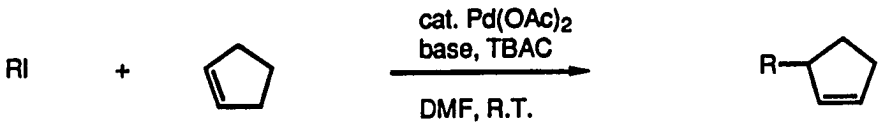
Scheme XXIII



R = Aryl, Vinylic, Alkynyl

use of non-activated cyclic alkenes (Scheme XXIV).[26]

Scheme XXIV

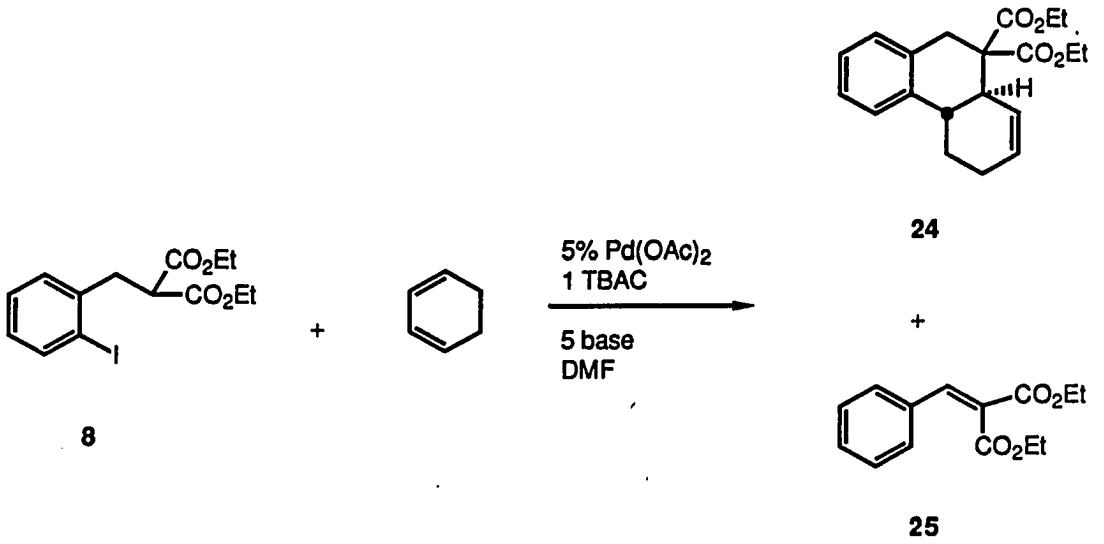


R = Aryl, Vinylic, Alkynyl

Initial studies were aimed at finding general reaction conditions for our palladium-catalyzed arylannulation process. The reaction between diethyl o-iodobenzylmalonate and 1,3-cyclohexadiene was chosen for the initial model study, and the results are summarized in Table I.

The mechanism for the desired reaction of 8 and 1,3-cyclohexadiene is envisioned as proceeding through a π-allyl-palladium intermediate (Scheme XXV). The palladium acetate is most likely reduced by the alkene present is solution. 2-Acetoxy-1,3-cyclohexadiene is not recovered from the solution, but only five percent of this product should be formed. Following oxidative addition of the palladium(0)

Table I. Reaction of Diethyl o-Iodobenzylmalonate and 1,3-Cyclohexadiene



Entry	Base	Temp.(°C)	Time(days)	% Yield 24[a]	% Yield 25[a]
1[b]	Na_2CO_3	25	14	-	-
2[b]	NaOAc	25	14	-	-
3	Na_2CO_3	80	1	82	10
4	NaOAc	80	1	85	-
5[c]	NaOAc	80	6	77	-
6[d]	NaOAc	80	7	76	-

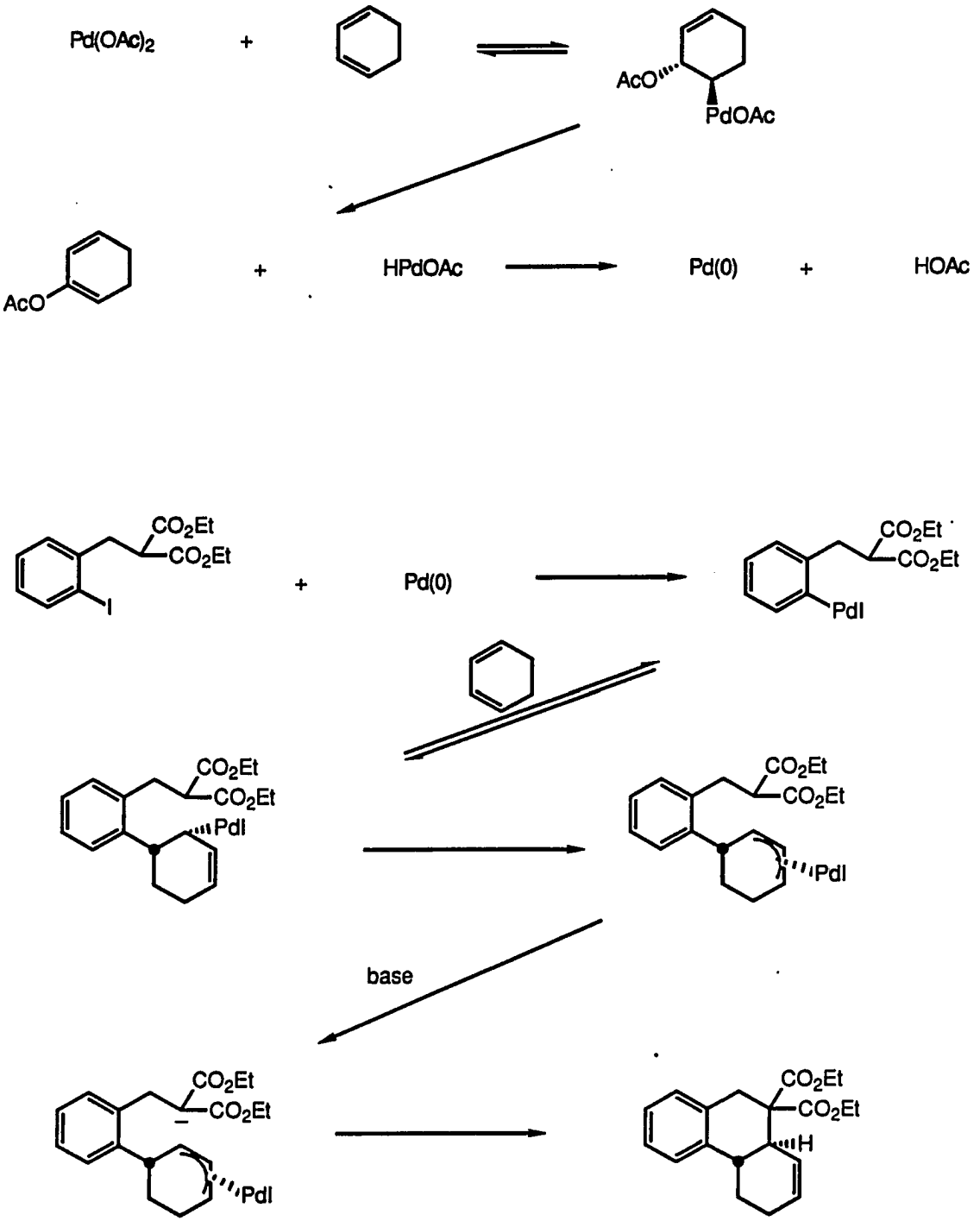
[a]Isolated yield.

[b]Over 90% of the starting aryl iodide was recovered.

[c]In this experiment, 2 equivalents of diene were used instead of 5 equivalents.

[d]In this experiment, 0.9 equivalents of diene were used instead of 5 equivalents.

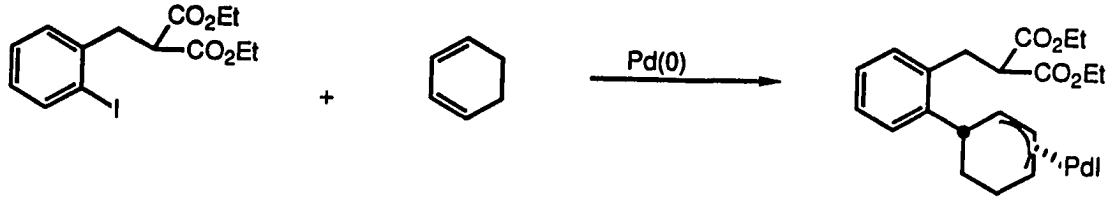
Scheme XXV


Pd(OAc)2
+
AcO
PdOAc
AcO
+
HPdOAc
Pd(0)
+
HOAc
CO2Et
CO2Et
I
+
Pd(0)
CO2Et
CO2Et
PdI
CO2Et
CO2Et
PdI
CO2Et
CO2Et
PdI
base
CO2Et
CO2Et
PdI
CO2Et
CO2Et
H

catalyst to the aryl iodide, the arylpalladium intermediate presumably adds to the diene in a cis fashion to yield a σ-allylpalladium complex. Collapse of the σ-allylpalladium species to the π-allylpalladium intermediate, followed by intramolecular trapping of the π-allylpalladium intermediate by backside attack, leads to the formation of the desired product.

The reaction of 8 and 1,3-cyclohexadiene was first attempted at room temperature using two different bases (Entries 1 and 2). The bases were chosen because they had generally performed well for either Dr. Bruce Baker[26a] or Dr. Srinivasan Babu[27] in their tetra-n-butylammonium chloride-mediated, palladium-catalyzed arylations. It is apparent from entries 1 and 2 that palladium-catalyzed arylannulation fails at room temperature. Even after stirring with the palladium catalyst for 14 days, significant amounts of the starting aryl iodide were isolated. It was thought that the palladium catalyst was being tied up as a π-allylpalladium complex, and was thus unable to mediate the desired reaction (Scheme XXVI). Generally, π-allylpalladium complexes are

Scheme XXVI



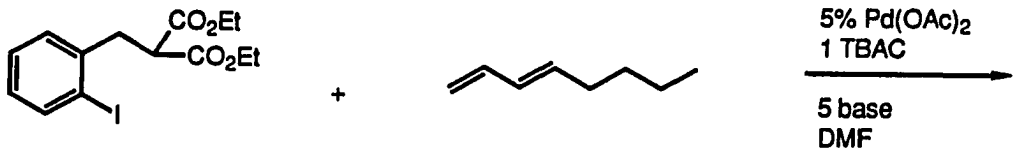
stable in the absence of nucleophiles or strong bases.[28]

While sodium carbonate and potassium carbonate have been shown to be efficient bases in the formation of the diethylmalonyl anion when the reaction is run in the presence of a phase transfer catalyst, these reactions require temperatures between 80°C and 100°C.[29] This report prompted us to try higher reaction temperatures. The reaction does proceed at 80°C with either sodium carbonate or sodium acetate as the base (Entries 3 and 4). Finally, the reaction can be run using less diene (Entries 5 and 6). When less than five equivalents of diene were used, the reaction slows, and the yield is slightly lower.

Having found general conditions for the annulation of 1,3-cyclohexadiene, we wished to explore the utility of linear dienes in the arylannulation process. 1,3-Octadiene was chosen as the model linear diene, and standard conditions utilizing sodium carbonate or sodium acetate were tried first. The results of this study are summarized in Table II.

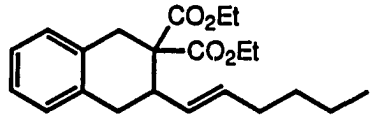
Initially, the base was varied to try to improve the yield of 26, and depress formation of side products such as 27 (Entries 1 - 8). Compound 27 presumably arises from the same π-allylpalladium intermediate as 26, with the ratio dependant on the relative rates of formation of 26 and 27. One possible route for the formation of 27 is through base-assisted β-hydride elimination of the π-allylpalladium complex (Scheme XXVII, Path a). Another route to 27 is direct β-hydride elimination from the π-allylpalladium

Table II. Reaction of Diethyl o-Iodobenzylmalonate and 1,3-Octadiene

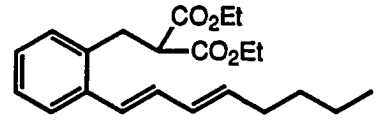


8

Entry	Palladium Source	Added Ligand	Base	Solvent
1	$Pd(OAc)_2$	-	Na_2CO_3	DMF
2	$Pd(OAc)_2$	-	NaOAc	DMF
3	$Pd(OAc)_2$	-	KOAc	DMF
4	$Pd(OAc)_2$	-	K_2CO_3	DMF
5	$Pd(OAc)_2$	-	$NaHCO_3$	DMF
6	$Pd(OAc)_2$	-	$KHCO_3$	DMF
7	$Pd(OAc)_2$	-	Et_3N	DMF
8	$Pd(OAc)_2$	-	Li_2CO_3	DMF
9	$Pd(OAc)_2$	-	Na_2CO_3	DMF
10	$Pd(OAc)_2$	-	Na_2CO_3	DMF
11	$Pd(OAc)_2$	-	Na_2CO_3	THF
12	$Pd(OAc)_2$	-	NaOAc	THF
13	$Pd(OAc)_2$	-	Na_2CO_3	CH_3CN
14	$Pd(OAc)_2$	-	NaOAc	CH_3CN



+



26 **27**

Temp(°C)	Time(days)	% Recovered 8	% Yield 26	% Yield 27
60	2	-	80	10
60	4	-	75	18
60	4	-	78	15
60	4	38	25	5
60	4	52	21	16
60	4	55	26	14
60	4	59	17	8
60	6	90	-	-
40	14	49	38	7
80	3	-	58	32
60	4	63	14	7
60	4	68	12	4
60	5	-	31	42
60	5	31	31	5

Table II. (continued)

Entry	Palladium Source	Added Ligand	Base	Solvent
15	$Pd(OAc)_2$	-	Na_2CO_3	DMF-HMPA[a]
16	$Pd(OAc)_2$	-	NaOAc	DMF-HMPA[a]
17[b]	$Pd(OAc)_2$	-	NaOAc	DMF
18[b]	$Pd(OAc)_2$	-	KOAc	DMF
19[b,c]	$Pd(OAc)_2$	-	Na_2CO_3	DMF
20[b,c]	$Pd(OAc)_2$	-	NaOAc	DMF
21[b]	$Pd(OAc)_2$	12% dppe[d]	-	THF
22	$Pd(dba)_2$	-	Na_2CO_3	DMF
23	$Pd(dba)_2$	-	NaOAc	DMF
24	$Pd(OAc)_2$	10% PPh_3	Na_2CO_3	DMF
25	$Pd(OAc)_2$	5% PPh_3	Na_2CO_3	DMF
26	$Pd(OAc)_2$	5% P(o-Tol)$_3$	Na_2CO_3	DMF

[a]A 9 : 1 mixture of DMF : HMPA was used as the solvent.

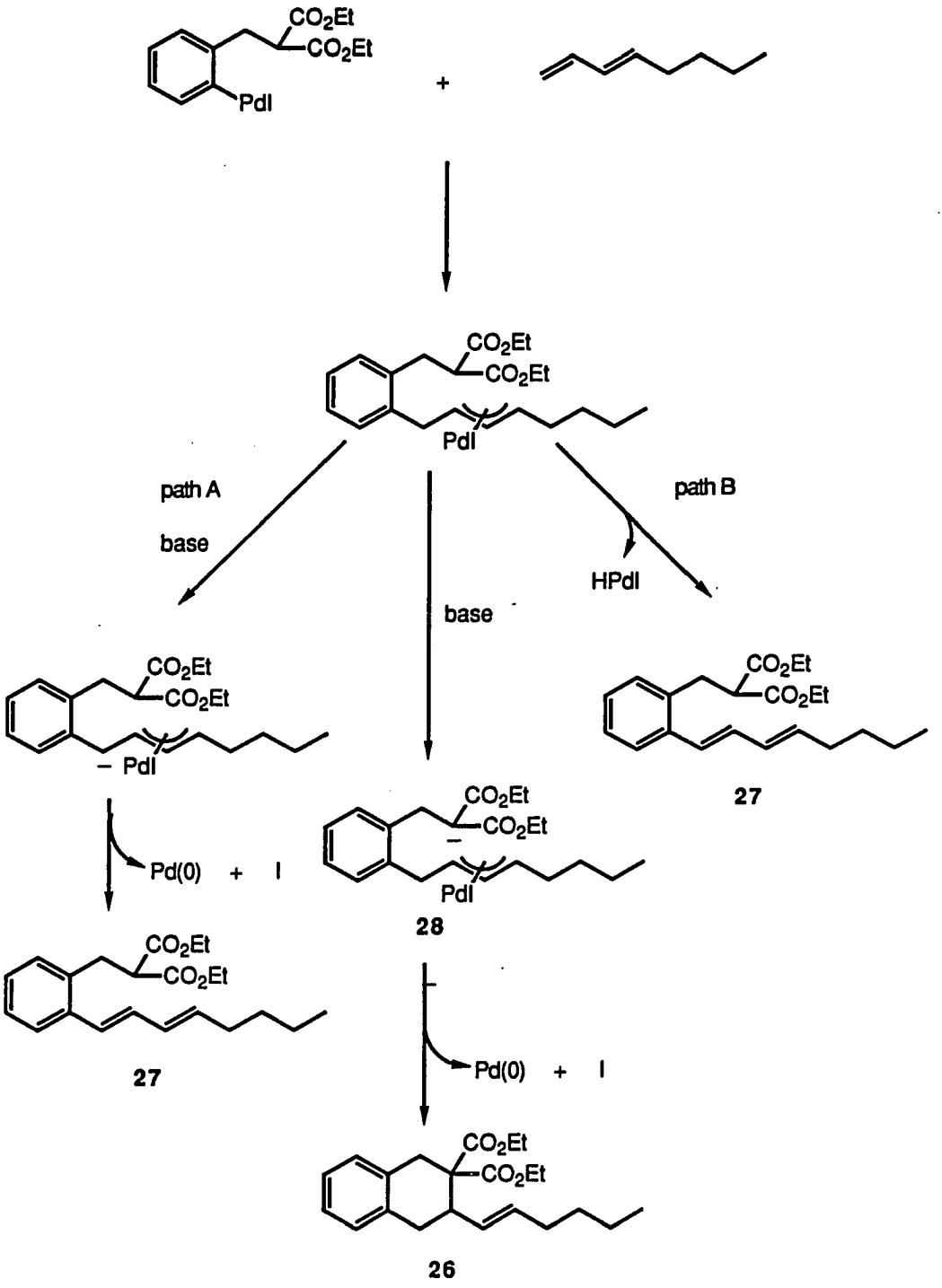
[b]The malonate anion was preformed using NaH.

[c]The only product found was reduced aryl iodide.

[d]Dppe stands for bis-1,2-diphenylphosphinoethane.

Temp(°C)	Time(days)	% Recovered 8	% Yield 26	% Yield 27
60	4	-	54	36
60	4	-	64	32
25	1	94	-	-
25	1	94	-	-
60	1	-	-	-
60	1	-	-	-
50	1 hr	72	-	-
60	4	-	67	14
60	4	-	67	20
60	4	7	37	28
60	1	-	87	-
60	1	-	88	-

Scheme XXVII



intermediate (Scheme XXVII, Path b). A plausible method of stopping path a from occurring is to use a weaker base. For this reason, sodium bicarbonate, potassium bicarbonate and lithium carbonate were tried (Entries 5, 6 and 8). Neither of the bicarbonates prevented formation of side product 27, and only starting material was recovered from the reaction utilizing lithium carbonate as the base. Two other bases, potassium carbonate and triethylamine, that had shown promise in other tetra-n-butylammonium chloride-mediated, palladium-catalyzed arylations were tried (Entries 4 and 7). Formation of 27 was not suppressed with either of these bases. From these studies, it was concluded that sodium carbonate, sodium acetate or potassium acetate are all suitable bases for this reaction (Entries 1 - 3). Sodium carbonate was chosen as the base in most of the subsequent studies, because the reaction using sodium carbonate proceeded faster than the reactions utilizing either of the acetate bases.

The effect of temperature on this reaction was studied (Entries 1, 9 and 10). It was found that 60°C was better than 80°C or 40°C for this reaction. Raising the temperature to 80°C resulted in formation of a significant amount of 27 (Entry 10) while at 40°C, the reaction was cumbersomely slow (Entry 9).

Various solvents were also tried as a means of controlling the arylannulation of linear dienes (Entries 1, 2, 11 - 16). The effect of changes in polarity were examined

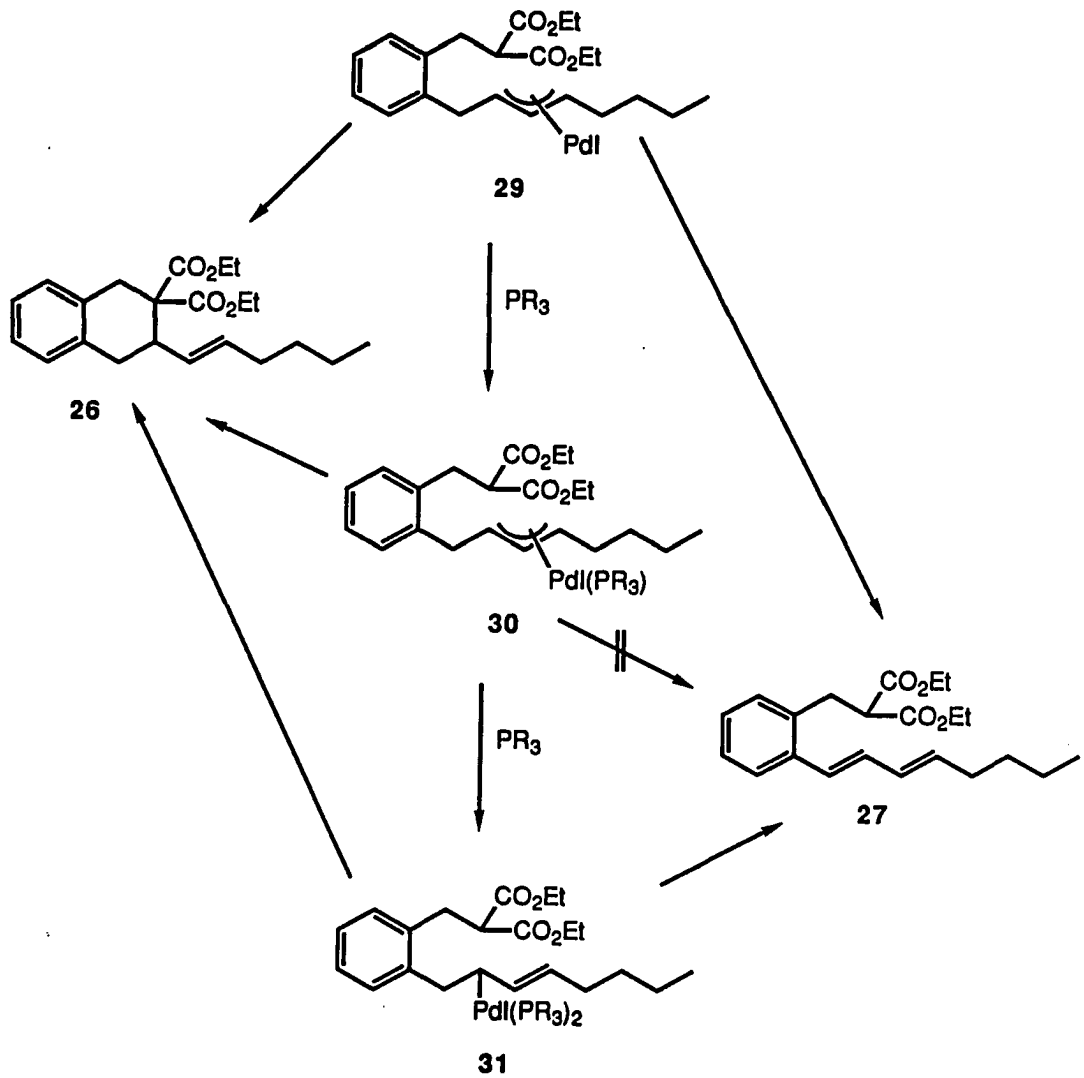
by comparing the results of reactions run in DMF (Entries 1 and 2), THF (Entries 11 and 12), acetonitrile (Entries 13 and 14) and DMF/HMPA (Entries 15 and 16). Use of solvents less polar then DMF slowed the reaction, and did not discourage formation of 27. Increasing the polarity by adding HMPA to DMF increased the rate of reaction, but significant amounts of 27 were still formed.

Formation of 27 through Path b may indicate that the carbanion 28 is not being formed. Therefore, the carbanion was preformed using sodium hydride and then used in the carboannulation reaction (Entries 17 - 21). The carbanion of diethyl o-iodobenzylmalonate does not undergo carboannulation.

The palladium source was also varied. When bis-dibenzylideneacetonyl palladium was used as the palladium source, the reaction was slower than the corresponding reaction run with palladium acetate. No other significant differences were found between the two catalyst sources.

Our final thought on preventing formation of 27 while maximizing the yield of 26, was to use various ligands (Entries 24 - 26). While use of 10 mole percent of phosphine decreases the ratio of 26 : 27 (Entry 24), using only 5 mole percent of phosphine results in exclusive formation of 26 (Entries 25 and 26). One possible explanation of these results is that π-allylpalladium intermediate 29 is stabilized by the addition of a phosphine (Scheme XXVIII).

Scheme XXVIII

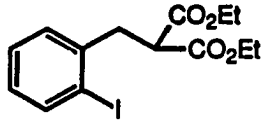
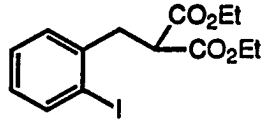
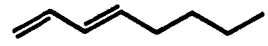
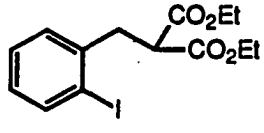


The new π-allylpalladium compound 30 can yield 27 by intramolecular nucleophilic attack, but it is not as susceptible to β-hydride elimination, and thus does not yield 27. On the other hand, addition of a second equivalent of phosphine stabilizes a σ-allylpalladium complex 31 which readily undergoes β-hydride elimination.

The studies on the reaction between 1,3-octadiene and diethyl o-iodobenzylmalonate indicate that the best procedure for a linear diene in the arylannulation reaction utilizes 5 mole percent of a phosphine ligand such as triphenylphosphine, sodium carbonate as the base and a reaction temperature of 60°C.

Having gained an understanding of what factors influence the reaction, the scope and limitations of the arylannulation procedure were explored. The optimized results of this work may be found in Table III. In each case, annulation was attempted using the two most effective bases (sodium carbonate and sodium acetate) under the initial conditions (5 mole percent palladium acetate, 1 equivalent of tetra-n-butylammonium chloride, in DMF at 80°C). Whenever these conditions resulted in poor product ratios, or did not yield any product, annulation was attempted using the two most effective bases under the alternate conditions (5 mole percent palladium acetate, 5 mole percent triphenylphosphine, 1 equivalent of tetra-n-butylammonium chloride, in DMF at 80°C). When linear dienes were used, or the aryl iodide used was a five-membered ring annulating agent, the initial conditions employed a reaction temperature of 60°C instead of 80°C. If neither of these sets of reactions provided adequate results, the base, the solvent, the ligand and the reaction temperature were varied. If no product was found

Table III[a]. Arylannulation of Conjugated Dienes

Entry	Arene	Diene	Base[b]
1	 **8**		NaOAc
2	 **8**		Na_2CO_3
3[e]	 **8**		Na_2CO_3

[a]Actual amounts of reagents used were as follows: 0.25 mmole arene, 1.25 mmole diene, 0.25 mmole $(\underline{n}\text{-Bu})_4NCl$, 0.0125 mmole $Pd(OAc)_2$, 1 ml DMF, 1.25 mmole base.

[b]In entries where more than one base is listed, results of separate trials using each base gave nearly identical results (± 5% yield).

[c]Triphenylphosphine (0.0125 mmole) or another ligand was occasionally used as part of the catalyst system; the ligand used is listed to the left of time and temperature.

[d]Numbers given are isolated yields of purified products obtained from flash column chromatography.

[e]The product is obtained as an 8 : 1 mixture of trans : cis olefins.

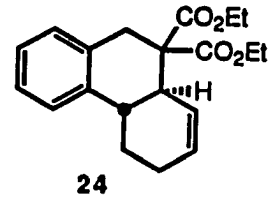
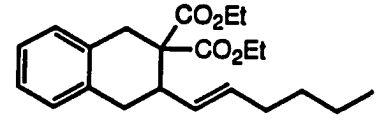
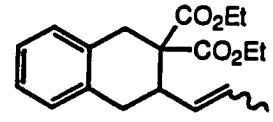
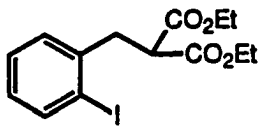
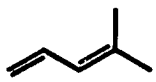
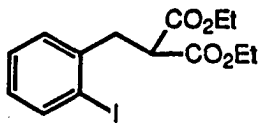
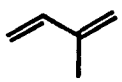
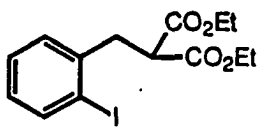
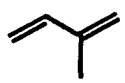
Reaction Conditions[c]	Product(s)	%Yield[d]
1d, 80°C	 **24**	85
PPh_3, 1d, 60°C	 **26**	87
PPh_3, 2d, 60°C	 **32**	95

Table III[a]. (continued)

Entry	Arene	Diene	Base[b]
4	 **8**		Na_2CO_3
5	 **8**		Na_2CO_3
6	 **8**		Na_2CO_3

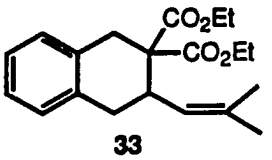
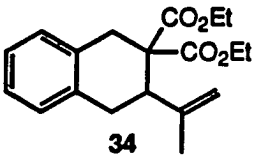
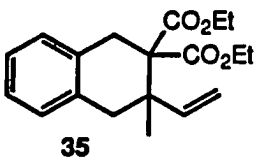
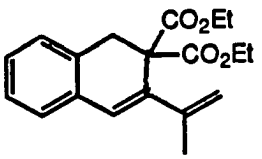
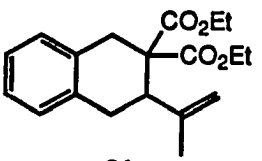
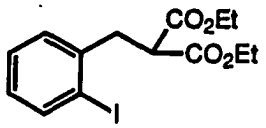
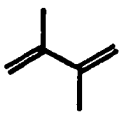
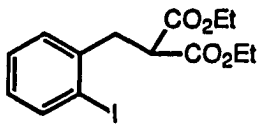
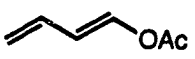
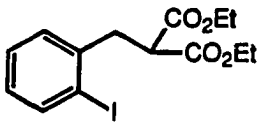
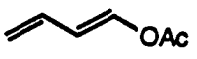
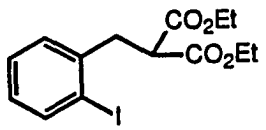
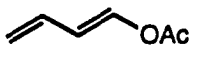
Reaction Conditions	Product(s)	%Yield[d]
PPh_3, 14d, 60°C	 **33**	87
3d, 60°C	 **34**	
	 **35**	64 (2 : 1)
	 **36**	26
PPh_3, 12d, 60°C	 **34**	92

Table III[a]. (continued)

Entry	Arene	Diene	Base[b]
7			Na_2CO_3
	8		
8[f]			Na_2CO_3
	8		
9[f]			NaOAc
	8		
10[f]			Na_2CO_3
	8		

[f]This reaction yielded a number of unidentifiable products.

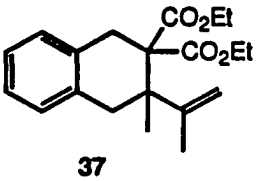
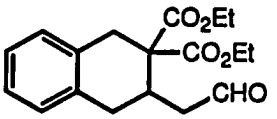
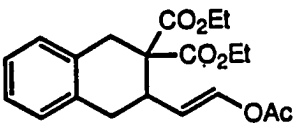
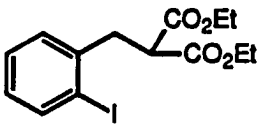
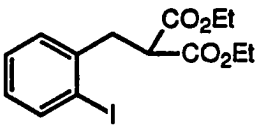
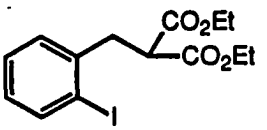
Reaction Conditions	Product(s)	%Yield[d]
PPh_3, 17d, 60°C	 **37**	84
1d, 60°C	 **38**	31
1d, 60°C	-	-
PPh_3, 3d, 60°C	 **39**	22

Table III[a]. (continued)

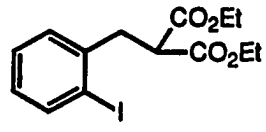
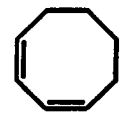
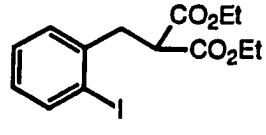
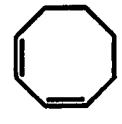
Entry	Arene	Diene	Base[b]
11[f]			Na_2CO_3, NaOAc or KOAc
	8		
12[f,g,h]			Na_2CO_3 or NaOAc
	8		
13[f]			Na_2CO_3 or NaOAc
	8		

[g]This reaction was run in the absence of light.

[h]Twenty percent of the starting aryl iodide was recovered from the reaction mixture.

Reaction Conditions	Product(s)	%Yield[d]
3d, 60°C	-	-
5d, 60°C	-	-
PPh_3, 2d, 60°C	-	-

Table III[a]. (continued)

Entry	Arene	Diene	Base[b]
14	 8		Na_2CO_3 or NaOAc
15	 8		KOAc

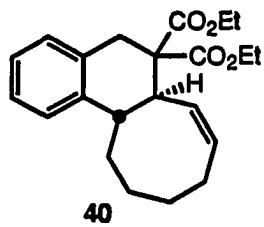
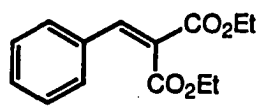
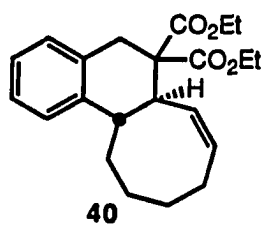
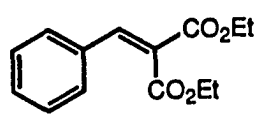
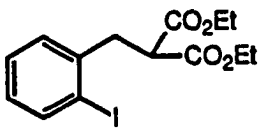
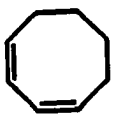
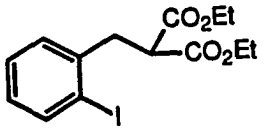
Reaction Conditions	Product(s)	%Yield[d]
1d, 80°C	 **40**	40
	 **25**	35
1d, 80°C	 **40**	27
	 **25**	45

Table III[a]. (continued)

Entry	Arene	Diene	Base[b]
16[i]	 8		Na_2CO_3
17	 8		Na_2CO_3

[i]Forty-three percent of the starting aryl iodide was recovered from the reaction mixture.

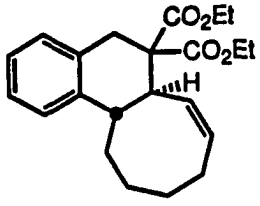
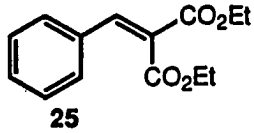
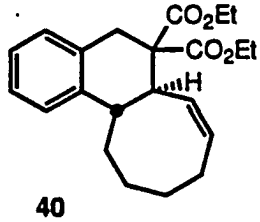
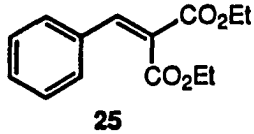
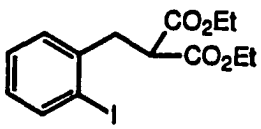
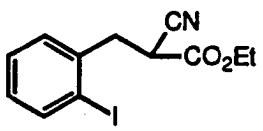
Reaction Conditions	Product(s)	%Yield[d]
5d, 60°C	 **40**	21
	 **25**	19
PPh_3, 1d, 80°C	 **40**	35
	 **25**	55

Table III[a]. (continued)

Entry	Arene	Diene	Base[b]
18			Na_2CO_3
	8		
19[j]			Na_2CO_3
	9		

[j]The desired product was isolated as a 2 : 3 mixture of diastereomers.

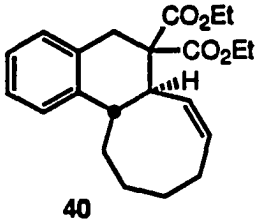
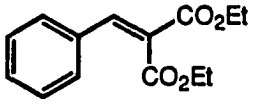
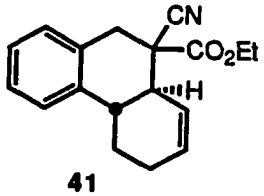
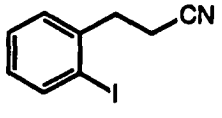
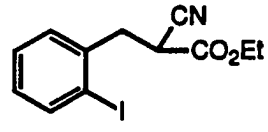
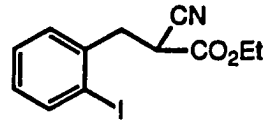
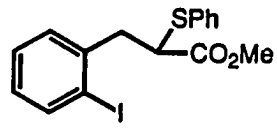
Reaction Conditions	Product(s)	%Yield[d]
$P(OPh)_3$, 2d, 80°C	 **40**	52
	 **25**	25
4d, 80°C	 **41**	70
	 **42**	11

Table III[a]. (continued)

Entry	Arene	Diene	Base[b]
20[k]	 **9**		Na_2CO_3
21[l]	 **9**		Na_2CO_3
22[m]	 **10**		NaOAc

[k]Eighty-four percent of the starting aryl iodide was recovered from the reaction mixture.

[l]The desired product was isolated as a 3 : 4 mixture of diastereomers.

[m]The desired product was isolated as a 4 : 5 mixture of diastereomers.

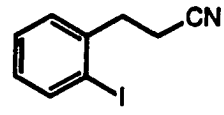
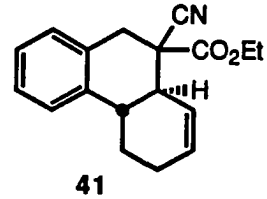
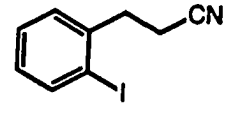
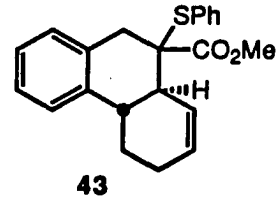
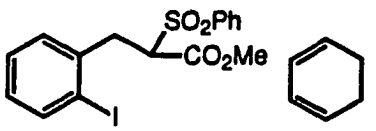
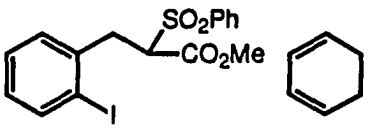
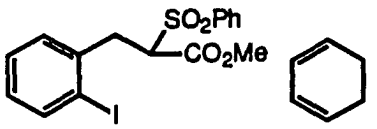
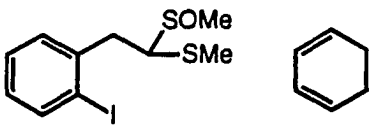
Reaction Conditions	Product(s)	%Yield[d]
5d, 60°C	 **42**	8
PPh_3, 3d, 80°C	 **41**	73
	 **42**	11
4d, 80°C	 **43**	96

Table III[a]. (continued)

Entry	Arene	Diene	Base[b]
23[f]	 11		Na_2CO_3, NaOAc or KOAc
24[f,n]	 11		Na_2CO_3 or NaOAc
25[f]	 11		Na_2CO_3
26	 12		Na_2CO_3

[n]Forty percent of the starting aryl iodide was recovered from the reaction mixture.

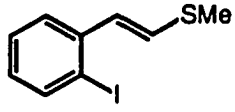
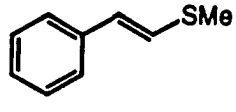
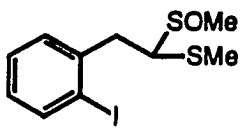
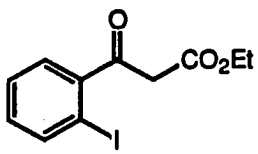
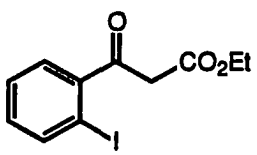
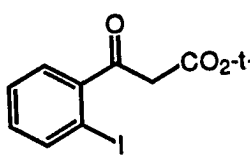
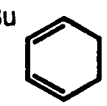
Reaction Conditions	Product(s)	%Yield[d]
1d, 80°C	-	-
5d, 60°C	-	-
PPh_3, 5d, 80°C	-	-
PPh_3, 1d, 80°C	 **44**	42
	 **45**	43

Table III[a]. (continued)

Entry	Arene	Diene	Base[b]
27	 **12**		Na_2CO_3
28	 **18**		Na_2CO_3
29	 **18**		Na_2CO_3
30[o]	 **19**		Na_2CO_3

[o]This product was isolated by base extraction.

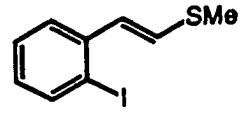
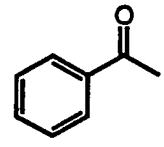
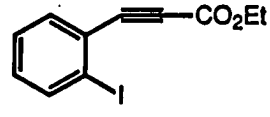
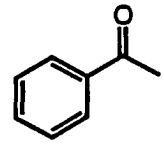
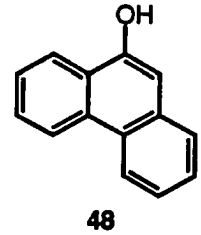
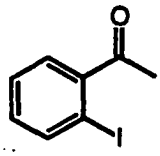
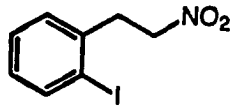
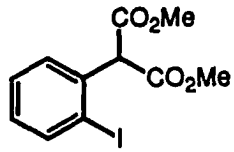
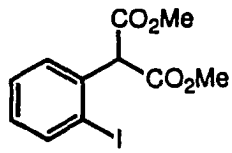
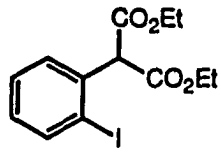
Reaction Conditions	Product(s)	%Yield[d]
PPh_3, 1d, 60°C	 **44**	95
3d, 80°C	 **46**	90
PPh_3, 6d, 60°C	 **47**	24
	 **46**	50
PPh_3, 1d, 80°C	 **48**	52

Table III[a]. (continued)

Entry	Arene	Diene	Base[b]
31	 **20**		KOAc
32	 **23**		Li_2CO_3
33	 **15**		Na_2CO_3
34[f]	 **15**		Na_2CO_3 or NaOAc
35	 **16**		Na_2CO_3

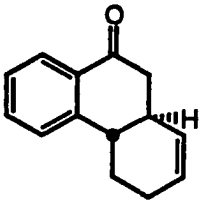
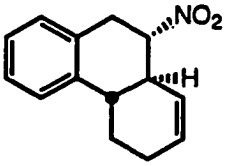
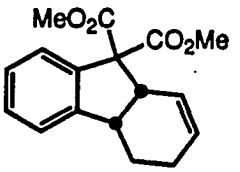
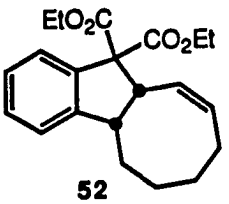
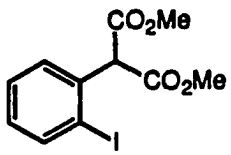
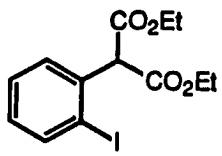
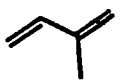
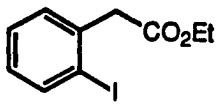
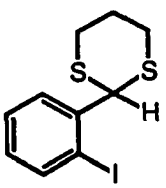
Reaction Conditions	Product(s)	%Yield[d]
PPh_3, 1d, 80°C	 **49**	56
PPh_3, 7d, 80°C	 **50**	73
1d, 60°C	 **51**	87
1d, 60°C	-	-
PPh_3, 10d, 60°C	 **52**	86

Table III[a]. (continued)

Entry	Arene	Diene	Base[b]
36	 **15**		Na_2CO_3
37	 **16**		Na_2CO_3
38[p]	 **14**		KOAc
39[q]	 **21**		Na_2CO_3

[p]The desired product was isolated as a 1.1 : 1 mixture of diastereomers.

[q]Eighty-seven percent of the starting aryl iodide was recovered from the reaction mixture.

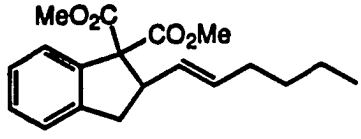
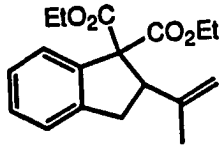
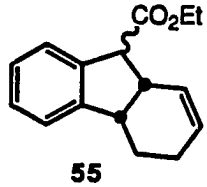
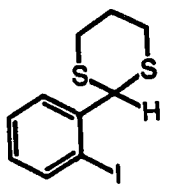
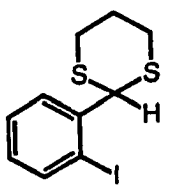
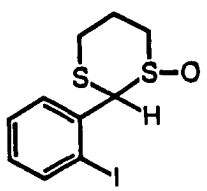
Reaction Conditions	Product(s)	%Yield[d]
1d, 60°C	 **53**	73
PPh_3, 8d, 60°C	 **54**	82
2d, 80°C	 **55**	85
9d, 80°C	-	-

Table III[a]. (continued)

Entry	Arene	Diene	Base[b]
40[r]	 **21**		Na_2CO_3
41[s]	 **21**		Cs_2CO_3
42[t]	 **22**		Na_2CO_3

[r]Seventy-eight percent of the starting aryl iodide was recovered from the reaction mixture.

[s]Thirty-three percent of the starting aryl iodide was recovered from the reaction mixture.

[t]Forty-one percent of the starting aryl iodide was recovered from the reaction mixture.

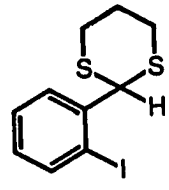
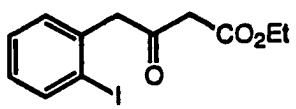
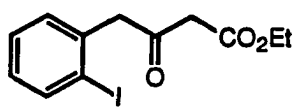
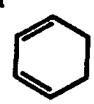
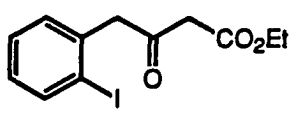
Reaction Conditions	Product(s)	%Yield[d]
6d, 100°C	-	-
6d, 100°C	-	-
6d, 80°C	 **21**	31

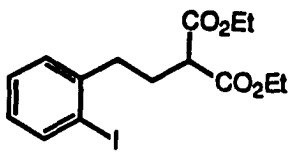
Table III[a]. (continued)

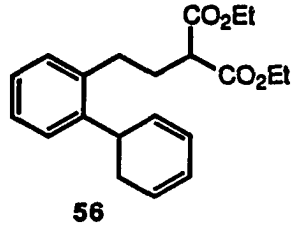
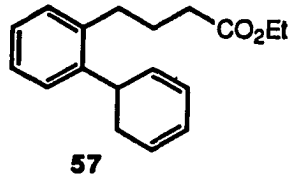
Entry	Arene	Diene	Base[b]
43[f]	 17		KOAc
44[f,u]	 17		KOAc
45	 17		Na_2CO_3

[u]This reaction was run using 3 ml of DMF instead of 1 ml of DMF.

Reaction Conditions	Product(s)	%Yield[d]
1d, 80°C	-	-
1d, 80°C	-	-
PPh_3, 1d, 100°C	-	-

Table III[a]. (continued)

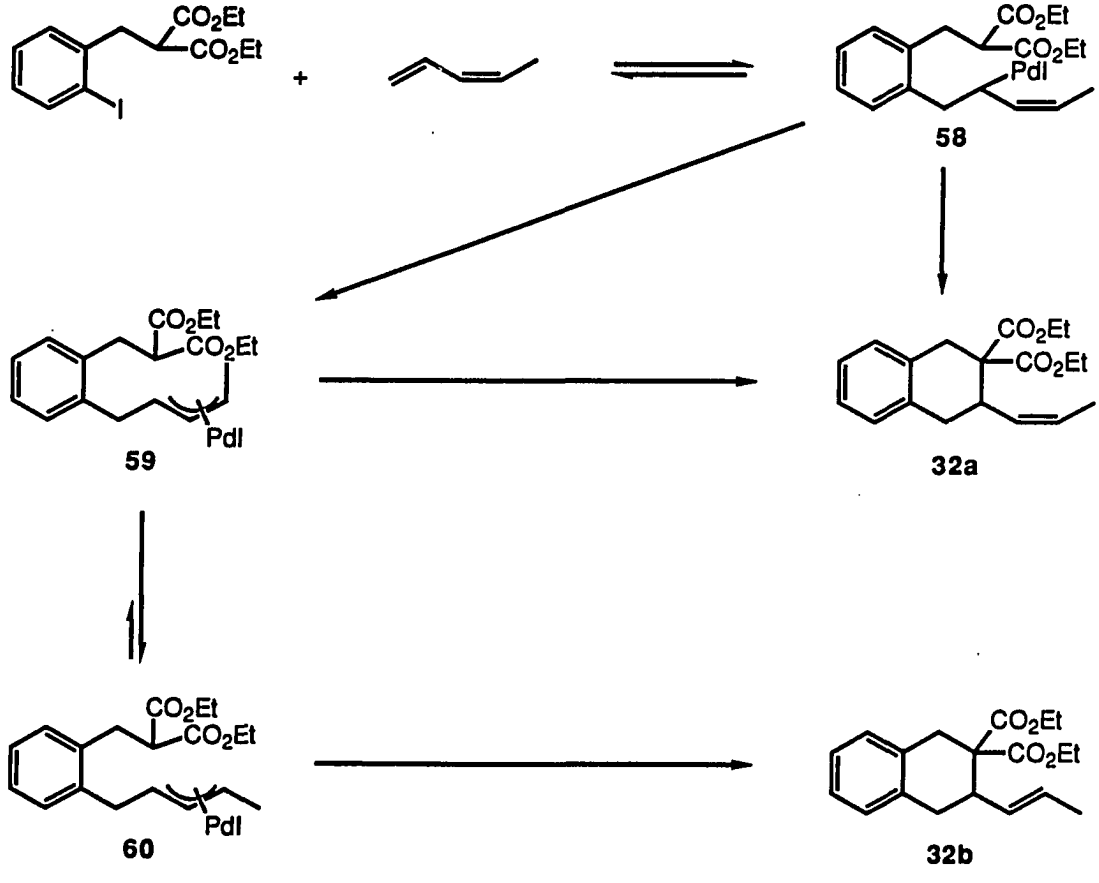
Entry	Arene	Diene	Base[b]
46	 13		Na_2CO_3

Reaction Conditions	Product(s)	%Yield[d]
PPh_3, 1d, 100°C	 **56**	51
	 **57**	47

under either of the standard conditions, very few further attempts were made.

Entries 1 - 18 summarize the studies of potential dienes for arylannulation. An E,Z-olefin, cis-1,3-pentadiene (Entry 3), was tried in the reaction to test the theory that trapping of a σ-allylpalladium intermediate, rather than trapping of a π-allylpalladium complex results in the desired product (Scheme XXIX). If the initially formed σ-allyl-

Scheme XXIX



palladium intermediate 58 is trapped before it collapses to the anti-π-allylpalladium complex 59, the internal double bond will retain its stereochemistry yielding the cis-product 32a. The anti-π-allylpalladium complex 59 would also be expected to yield 32a. However, anti-π-allylpalladium complexes are known to readily isomerize to syn-π-allylpalladium complexes.[30] Isomerization of the anti-π-allylpalladium complex 59 to the syn-π-allylpalladium complex 60 should be rapid, and cyclization of 60 will afford the trans-product 32b. The reaction of 8 with cis-1,3-pentadiene gives an 8 : 1 mixture of the trans- : cis-products. This ratio indicates that closure to the annulated product is proceeding primarily through a π-allylpalladium intermediate.

The effect of the substitution pattern of the linear dienes on arylannulation was studied (Entries 4 - 7). Steric hindrance seems to slow the reaction, but high yields are still attainable. Placing gem dimethyl groups at the terminal end of the diene slows the reaction from a two day process to a two week process (Entry 4). Placing one methyl group on an internal carbon again slows the reaction to almost two weeks (Entry 6). The reaction with isoprene is unique in that structural isomers may result from attack at opposite ends of the diene system (Entries 5 and 6). After comparing entries 5 and 6, it was concluded that the phosphine not only eliminates formation of diene product 36,

but also controls the regiochemistry of the original attack. It is presumed that the steric bulk of an arylpalladium phosphine complex prohibits its approach to the more substituted end of isoprene. The steric bulk of the arylpalladium phosphine complex, or the steric bulk of the π-allylpalladium phosphine complex is also the most likely cause of the long reaction times. The reaction of diethyl o-iodobenzyl malonate with isoprene proceeds four times as fast without triphenylphosphine in the reaction mixture (Entries 5 and 6).

A brief exploration of functional group tolerance was made using 1-acetoxy-1,3-butadiene (Entries 8 - 10). The reaction of 1-acetoxy-1,3-butadiene and diethyl o-iodobenzyl malonate yields two different identifiable products depending on the reaction conditions. Under standard arylannulation conditions without added phosphine, the reaction yields cyclized aldehyde (Entry 8). The aldehyde presumably results from hydrolysis of the vinylic acetate. When triphenylphosphine is used in the reaction, the only identifiable product found was annulated vinylic acetate (Entry 10). Numerous products were seen in these reactions with 1-acetoxy-1,3-butadiene by TLC and GC, but none of these products were identified. One problem with 1-acetoxy-1,3-butadiene is that vinylic acetate groups are readily hydrolyzed to ketones and aldehydes.[31] Hydrolysis of 1-acetoxy-1,3-butadiene initially yields 3-butenal, which can

isomerize to crotonaldehyde. To prevent formation of crotonaldehyde, anhydrous reaction conditions were tried. Tetra-n-butyl-ammonium chloride, sodium carbonate, palladium acetate and triphenylphosphine were dried under vacuum at 120°C. The reaction was run under argon, and the anhydrous conditions were rigorously maintained for two weeks. The starting aryl iodide 8 (95%) was recovered from the reaction mixture.

Cyclic dienes were examined to determine how the reaction is effected by a change in ring size (Entries 1, 11 - 18). Dicyclopentadiene was cracked to give 1,3-cyclopentadiene which was immediately used in the reaction (Entries 11 - 13). In all cases, what appeared to be a single product by TLC was isolated from the reaction of 8 and 1,3-cyclopentadiene. The fraction isolated by column chromatography showed a clean ^{1}H NMR spectrum, but the ^{13}C NMR spectrum had over forty peaks, and GC of the fraction showed seven peaks. When the reaction of diethyl o-iodobenzylmalonate and 1,3-cyclopentadiene was run using the initial catalyst system without triphenylphosphine, the reaction immediately turned deep purple (Entry 11). It was thought that the purple color might be arising from the formation of iodine through a free radical process. Therefore, the reaction was rerun omitting light (Entry 12). These reactions do not produce the same purple color, but the only fraction isolated was identical to the fraction found in

entry 11. Addition of triphenylphosphine did not change the reaction (Entry 13).

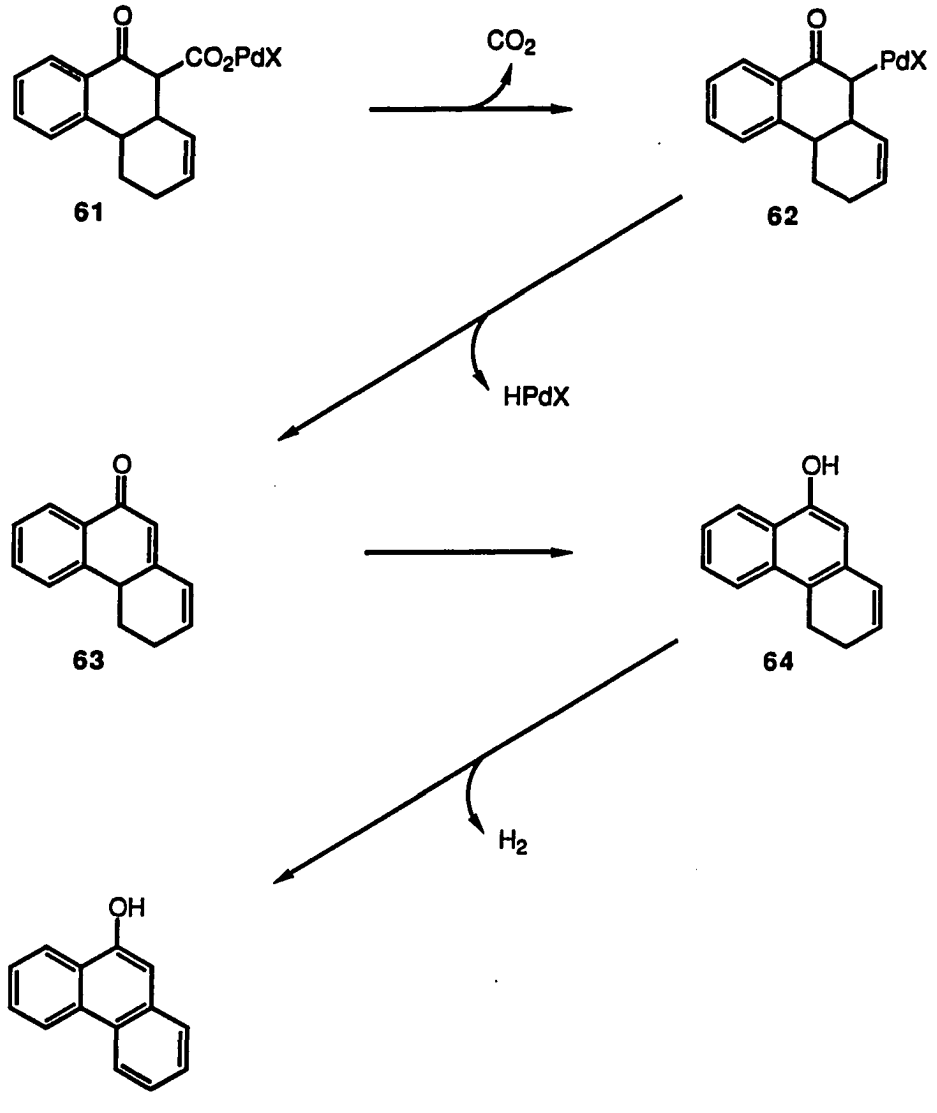
When 1,3-cyclooctadiene is used in the reaction, the desired annulated product along with styrenyl product 25 is formed (Entries 14 - 18). Variation of the base (Entries 14 and 15), lowering the reaction temperature (Entry 16) and the addition of various phosphorus ligands does not significantly alter the product ratios.

The effectiveness of various carbanion stabilizing groups in the arylannulation was examined next (Entries 19 - 32). Nitrile esters (Entries 19 - 21), sulphide esters (Entry 22), 2-iodoacetophenone (Entry 31) and nitro compounds (Entry 32) are all efficient in the palladium-catalyzed annulation procedure. With nitrile esters (Entries 19 - 21), one problem that could not be overcome was decarboxylation to yield 3-(2'-iodophenyl)proprionitrile (42). This side product is easily separated from the desired product, and the desired product is obtained in high yield (Entries 19 and 21). Arylannulation of 1,3-cyclohexadiene using sulfone ester 11, completely fails under a number of different reaction conditions (Entries 23 - 25). Under all reaction conditions, at least five different fractions are isolated by preparative TLC. Each of these fractions shows at least two peaks when examined by GC, and none of the fractions shows both arene protons and olefinic protons by ^{1}H NMR spectral analyses. Under the reaction conditions employed, the

sulfoxide sulfide 12 undergoes sulfoxide elimination to yield styrenyl sulphide 44 (Entries 26 and 27). Ethyl β-ketoester 18 is readily decarboxylated under the reaction conditions to yield acetophenone (Entries 28 and 29). An interesting and useful reaction occurs when the ethyl group of the β-ketoester 18 is replaced with a t-butyl group (Entry 30). Under the standard reaction conditions using triphenylphosphine, t-butyl 3-(2'-iodophenyl)-3-oxopropanoate 19 and 1,3-cyclohexadiene affords 9-phenanthrol as the only product. The fully aromatized product is thought to arise from the annulated palladium carboxylate 61 which undergoes loss of CO_2 to yield the σ-palladium intermediate 62 (Scheme XXXII). Elimination of HPdX affords dienone 63 which tautomerizes to the corresponding phenol 64. Then loss of hydrogen, which is known to occur over a palladium catalyst, leads to 9-phenanthrol. The palladium carboxylate is presumably formed via attack of the anionic palladium species PdX^- on the ester.

The next set of experiments explored formation of a five-membered ring instead of a six-membered ring (Entries 33 - 42). In the examination of dienes, either dimethyl o-iodophenylmalonate or diethyl o-iodophenylmalonate were used (Entries 33 - 37). The reaction with o-iodophenylmalonate and every diene except 1,3-cyclopentadiene gives high yields of the desired product without any accompanying side products. Like the reaction with diethyl o-iodobenzyl-

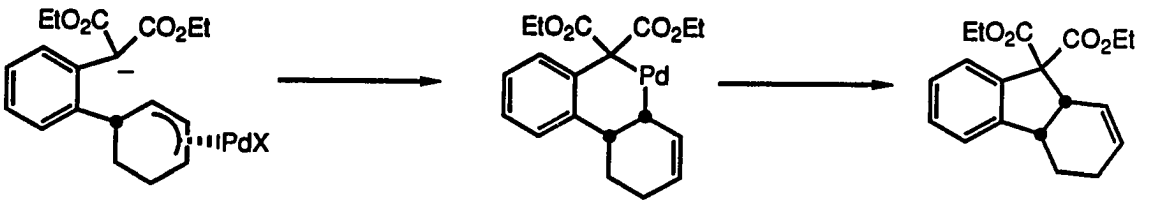
Scheme XXXII



malonate, the reaction of dimethyl o-iodophenylmalonate and 1,3-cyclopentadiene yields what appears to be a single product by TLC, but GC analysis shows eight peaks, and the ^{13}C NMR spectrum had 38 peaks (Entry 34). Surprisingly, 1,3-cyclooctadiene works well with this three carbon annulating agent, but works poorly with the four carbon annulating agent

(Entry 35). Unlike the six-membered rings that were formed during arylannulation, the five-membered rings are cis-fused. This stereochemistry is thought to arise from attack of the intermediate carbanion 65 onto the palladium to yield metallocycle 66 (Scheme XXXIII). Reductive elimination of

Scheme XXXIII



65 66

the palladium from the metallocycle furnishes the cis-fused ring.

The types of carbanion-stabilizing groups that can be used on the three carbon annulating arene were also explored (Entries 38 - 42). Interestingly, ethyl o-iodophenylacetate produces high yields of the desired product (Entry 38). On the other hand, a dithiane (Entries 39 - 41) and a sulfoxide sulphide (Entry 42) cannot be used in the arylannulation reaction.

Formation of seven-membered rings via the palladium-catalyzed annulation method also proved to be unsuccessful (Entries 43 - 46). The ethyl β-ketoester 17 yields numerous products as is seen with the four carbon annulating ethyl β-keto ester 18 (Entries 43 - 45). When the five carbon annulating malonate 13 is used, the arene does indeed add to the diene, but the π-allylpalladium intermediate apparently undergoes elimination to form two diene products (Entry 46). It is felt that the π-allylpalladium intermediate in this case may be too crowded to allow nucleophilic attack at the carbon center, and thus prevents annulation.

CONCLUSION

The palladium-catalyzed intermolecular reaction of three- and four-carbon annulating agents and 1,3-dienes presented in this section provides a valuable route to polycyclic compounds. High yields of five- and six-membered rings annulated to arene rings can be readily obtained. The reaction proceeds under relatively mild conditions, and makes use of a catalytic amount of palladium. A wide variety of electron-withdrawing groups can be used to stabilize the carbanion. Substitution patterns about the diene system result in variations of the reaction time, but they do not stop the reaction. Further exploration on the tolerance of olefin functional groups, and on the formation of rings larger than six-membered rings could further expand the utility of this arylannulation. Currently, the reaction is being extended to the formation of heterocycles, and to the use of vinylic iodides. These two extensions provide further avenues for exploration.

EXPERIMENTAL SECTION

Equipment

NMR spectra were recorded on a Nicolet NT-300 spectrometer (^{1}H NMR, 300 MHz; ^{13}C NMR, 75 MHz), and chemical shifts are reported in ppm relative to TMS (δ 0.00) as an internal standard. IR spectra were obtained on an IBM IR98. High-resolution mass spectra were recorded on a Kratos MS-30 spectrometer.

Reagents

All chemicals were used directly as obtained commercially unless otherwise noted. N,N-Dimethylformamide and dimethyl sulfoxide were distilled from calcium hydride under reduced pressure and stored over 4 Å molecular sieves. Acetonitrile was distilled over calcium hydride and stored over 4 Å molecular sieves. Tetrahydrofuran was distilled over sodium benzophenone ketal and used immediately. Methanol was distilled over sodium methoxide and stored over 4 Å molecular sieves. Triphenylphosphine was recrystallized from absolute ethanol. Sodium methoxide was obtained from Aldrich or prepared from sodium and methanol.

Preparation of diethyl o-iodobenzylmalonate 8

Diethyl o-iodobenzylmalonate was prepared from o-iodobenzyl alcohol. 2-Iodobenzyl alcohol was converted to

2-iodobenzyl bromide by the method of Hooz and Gilani.[32] Carbon tetrabromide (6.6 g, 20 mmole) and 2-iodobenzyl alcohol (2.3 g, 10 mmole) were weighed into a 50-ml round-bottom flask equipped with a septum inlet and a magnetic stirring bar. Ether (20 ml) was added via syringe, and the mixture was stirred until everything dissolved. The mixture was placed in an ice bath and triphenylphosphine (5.25 g, 20 mmole) was added all at once. The mixture was stirred for 2 hr, then the diethyl ether and bromoform were distilled off under reduced pressure. The residue was purified by flash column chromatography over silica gel using 5 : 1 hexanes : ethyl acetate. 2-Iodobenzyl bromide (2.97 g, 100%) was afforded as a white solid. ^{1}H NMR δ 4.96 (s, 2H, $ArCH_2$), 6.98 (t, J = 5.1 Hz, 1H, ArH), 7.33 (t, J = 7.5 Hz, 1H, ArH), 7.47 (d, J = 5.1 Hz, 1H, ArH), 7.85 (d, J = 7.5 Hz, 1H, ArH). Sodium hydride (1.894 g, 80 mmole) was weighed into a flame-dried, 100-ml round-bottom flask equipped with a septum inlet and a magnetic stirring bar. The flask was flushed with nitrogen, then DMF-THF (2 : 1, 45 ml) was added via syringe. The suspension was stirred under nitrogen, and diethyl malonate (12 ml, 80 mmole) was added in a dropwise fashion over a half hour. The reaction was stirred for an additional 15 min at room temperature. A solution of 2-iodobenzyl bromide (1.450 g, 5.0 mmole) in DMF-THF (2 : 1, 6 ml) was added via cannula and the reaction mixture was stirred overnight at room temperature. The reaction mixture was

poured into cold water, then extracted with ether (3 x 100 ml). The combined ether extracts were dried over magnesium sulfate. Flash column chromatography over silica gel using 5 : 1 hexanes : ethyl acetate afforded diethyl 2-iodobenzylmalonate (1.443 g, 78%). ^{1}H NMR δ 1.21 (t, J = 6.9 Hz, 6H, CH_3), 3.33 (d, J = 7.8 Hz, 2H, $ArCH_2$), 3.82 (t, J = 7.8 Hz, 1H, $CH(CO_2Et)_2$), 4.16 (d of q, J = 2.7 and 6.9 Hz, 4H, CO_2CH_2), 6.91 (m, 1H, ArH), 7.24 (m, 2H, ArH), 7.82 (d, J = 7.8 Hz, 1H, ArH); ^{13}C NMR δ 13.96, 39.19, 51.62, 61.42, 100.36, 127.33, 129.44, 131.58, 138.45, 140.38, 168.38; IR 2982, 2937, 1732 (C=O), 1468, 1443, 1391, 1369, 1331, 1292, 1225, 1177, 1151, 1113, 1096, 1032, 1013, 752, 646 cm^{-1}; HRMS calculated for $C_{14}H_{17}IO_4$ 376.01716, found 376.01679.

Synthesis of 2-iodoarenes

A number of the 2-iodoarene starting materials were prepared in two steps from 2-iodobenzyl alcohol. The synthesis of ethyl 2-cyano-3-(2'-iodophenyl)propanoate 9 is representative. 2-Iodobenzyl alcohol (1.1606 g, 5.0 mmole) was weighed into a 25-ml flame-dried, round-bottom flask equipped with a septum inlet and a magnetic stirring bar. The flask was flushed with nitrogen and placed in an ice bath. Triethylamine (1.10 ml, 8.0 mmole) and mesyl chloride (0.54 ml, 7.0 mmole) were added sequentially via syringe. The flask was warmed to room temperature. The reaction mixture was filtered and then evaporated to afford 2-

iodobenzyl mesylate as a crude mixture. Sodium hydride (0.1440 g, 6.0 mmole) was weighed into a 100-ml round-bottom, flame-dried flask. The flask was flushed with nitrogen, and then DMF (10 ml) and ethyl cyanoacetate (0.66 ml, 6.2 mmole) were added sequentially via syringe. The reaction mixture was stirred for 30 min. 2-Iodobenzyl mesylate, dissolved in THF (10 ml), was added via cannula. The reaction mixture was stirred overnight, poured into cold water (100 ml), extracted with methylene chloride (4 x 50 ml), and then dried over sodium sulfate. Flash column chromatography over silica gel using 5 : 1 hexanes : ethyl acetate afforded ethyl 2-cyano-3-(2'-iodophenyl)propanoate (1.2468 g, 76%) as a white solid. mp 71-72°C; ^{1}H NMR δ 1.31 (t, J = 7.2 Hz, 3H, CH_3), 3.22 (d of d, J = 9.9 and 13.8 Hz, 1H, $ArCH_2$), 3.47 (d of d, J = 6 and 13.8 Hz, 1H, $ArCH_2$), 3.91 (d of d, J = 6 and 9.9 Hz, 1H, $CH(CN)CO_2Et$), 4.28 (q, J = 7.2 Hz, 2H, CO_2CH_2), 7.00 (m, 1H, ArH), 7.35 (m, 2H, ArH), 7.87 (m, 1H, ArH); ^{13}C NMR δ 37.75, 40.54, 45.54, 63.10, 100.26, 128.56, 128.84, 129.68, 130.26, 131.02, 139.90, 165.17; IR 3063, 2984, 2937, 2251 (C≡N), 1744 (C=O), 1587, 1564, 1468, 1439, 1369, 1259, 1096, 752, 717 cm^{-1}; HRMS calculated for $C_{12}H_{12}INO_2$ 328.99128, found 328.99143.

Methyl 2-thiophenyl-3-(2'-iodophenyl)propanoate 10

Obtained in 25% yield from methyl thiophenylacetate as a white solid. ^{1}H NMR δ 3.17 (d of d, J = 6.3 and 13.8 Hz, 1H,

$ArCH_2$), 3.31 (d of d, J = 9.3 and 13.8 Hz, 1H, $ArCH_2$), 3.59 (s, 3H, CH_3), 4.03 (d of d, J = 6.3 and 9.3 Hz, 1H, $CH(SPh)CO_2Me$), 6.91 (m, 1H, ArH), 7.15-7.35 (m, 5H, ArH), 7.46 (m, 2H, ArH), 7.80 (d, J=7.2 Hz, 1H, ArH); ^{13}C NMR δ 42.79, 50.59, 52.05, 100.57, 128.22, 128.70, 128.93, 130.83, 132.12, 133.06, 133.53, 139.65, 140.27, 171.60; IR 3059, 2949, 1736 (C=O), 1643, 1468, 1439, 1302, 1258, 1225, 1190, 1153, 1013, 748, 690, 646 cm^{-1}; HRMS calculated for $C_{16}H_{15}IO_2S$ 397.98376, found 397.98285.

Methyl 2-phenylsulfonyl-3-(2'-iodophenyl)propanoate 11

Obtained in 86% yield from methyl phenylsulfonylacetate as a light yellow liquid. ^1H NMR δ 3.4 (m, 2H, $ArCH_2$), 3.587 (s, 3H, CH_3), 4.392 (d of d, J = 9.9 and 5.4 Hz, 1H, $CH(SO_2Ph)CO_2Me$), 6.912 (d of t, J = 1.2 and 7.5 Hz, 1H, ArH), 7.18 (m, 2H, ArH), 7.609 (m, 2H, ArH), 7.694 (d, J = 7.2 Hz, 1H, ArH), 7.762 (d, J = 8.7 Hz, 1H, ArH), 7.97 (m, 2H, ArH); ^{13}C NMR δ 43.25, 54.45, 54.78, 100.46, 127.95, 128.57, 128.73, 130.10, 130.87, 133.12, 133.53, 138.97, 140.25, 172.05; IR 3003, 2952, 1742 (C=O), 1447, 1437, 1356, 1325, 1231, 1202, 1175, 1150, 1084, 1016, 756, 723, 689, 646 cm^{-1}; HRMS calculated for $C_{16}H_{15}IO_4S$ 429.973358, found 429.97403.

Ethyl 2-carboethoxy-4-(2'-iodophenyl)butanoate 13

Obtained in 5% yield from the mesylate of 2-iodophenethyl alcohol and diethyl malonate as a colorless oil. ^1H

NMR δ 1.28 (t, J = 7.2 Hz, 6H, CH_3), 2.19 (d of d of d, J = 5.7, 7.5 and 7.8 Hz, 2H, $ArCCH_2$), 2.78 (d of d, J = 5.7 and 7.8 Hz, 2H, $ArCH_2$), 3.39 (t, J = 7.5 Hz, 1H, $CH(CO_2Et)$), 4.21 (q, J = 7.2 Hz, 4H, CO_2CH_2), 6.89 (d of t, J = 1.8 and 7.8 Hz, 1H, ArH), 7.22 (d of d, J = 1.8 and 7.5 Hz, 1H, ArH), 7.27 (d of t, J = 1.2 and 7.5 Hz, 1H, ArH), 7.80 (d of d, J = 1.2 and 7.8 Hz, 1H, ArH); ^{13}C NMR δ 14.14, 38.24, 41.68, 51.38, 61.44, 100.34, 128.06, 128.40, 129.55, 139.55, 143.36, 169.09; IR 2980, 2930, 1732 (C=O), 1466, 1369, 1223, 1151, 1115, 1020, 752 cm^{-1}; HRMS calculated for $C_{15}H_{19}O_4I$ 390.03281, found 390.03279.

Preparation of 2-iodophenethyl alcohol

Reduction of o-iodophenylacetic acid was accomplished by the method of Yoon et al.[33] A clean, dry 25-ml flask equipped with a side arm fitted with a septum inlet, a magnetic stirring bar and a reflux condenser connected to a mercury bubbler was cooled under nitrogen. 2-Iodophenylacetic acid (1.259 g, 4.8 mmole) was placed in the flask. THF (2 ml) was added, and the flask was cooled to 0°C. Borane-THF (10 ml of 1 M, 10 mmole) was added slowly over a period of 15 min, and the solution was vigorously stirred for an additional 2 hr. Excess hydride was carefully destroyed with a 1 : 1 mixture of THF-H_2O (10 ml), and the water layer was saturated with potassium carbonate (2 g). The THF layer was separated, and the aqueous phase was extracted with ether (4

x 25 ml). The combined organic extracts were dried over $MgSO_4$. Flash column chromatography over silica gel using 2 : 1 hexanes : ethyl acetate afforded o-iodophenethyl alcohol (0.843 g, 71 %). ^1H NMR δ 1.52 (br s, 1H, OH), 3.02 (t, J = 6.7 Hz, 2H, $ArCH_2$), 3.86 (t, J = 6.7 Hz, 1H, $C\underline{H}_2OH$), 6.92 (d of d of d, J = 2.4, 6.6 and 6.9 Hz, 1H, ArH), 7.27 (m, 2H, ArH), 7.83 (d, J = 7.8 Hz, 1H, ArH).

Synthesis of 2-(2'-iodophenyl)-1-methylsulfinyl-1-thiomethylethane 12

2-(2'-Iodophenyl)-1-methylsulfinyl-1-thiomethylethane was prepared by the method of Richman et al.[34] in 25% yield as a diastereomeric mixture in a 1 : 1 ratio. ^1H NMR (diastereomer A) δ 2.17 (s, 3H, SCH_3), 2.78 (s, 3H, $SOCH_3$), 2.89 (d of d, J = 11.4 and 14.4 Hz, 1H, $ArCH_2$), 3.54 (d of d, J = 3.9 and 14.4 Hz, 1H, $ArCH_2$), 3.95 (d of d, J = 3.9 and 11.4 Hz, 1H, CHS_2), 6.98 (d of t, J = 2.4 and 7.2 Hz, 1H, ArH), 7.3-7.4 (m, 3H, ArH); (diastereomer B) δ 2.20 (s, 3H, SCH_3), 2.68 (s, 3H, $SOCH_3$), 3.03 (d of d, J = 9.9 and 13.8 Hz, 1H, $ArCH_2$), 3.73 (d of d, J = 4.8 and 13.8 Hz, 1H, $ArCH_2$), 3.81 (d of d, J = 4.8 and 9.9 Hz, 1H, CHS_2), 6.98 (d of t, J = 2.4 and 7.2 Hz, 1H, ArH), 7.3-7.4 (m, 3H, ArH); ^{13}C NMR (mixture of diastereomers) δ 14.79, 15.58, 33.17, 35.76, 37.02, 37.84, 65.26, 66.98, 100.23, 100.52, 127.99, 128.05, 128.67, 131.00, 138.92, 139.09, 139.42; IR (mixture of diastereomers) 2980, 1740, 1701, 1649, 1582, 1464, 1427,

1383, 1319, 1267, 1196, 1151, 1022, 760 cm^{-1}; HRMS calculated for $C_{10}H_{13}IOS_2$ 317.97530, found 317.97527.

Preparation of dimethyl 2-iodophenylmalonate 15

Dimethyl 2-iodophenylmalonate was prepared in three steps from phenylacetic acid. Phenylacetic acid (3.50 g, 26 mmole) was iodinated by the thallation/iodination procedure of McKillop et al.[35] to afford 2-iodophenylacetic acid (3.60 g, 58%) as a white solid. ^1H NMR δ 3.85 (s, 2H, $ArCH_2$), 6.98 (d of t, J = 2.1 and 7.2 Hz, 1H, ArH), 7.30 (m, 2H, ArH), 7.85 (d, J = 7.8 Hz, 1H, ArH). Methyl 2-iodophenylacetate was prepared by the method of Harrison[36] from 2-iodophenylacetic acid (1.543 g, 5.9 mmole) to afford the ester (1.453 g, 89%) as a clear oil. ^1H NMR δ 3.71 (s, 3H, CO_2CH_3), 3.80 (s, 2H, $ArCH_2$), 6.95 (d of t, J = 2.1 and 10.5 Hz, 1H, ArH), 7.28 (m, 2H, ArH), 7.83 (d, J = 8.7 Hz, 1H, ArH). Sodium hydride (0.463 g, 19 mmole) was weighed into a flame-dried, 50-ml round-bottom flask equipped with a septum inlet and a magnetic stirring bar. The flask was flushed with nitrogen. A solution of methyl 2-iodophenylacetate (1.453 g, 5.3 mmole) dissolved in dimethyl carbonate (20 ml) was added via cannula. The reaction mixture was stirred under nitrogen at room temperature overnight. The solution was poured into a cold saturated solution of ammonium chloride (100 ml) and extracted with methylene chloride (4 x 50 ml). The combined methylene chloride extracts were dried over magnesium

sulfate. Removal of the solvent in vacuo afforded dimethyl 2-iodophenyl malonate (1.376 g, 78%) as a white solid. mp. 65°C; ^{1}H NMR δ 3.78 (s, 6H, CO_2CH_3), 5.18 (s, 1H, $CH(CO_2Me)$), 7.02 (d of t, J = 1.8 and 7.5 Hz, 1H, ArH), 7.37 (d of t, J = 0.9 and 7.8 Hz, IH, ArH), 7.47 (d of d, J = 1.5 and 7.8 Hz, 1H, ArH), 7.87 (d of d, J = 1.2 and 8.1 Hz, 1H, ArH); ^{13}C NMR δ 52.99, 61.91, 101.53, 128.60, 129.69, 129.85, 136.16, 139.63, 168.09; IR 3005, 2955, 2843, 1753 (C=O), 1736 (C=O), 1472, 1433, 1310, 1263, 1215, 1194, 1150, 1011, 989, 905, 746 cm^{-1}; HRMS calculated for $C_{11}H_{11}IO_4$ 333.97021, found 333.96992.

Preparation of diethyl 2-iodophenyl malonate 16

Diethyl 2-iodophenylmalonate was prepared in the same method as dimethyl 2-iodophenylmalonate. Ethyl 2-iodophenylacetate (14) was obtained as an intermediate. ^{1}H NMR δ 1.26 (t, J = 7.2 Hz, 3H, CH_3), 3.79 (s, 2H, $ArCH_2$), 4.18 (q, J = 7.2 Hz, 2H, CO_2CH_2), 6.99 (m, 1H, ArH), 7.35 (m, 2H, ArH), 7.83 (d, J = 7.5 Hz, 1H, ArH). Diethyl 2-iodophenyl malonate (2.924 g, 93%) was obtained as a yellow oil. ^{1}H NMR δ 1.28 (t, J = 7.2 Hz, 6H, CH_3), 4.25 (d of q, J = 1.5 and 7.2 Hz, 4H, CO_2CH_2), 5.12 (s, 1H, ArCH), 7.01 (d of t, J = 1.5 and 7.8 Hz, 1H, ArH), 7.37 (d of q, J = 1.2 and 7.8 Hz, 1H, ArH), 7.47 (d of d, J = 1.5 and 7.8 Hz, 1H, ArH), 7.87 (d of d, J = 1.2 and 7.8 Hz, 1H, ArH); ^{13}C NMR δ 14.05, 29.74, 61.96, 101.63, 128.49, 129.63, 129.67, 136.41, 139.55, 167.66; IR

2955, 2924, 1753 (C=O), 1736 (C=O), 1468, 1304, 1259, 1217, 1175, 1030, 745, 648 cm^{-1}; HRMS calculated for $C_{13}H_{15}IO_4$ 362.00151, found 362.00131.

Preparation of β-ketoesters 17 - 19

The synthesis of ethyl 3-(2'-iodophenyl)-3-oxopropanoate (18) is representative. The synthesis of ethyl 3-(2'-iodophenyl)-3-oxopropanoate was carried out using the general procedure of Ohta et al.[19] Diisopropylamine (2.8 ml, 20 mmole) and THF (5 ml) were added to a flame-dried 50-ml round-bottom flask equipped with a magnetic stirring bar and septum inlet. The flask was cooled to -78°C. n-Butyllithium (8.0 ml, 2.5 M solution in hexanes, 20 mmole) was added to the stirring solution. The flask was warmed to 0°C and stirred for 5 min before recooling to -78°C. Ethyl acetate (2.0 ml, 20 mmole) was added and the solution was stirred for 20 min. The resulting mixture was than transferred in a dropwise fashion via cannula to a flask containing ethyl o-iodobenzoate (2.76 g, 10 mmole) and THF (25 ml). The resulting yellow solution was stirred for 2 hr. Acetic acid (10 ml) was added followed by water (50 ml) and ether (150 ml). The organic layer was washed with 20% potassium carbonate (2 x 50 ml) and brine (1 x 50 ml), and then dried over sodium sulfate. Addition of hexanes to the concentrated crude product yielded ethyl 3-(2'-iodophenyl)-3-oxopropanoate as a pale yellow oil. ^1H NMR (mixture of keto

and enol forms) δ 1.24 and 1.26 (t, J = 7.2 Hz, 3H, CH_3), 3.97 (s, 1.5 H, $C(O)CH_2C(O)$), 4.12 and 4.19 (q, J = 7.2 Hz, 2H, $C(O)CH_2Ar$), 5.34 (s, 0.25H, C(OH)=CHC(O)), 7.0-7.2 (m, 1H, ArH), 7.35-7.55 (m, 2H, ArH), 7.9-8.0 (m, 1H, ArH); ^{13}C NMR δ 14.08, 14.28, 48.14, 60.54, 61.54, 91.44, 92.89, 94.31, 127.94, 128.05, 128.78, 129.53, 131.10, 132.27, 139.80, 140.23, 141.02, 142.51, 166.63, 172.41, 174.03, 195.76; IR 2980, 1740 (C=O), 1701 (C=O), 1649, 1582, 1464, 1427, 1383, 1319, 1267, 1196, 1151, 1022, 760 cm^{-1}; HRMS calculated for $C_{11}H_{11}IO_3$ 317.97530, found 317.97527.

Ethyl-4-(2'-iodophenyl)-3-oxobutanoate 17

Obtained in 9% yield as a yellow oil. ^1H NMR δ 1.27 (t, J = 7.2 Hz, 3H, CH_3), 3.52 (s, 2H, $ArCH_2$), 4.03 (s, 2H, $C(O)CH_2C(O)$), 4.20 (q, J = 7.2 Hz, 2H, CO_2CH_2), 6.98 (m, 1H, ArH), 7.24 (d of d, J = 1.8 and 7.5 Hz, 1H, ArH), 7.33 (t, J = 7.5 Hz, 1H, ArH), 7.86 (d, J = 7.8 Hz, 1H, ArH); ^{13}C NMR δ 14.14, 49.14, 54.44, 61.44, 101.19, 128.51, 129.06, 130.99, 137.41, 139.49, 166.87, 199.00; IR 3061, 2981, 2935, 1744 (C=O), 1720 (C=O), 1466, 1317, 1259, 1227, 1194, 1030, 1015, 746 cm^{-1}; HRMS calculated for $C_{12}H_{13}IO_3$ 331.99095, found 331.99114.

t-Butyl-3-(2'-iodophenyl)-3-oxopropanoate 19

Obtained in 72% yield as a white powder. mp 145°C; ^1H NMR δ 1.51 (s, 9H, t-Bu), 4.83 (s, 2H, $C(O)CH_2C(O)$), 6.87 (d

of t, J = 1.8 and 7.5 Hz, 1H, ArH), 7.21 (d of t, J = 0.9 and 7.5 Hz, 1H, ArH), 7.38 (d of d, J = 1.8 and 7.5 Hz, 1H, ArH), 7.77 (d of d, J = 0.9 and 7.5 Hz, 1H, ArH); ^{13}C NMR δ 29.06, 46.20, 87.41, 94.72, 127.24, 128.74, 128.80, 139.64, 148.70, 172.31, 182.57; IR 2976, 2885, 1637(C=O), 1583, 1528, 1456, 1391, 1290, 1267, 1157, 928, 914, 733 cm^{-1}; HRMS calculated for $C_{13}H_{15}O_3I$ 346.00660, found 346.00616.

Preparation of o-iodoacetophenone 20

Ethyl 3-(2'-iodophenyl)-3-oxopropanoate (1.0145g, 3.2 mmole) was weighed into a 25-ml round-bottom flask equipped with a magnetic stirring bar and reflux condenser. Propionic acid (1.9 ml, 25.6 mmole) was added via syringe followed by sulfuric acid (0.016 ml). The solution was brought to reflux for 3 hr. After cooling, the solution was poured into a cold water (40 ml)-ether (20 ml) mixture. The aqueous layer was extracted with ether (2 x 20 ml). The combined ether layers were washed with saturated sodium chloride (1 x 20 ml) and 10% sodium bicarbonate (2 x 20 ml), then dried over magnesium sulfate. Flash column chromatography over silica gel using 6 : 1 hexanes : ethyl acetate afforded o-iodoacetophenone (0.716 g, 91%). ^1H NMR δ 2.64 (s, 3H, CH_3), 7.12 (d of t, J = 1.8 and 7.5 Hz, 1H, ArH), 7.41 (d of t, J = 0.9 and 7.5 Hz, 1H, ArH), 7.46 (d of d, J = 1.8 and 7.5 Hz, 1H, ArH), 7.94 (d of d, J = 0.9 and 7.5 Hz, 1H, ArH).

Preparation of 2-(2'-iodophenyl)-1,3-dithiane 21

2-(2'-Iodophenyl)-1,3-dithiane was prepared by the method of Stütz and Stadler,[20] and was obtained as a white solid. ^{1}H NMR δ 1.91 (d of d of d of d of d, J = 3.6, 3.6, 12.3, 12.3, 14.1 Hz, 1H, $SCCH_2CS$), 2.17 (d of d of d of d of d, J = 2.4, 2.4, 3.6, 3.6, and 14.1 Hz, 1H, $SCCH_2CS$), 2.19 (d of d of d, J = 3.6, 3.6 and 13.8 Hz, 2H, SCH_2), 3.11 (d of d of d, J = 2.4, 12.3, 13.8 Hz, 2H, SCH_2), 5.41 (s, 1H, SCHS), 6.97 (d of d of d, J = 1.5, 7.5 and 7.5 Hz, 1H, ArH), 7.35 (d of d of d, J = 0.9, 7.5 and 7.5 Hz, 1H, ArH), 7.65 (d of d, J = 1.5 and 7.5 Hz, 1H, ArH), 7.81 (d of d, J = 0.9 and 7.5 Hz, 1H, ArH); ^{13}C NMR δ 25.00, 32.28, 56.55, 99.48, 128.93, 129.94, 132.78, 139.48, 141.26; IR 2947, 2930, 1462, 1433, 1275, 1175, 1161, 1011, 910, 744, 721 cm^{-1}; HRMS calculated for $C_{10}H_{11}IS_2$ 321.93470, found 321.93459.

Synthesis of 2-(2'-iodophenyl)-1-oxo-1,3-dithiane 22

Sodium periodate (1.11 g, 5.2 mmole) was weighed into a 250-ml round-bottom flask equipped with a magnetic stirring bar and septum inlet. Water (25 ml) was added and the solution was placed in a ice bath. 2-(2'-Iodophenyl)-1,3-dithiane, dissolved in methanol (50 ml), was added all at once. Stirring was continued at 0°C overnight. Flash column chromatography over silica gel using ethyl acetate afforded 2-(2'-iodophenyl)-1-oxo-1,3-dithiane as two diastereomers, both were slightly yellow solids. Compound A: mp. 105-

106°C; ^{1}H NMR δ 1.85 (m, 1H, $SCCH_2CSO$), 2.8 (m, 2H, $SCCH_2CSO$ and SCH_2), 3.2 (m, 2H, SCH_2 and $SOCH_2$), 3.7 (m, 1H, $SOCH_2$), 5.260 (s, 1H, SCHSO), 7.05 (d of d of d, J = 1.5, 7.8 and 7.8 Hz, 1H, ArH), 7.37 (d of d of d, J = 0.9, 7.5 and 7.5 Hz, 1H, ArH), 7.53 (d of d, J = 1.5 and 7.8 Hz, 1H, ArH), 7.88 (d of d, J = 0.9 and 7.8 Hz, 1H, ArH); ^{13}C NMR δ 29.92, 47.68, 63.85, 69.17, 100.52, 129.12, 130.03, 130.67, 137.96, 139.50; IR 3057, 2912, 1462, 1421, 1261, 1081, 1061, 1013, 958 cm^{-1}; HRMS calculated for $C_{10}H_{11}IOS_2$ 337.92961, found 337.9294. Compound B: mp. 101-101.5°C; ^{1}H NMR δ 2.67 (m, 1H, $SCCH_2CSO$), 2.88 (m, 2H, $SCCH_2CSO$ and SCH_2), 3.33 (m, 1H, SCH_2), 3.61 (m, 1H, $SOCH_2$), 3.73 (m, 1H, $SOCH_2$), 5.15 (s, 1H, SCHSO), 7.04 (d of d of d, J = 1.8, 7.2 and 7.2 Hz, 1H, ArH), 7.41 (d of d of d, J = 1.2, 7.2 and 7.2 Hz, 1H, ArH), 7.48 (d of d, J = 1.5 and 7.8 Hz, 1H, ArH), 7.89 (d of d, J = 1.8 and 7.2 Hz, 1H, ArH); ^{13}C NMR δ 29.83, 54.87, 63.35, 73.02, 102.27, 128.73, 129.21, 130.55, 136.27, 140.15; IR 2918, 1464, 1423, 1423, 1261, 1086, 1055, 1011, 906, 837, 787, 754 cm^{-1}; HRMS calculated for $C_{10}H_{11}IOS_2$ 337.92961, found 337.9288.

Synthesis of 2-(2'-iodophenyl)-1-nitroethane 23

2-(2'-Iodophenyl)-1-nitroethane was synthesized from 2-iodobenzyl alcohol in four steps. 2-Iodobenzyl alcohol was oxidized by the method of Corey and Suggs.[37] Pyridinium chlorochromate (5.40 g, 25 mmole) was weighed into an

Erlenmeyer flask equipped with a magnetic stirring bar, and suspended in methylene chloride (25 ml). 2-Iodobenzyl alcohol (3.86 g, 16 mmole) dissolved in methylene chloride (30 ml) was added all at once to the vigorously stirred solution. The reaction mixture immediately turned black and was allowed to stand for 2 hr. The mixture was diluted with ether (130 ml) and filtered through Celite twice. Flash column chromatography over silica gel using 6 : 1 hexanes : ethyl acetate afforded o-iodobenzaldehyde (3.56 g, 96%) ^{1}H NMR δ 7.29 (d of t, J = 1.8 and 7.8 Hz, 1H), 7.47 (t, J = 7.5 Hz, 1H), 7.88 (d of d, J = 1.8 and 7.8 Hz, 1H), 7.96 (d of d, J = 0.9 and 7.5 Hz, 1H), 10.07 (s, 1H). 2-Iodobenzaldehyde was condensed with nitromethane, and the intermediate nitro alcohol was eliminated by the method of Stevens et al.[38] 2-Iodobenzaldehyde (2.32 g, 10 mmole), nitromethane (2.0 ml, 37 mmole), potassium fluoride dihydrate (94.13 g, 5 mmole) and isopropanol (20 ml) were placed in a 50-ml round-bottom flask equipped with a septum inlet and a magnetic stirring bar. The flask was flushed with nitrogen and stirring continued overnight. The reaction mixture was concentrated on a rotary evaporator. Water (10 ml) was added and the mixture was extracted with methylene chloride (3 x 20 ml). The combined organic extracts were washed with brine (10 ml) and were dried over sodium sulfate. Removal of the solvent afforded 1-(2'-iodophenyl)-2-nitroethanol (2.65 g, 90%). ^{1}H NMR δ 3.49 (d, J = 3.9 Hz, 1H, OH), 4.39 (d of d, J = 9.9 and 13.5

Hz, 1 H, $CHNO_2$), 4.45 (d of d, J = 2.4 and 13.5 Hz, 1H, $CHNO_2$), 5.66 (d of t, J = 3.0 and 9.9 Hz, 1H, ArC<u>H</u>OH), 7.06 (d of t, J = 1.5 and 7.8 Hz, 1H, ArH), 7.43 (d of t, J = 0.9 and 7.8 Hz, 1H, ArH), 7.63 (d of d, J = 1.5 and 7.8 Hz, 1H, ArH), 7.84 (d of d, J = 0.9 and 7.8 Hz, 1H, ArH). 1-(2'-Iodophenyl)-2-nitroethanol (2.65 g, 9.0 mmole) was dissolved in ethyl acetate (20 ml). The reaction flask was flushed with nitrogen, and cooled on an ice bath. Mesyl chloride (1.86 ml, 24 mmole) was added all at once and triethylamine (4.04 ml, 29 mmole) was added over 20 min. The mixture was stirred for 2 hr at 0°C. 2N Hydrochloric acid (10 ml) was added. The aqueous layer was extracted with ethyl acetate (2x20 ml). The combined organic layers were washed with saturated potassium carbonate (1 x 20 ml) and brine (1 x 20 ml) and then dried over sodium sulfate. Removal of the solvent afforded 2-(2'-iodophenyl)nitroethene (2.48 g, 100%). ^{1}H NMR δ 7.16 (d of t, J = 1.5 and 7.8 Hz, 1H, ArH), 7.41 (t, J = 7.8 Hz, 1H, ArH), 7.43 (d, J = 13.5 Hz, 1H, -CH), 7.54 (d of d, J = 1.5 and 7.8 Hz, 1H, ArH), 7.96 (d of d, J = 0.9 and 7.8 Hz, 1H, ArH), 8.26 (d, J = 13.5 HZ, 1H, -CH). The nitro alkene was reduced by the method of Chikashita et al.[39] To a stirred solution of 2-(2'-iodophenyl)nitroethene (1.4051 g, 3.8 mmole) and benzaldehyde (0.4882 g, 4.6 mmole) in 1-butanol (15 ml) under nitrogen at room temperature was added <u>o</u>-phenylenediamine (0.4974 g, 4.6 mmole). After refluxing for 5 hr, the solvent was evaporated under reduced pressure.

Dichloromethane was added and the insoluble imidazole was filtered off. The dichloromethane solution was thoroughly washed with 0.1 M hydrochloric acid, 5% sodium bicarbonate and saturated sodium bisulfite. Flash column chromatography over silica gel using 6 : 1 hexanes : ethyl acetate afforded 2-(2'-iodophenyl)-1-nitroethane as a bright yellow oil: ^{1}H NMR δ 3.42 (t, J = 7.35 Hz, 2H, $ArCH_2$), 4.60 (t, J = 7.35 Hz, 2H, CH_2NO_2), 6.96 (d of t, J = 1.8 and 7.5 Hz, 1H, ArH), 7.23 (d of d, J = 1.8 and 7.5 Hz, 1H, ArH), 7.29 (d of t, J = 1.2 and 7.5 Hz, 1H, ArH), 7.83 (d of d, J = 0.9 and 7.8 Hz, 1H, ArH); ^{13}C NMR δ 38.11, 74.50, 100.02, 128.84, 129.31, 130.16, 138.24, 139.89; IR 3025, 2920, 1555, 1468, 1450, 1379, 1342, 1286, 1219, 1180, 1011, 870, 858, 754, 729 cm^{-1}; HRMS calculated for $C_8H_8INO_2$ 276.95998, found 276.95983.

General procedure for carboannulation reactions

Palladium acetate (0.0028 g, 0.0125 mmole), triphenylphosphine (0.0033 g, 0.0125 mmole), base (1.25 mmole), aryl halide (0.25 mmole) and tetra-n-butylammonium chloride (0.0695 g, 0.25 mmole) were weighed into a 2 dram vial equipped with a magnetic stirring bar and septum inlet. DMF (1 ml) and diene (1.25 mmole) were added sequentially via syringe. Stirring was continued at the appropriate temperature for the required amount of time. The reaction mixture was diluted with ether (10 ml), washed with saturated ammonium chloride (5 x 10 ml) and dried over sodium sulfate.

Following removal of the solvents, the compounds were purified by flash column chromatography. Occasionally other solvents, palladium salts or additives were used, but the general procedure remained the same. The following compounds were obtained from the above procedure.

Compound 24

Compound 24 was isolated in 85% yield from diethyl o-iodobenzyl malonate and 1,3-cyclohexadiene when the reaction was run in the presence of sodium acetate for 1 day at 80°C. ^{1}H NMR δ 1.18 (t, J = 7.2 Hz, 3H, CH_3), 1.29 (t, J = 7.2 Hz, 3H, CH_3), 1.62 (m, 1H, ArCCHC=C), 2.27 (m, 2H, $ArCCH_2$), 2.55 (q of d, J = 3.3 and 12.6 Hz, 1H, C=CCH_2), 2.68 (t, J = 11.7 Hz, 1H, ArCH), 2.83 (q of d, J = 2.6 and 11.1 Hz, 1H, C=CCH_2), 3.25 (d, J = 16.2 Hz, 1H, $ArCH_2$), 3.51 (d, J = 16.2 Hz, 1H, $ArCH_2$), 4.14 (d of q, J = 2.7 and 7.2 Hz, 2H, CO_2CH_2), 4.25 (q, J = 7.2 Hz, 2H, CO_2CH_2); 5.75 (q of d, J = 3 and 10.2 Hz, 1H, $CH_2C\underline{H}$=C), 5.82 (d of d, J = 1.8 and 10.2 Hz, 1H, CHC<u>H</u>=C), 7.1-7.3 (m, 4H, ArH); ^{13}C NMR δ 14.07, 14.15, 25.92, 27.21, 36.55, 37.17, 43.88, 57.65, 61.05, 61.50, 124.56, 126.19, 126.92, 128.35, 129.63, 130.38, 134.00, 139.24, 170.34, 171.93; IR 2980, 2922, 1728 (C=O), 1240, 1121, 1184, 1097, 1051, 1028 cm^{-1}; HRMS calculated for $C_{20}H_{24}O_4$ 328.16746, found 328.16737. Anal. Calculated for $C_{20}H_{24}O_4$: C, 73.15%; H, 7.37%. Found: C, 73.16%; H, 7.25%.

Compound 25

Compound 25 was isolated in 51% yield when the reaction of diethyl o-iodobenzyl malonate and 1,3-cyclohexadiene was run in the presence of potassium carbonate for 1 day at 80°C. ^{1}H NMR δ 1.28 (m, 6H, CH_3), 4.27 (m, 4H, CO_2CH_2), 7.21 (m, 1H, ArH), 7.38 (m, 2H, ArH), 7.45 (m, 2H, ArH), 7.74 (s, 1H, vinylic); ^{13}C NMR δ 13.97, 14.22, 61.47, 61.54, 109.05, 126.65, 128.49, 128.79, 129.48, 130.46, 133.12, 142.12, 164.15, 196.02; IR 2982, 2928, 1730 (C=O), 1630, 1448, 1369, 1294, 1259, 1213, 1200, 1096, 1082, 1020, 692 cm^{-1}; HRMS calculated for C14H1604 248.10486, found 248.10442.

Compound 26

Compound 26 was isolated in 87% yield from diethyl 2-iodobenzyl malonate and 1,3-octadiene when the reaction was run in the presence of triphenylphosphine, using sodium carbonate as the base for 1 day at 60°C. ^{1}H NMR δ 0.86 (t, J = 6.9 Hz, 3H, $C=CC_3CH_3$), 1.18 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 1.20 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 1.27 (m, 4H, $C=CCCH_2CH_2$), 1.95 (m, 2H, $C=CCH_2$), 2.85 (m, 1H, C=CCH), 3.16 (m, 2H, $ArC\underline{H}_2CH$), 3.34 (br s, 2H, $ArCH_2C(CO_2Et)_2$), 4.11 (q, J = 7.2 Hz, 2H, CO_2CH_2), 4.13 (q, J = 7.2 Hz, 2H, CO_2CH_2), 5.54 (m, 2H, C=CH), 7.09 (m, 4H, ArH); ^{13}C NMR δ 13.85, 13.89, 13.95, 22.06, 31.50, 32.10, 32.76, 33.55, 42.09, 57.64, 60.97, 61.19, 125.64, 126.09, 128.65, 128.69, 129.23, 133.09, 133.23, 134.20, 169.85, 170.77; IR 2980, 2959, 1730 (C=O),

1466, 1454, 1366, 1252, 1182, 1113, 1096, 1042, 974, 746 cm^{-1}. Anal. Calculated for $C_{22}H_{30}O_4$: C, 73.71%; H, 6.34%. Found: C, 73.68%; H, 6.37%.

Compound 27

Compound 27 was isolated in 42% yield from diethyl o-iodobenzyl malonate and 1,3-octadiene when the reaction was run in the presence of sodium carbonate for 5 days at 60°C in acetonitrile. ^1H NMR δ 0.92 (t, J = 7.2 Hz, 3H, C=CC$_3$CH$_3$), 1.20 (t, J = 7.2 Hz, 6H, CO$_2$CCH$_3$), 1.3-1.5 (m, 4H, C=CCCH$_2$CH$_2$), 2.16 (q, J = 6.6 Hz, 2H, C=CCH$_2$), 3.30 (d, J = 7.5 Hz, 2H, ArCH$_2$), 3.62 (t, J = 7.5 Hz, 1H, CH(CO$_2$Et)$_2$), 4.13 (q, J = 7.2 Hz, 4H, CO$_2$CH$_2$), 5.84 (m, 1H, ArC=CC=CH), 6.1-6.3 (m, 2H, ArC=CHCH=C), 6.68 (d, J = 5 Hz, 1H, ArCH=C), 7.0-7.5 (m, 4H, ArH), ^{13}C NMR δ 13.84, 13.89, 22.07, 25.07, 31.50, 42.10, 57.64, 61.00, 125.70, 125.82, 126.19, 127.00, 127.15, 127.98, 130.24, 134.95, 136.88, 137.00, 168.92; IR 2982, 1732 (C=O), 1369, 1300, 1256, 1178, 1155, 1096, 1067, 1032 cm^{-1}; HRMS calculated for $C_{22}H_{30}O_4$ 358.21450, found 358.2148.

Compound 32

Compound 32 was isolated in 95% yield as an 8:1 E:Z mixture from the reaction of diethyl o-iodobenzyl malonate and cis-1,3-pentadiene when the reaction was run in the presence of sodium carbonate and 5% triphenylphosphine for 2

days at 60°C. ^{1}H NMR δ 1.18 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 1.29 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 1.62 (d, J = 4.8 Hz, 3H, $C{=}CCH_3$), 2.86 (d of d, J = 8.4 and 19.2 Hz, 1H, $ArC\underline{H}_2CH$), 3.1-3.2 (m, 2H, $ArCH_2CH$), 3.3-3.4 (m, 2H, $ArCH_2$), 5.53 (d of t, J = 15.3 and 6 Hz, 1H, $C{=}C\underline{H}CH_2$), 5.61 (d of d, J = 7.2 and 15.3 Hz, 1H, $C{=}C\underline{H}CH$), 7.0-7.2 (m, 4H, ArH); ^{13}C NMR δ 14.07, 17.98, 32.73, 33.63, 36.03, 42.18, 57.61, 61.15, 61.43, 125.75, 125.81, 126.19, 127.72, 128.76, 130.51, 133.16, 134.29, 170.04, 170.92. IR 2982, 2935, 1730 (C=O), 1497, 1452, 1367, 1250, 1225, 1182, 1113, 1059, 1015, 746 cm^{-1}; Anal. Calculated for $C_{19}H_{24}O_4$: C, 72.13; H, 7.65. Found: C, 72.16; H, 7.01.

Compound 33

Compound 33 was isolated in 87% yield from diethyl o-iodobenzylmalonate and 4-methyl-1,3-pentadiene when the reaction was run in the presence of 5% triphenylphosphine using sodium carbonate as the base for 14 days at 60°C. ^{1}H NMR δ 1.17 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 1.17 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 1.66 (br s, 6H, $=CCH_3$), 2.75 (d of d, J = 6.3 and 17.1 Hz, 1H, $ArCH_2$), 3.26 (d of d, J = 6.3 and 17.1 Hz, 1H, $ArCH_2$), 3.34 (d, J = 16.8 Hz, 1H, $ArCH_2$), 3.42 (d, J = 16.8 Hz, 1H, $ArCH_2$), 3.47 (d of d of d, J = 6.3, 6.3 and 10.5 Hz, 1H, $=CCH$), 4.05-4.15 (m, 4H, CO_2CH_2), 5.33 (d of q, J = 10.5 and 1.2 Hz, 1H, C=CH), 7.09 (m, 4H, ArH); ^{13}C NMR δ 13.99, 14.00, 17.96, 26.01, 33.19, 33.74, 37.40, 57.22,

61.01, 61.27, 123.88, 125.68, 126.12, 128.70, 128.76, 133.15, 133.65, 134.52, 170.14, 170.14; IR 2978, 2930, 1732 (C=O), 1450, 1365, 1258, 1221, 1096, 860 cm^{-1}; Anal. Calculated for $C_{20}H_{26}O_4$: C, 72.70, H, 7.93.

Compounds 34 and 35

A 2 : 1 mixture of 34 : 35 was isolated in a 64% yield from diethyl o-iodobenzyl malonate and isoprene when the reaction was run in the presence of sodium carbonate for 3 days at 60°C. Compound 31: ^1H NMR δ 1.14 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 1.23 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 1.71 (s, 3H, C=CCH_3), 2.96 (d of d, J = 3 and 16.2 Hz, 1H, $ArC\underline{H}_2CH$), 3.37 (m, 4H, $ArCH_2CH$ and $ArCH_2$), 4.1 (m, 4H, CO_2CH_2), 4.74 (s, 1H, C=CH), 4.82 (s, 1H, C=CH), 7.06 (m, 4H, ArH); ^{13}C NMR δ 14.00, 22.31, 32.18, 34.52, 39.17, 44.28, 57.41, 61.27, 61.40, 112.93, 114.52, 125.64, 126.39, 128.30, 128.62, 133.12, 145.49, 170.39, 170.86; IR 3082, 2982, 1730 (C=O), 1454, 1256, 1180, 1069, 746 cm^{-1}. Compound 32: ^1H NMR δ 1.16 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 1.20 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 1.33 (s, 3H, C=$CCCH_3$), 2.98 (d, J = 16.2 Hz, 1H, $ArCH_2CC$=C), 3.16 (d, J = 16.2 Hz, 1H, $ArCH_2CC$=C), 3.33 (d, J = 15.9 Hz, 1H, $ArCH_2C(CO_2Et)_2$), 3.43 (d, J = 15.9 Hz, 1H, $ArCH_2C(CO_2Et)_2$), 4.15 (m, 4H, CO_2CH_2), 5.00 (d, J = 11.1 Hz, 1H, C=CH_2), 5.01 (d, J = 17.1 Hz, 1H, C=CH_2), 6.27 (d of d, J = 11.1 and 17.1 Hz, 1H, $C\underline{H}$=CH_2), 7.08 (m, 4H, ArH); ^{13}C NMR δ 13.84, 22.76, 33.25, 36.01, 40.57, 44.73, 59.39, 60.97,

61.04, 112.93, 125.63, 126.11, 126.51, 128.53, 128.62, 134.58, 143.32, 170.12, 170.39; IR 3064, 2940, 1732 (C=O), 1452, 1227, 1180, 1055, 746 cm^{-1}; Anal. Calculated for $C_{19}H_{24}O_4$: C, 72.13; H, 7.65.

Compound 36

Compound 36 was isolated in 66% yield from diethyl o-iodobenzyl malonate and isoprene when the reaction was run in the presence of sodium acetate for 3 days at 60°C. ^1H NMR δ 1.21 (t, J = 7.2 Hz, 6H, CO_2CCH_3), 1.72 (s, 3H, $C=CCH_3$), 3.33 (d of d, J = 0.96 and 10.5 Hz, 2H, $ArCH_2$), 4.16 (m, 4H, CO_2CH_2), 5.10 (d, J = 1.5 Hz, 1H, $C=CH_2$), 5.15 (d, J = 1.5 Hz, 1H, $C=CH_2$), 6.79 (s, 1H, ArCH=C), 7.1-7.3 (m, 4H, ArH); ^{13}C NMR δ 13.83, 22.49, 42.12, 57.66, 61.19, 115.95, 121.30, 125.84, 126.21, 127.01, 127.15, 127.95, 130.28, 134.90, 136.85, 169.32; IR 3021, 2929, 1735 (C=O), 1476, 1236, 1177, 743 cm^{-1}; HRMS calculated for $C_{19}H_{22}O_4$ 314.15174, found 314.1516.

Compound 37

Compound 37 was isolated in 84% yield from diethyl o-iodobenzyl malonate and 2,3-dimethyl-1,3-butadiene when the reaction was run in the presence of 5% triphenylphosphine and sodium carbonate for 17 d at 60°C. ^1H NMR δ 1.21 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 1.23 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 1.49 (s, 3H, $ArCH_2CC\underline{H}_3$), 1.75 (s, 3H, $C=CCH_3$), 3.30 (d, J = 18 Hz, 1H,

$ArCH_2$), 3.37 (d, J = 18 Hz, 1H, $ArCH_2$), 3.57 (s, 2H, $ArCH_2$), 4.75 (d, J = 1.8 Hz, 1H, C=CH), 4.88 (d, J = 1.8 Hz, 1H, C=CH), 7.0-7.3 (m, 4H, ArH), ^{13}C NMR δ 13.93, 13.97, 21.59, 23.66, 35.40, 40.99, 43.88, 59.15, 61.04, 61.25, 113.56, 125.47, 126.22, 128.10, 128.28, 132.97, 135.82, 149.64, 170.57, 171.06; IR 2980, 2932, 1730 (C=O), 1454, 1366, 1259, 1242, 1177, 1138, 1047, 1036, 744 cm^{-1}; Anal. Calculated for $C_{20}H_{26}O_4$: C, 72.70; H, 7.93.

Compound 38

Compound 38 was isolated in 31% yield from diethyl o-iodobenzyl malonate and 1-acetoxy-1,3-butadiene when the reaction was run in the presence of sodium carbonate for 1 d at 60°C. ^1H NMR δ 1.20 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 1.24 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 2.19 (d of d, J = 0.9 and 9.6 Hz, 2H, $C\underline{H}_2CHO$), 2.64 (d, d of t, J = 3, 6.9 and 9.6 Hz, 1H, $ArCH_2C\underline{H}$), 2.84 (d of d, J = 3 and 17.7 Hz, 1H, $ArC\underline{H}_2CH$), 3.16 (d of d, J = 6.9 & 17.7 Hz, 1H, $ArC\underline{H}_2CH$), 3.27 (d, J = 18 Hz, 1H, $ArCH_2C(CO_2Et)_2$), 3.37 (d, J = 18 Hz, 1H, $ArCH_2C(CO_2Et)_2$), 4.16 (q, J = 7.2 Hz, 2H, CO_2CH_2), 4.17 (q, J = 7.2 Hz, 2H, CO_2CH_2), 7.0-7.2 (m, 4H, ArH), 9.79 (d, J = 0.9 Hz, 1H, CHO); ^{13}C NMR δ 13.40, 13.89, 26.01, 33.19, 33.74, 47.89, 57.22, 61.30, 61.69, 124.80, 125.15, 125.89, 128.76, 132.89, 133.65, 168.89, 170.10, 199.79; IR 3001, 2915, 2750 (C(O)H), 1740 (C=O), 1728 (C=O), 1470, 1367, 1250, 1225, 1015 cm^{-1}; HRMS calculated for $C_{18}H_{22}O_5$ 318.14676, found 318.1458.

Compound 39

Compound 39 was isolated in 22% yield from diethyl o-iodobenzyl malonate and 1-acetoxy-1,3-butadiene when the reaction was run in the presence of 5% triphenylphosphine using sodium carbonate as the base for 3 days at 60°C: ^{1}H NMR δ 1.19 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 1.20 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 2.08 (s, 3H, $C(O)CH_3$), 2.87 (d of d, J = 6.3 and 16.8 Hz, 1H, $ArCH_2$), 3.17 (d of d, J = 3.3 and 16.8 Hz, 1H, $ArCH_2$), 3.36 (br s, 2H, $ArCH_2$), 3.45 (d of d, J = 3.3 and 6.3 Hz, 1H, -CCH), 4.15 (m, 4H, CO_2CH_2), 5.61 (d, J = 12.3 Hz, 1H, C-CH), 5.65 (d, J = 12.3 Hz, 1H, C-CH), 7.100 (br s, 4H, ArH); IR 2980, 2940, 1760 (CH_3C-O), 1732 (C-O), 1452, 1180 (C(O)-O), 1055, 762 cm^{-1}; HRMS calculated for $C_{20}H_{24}O_5$ 344.16242, found 344.1632.

Compound 40

Compound 40 was isolated in 52% yield from diethyl o-iodobenzyl malonate and 1,3-cyclooctadiene when the reaction was run in the presence of 5% triphenylphosphite using sodium carbonate as the base for 2 days at 80°C. ^{1}H NMR δ 1.0-2.0 (m, 12H, aliphatic), 2.2-2.6 (m, 3H, allylic), 3.16 (d, J = 13.2 Hz, 1H, $ArCH_2$), 3.23 (d, J = 13.2 Hz, 1H, $ArCH_2$), 3.85 (m, 1H, ArCH), 4.14, (m, 4H, CO_2CH_2), 5.6-6.0 (m, 2H, C-CH), 7.04-7.32 (m, 4H, ArH); ^{13}C NMR δ 14.05, 14.09, 22.87, 23.11, 29.28, 32.22, 33.10, 53.03, 61.30, 61.35, 61.43, 61.50, 125.46, 126.46, 126.64, 126.76, 129.37,

131.32, 131.70, 134.66, 168.86, 169.05; IR 2982, 2932, 1751 (C=O), 1734 (C=O), 1447, 1364, 1298, 1267, 1225, 1177, 1096, 1034, 756, 675 cm^{-1}; Anal. Calculated for $C_{22}H_{28}O_4$: C, 74.13; H, 7.92.

Compound 41

Compound 41 was isolated as a 3 : 4 mixture of diastereomers in 73% yield from ethyl 2-cyano-3-(2'-iodophenyl)propanoate and 1,3-cyclohexadiene when the reaction was run in the presence of 5% triphenylphosphine and sodium carbonate for 3 days at 80°C. ^1H NMR δ 1.26 (t, J = 6.6 Hz, 3H, CH_3), 1.73 (m, 1H, $ArCCH_2$), 2.1-2.5 (m, 3H, $ArCCH_2$ and $C{=}CCH_2$), 2.95 (m, 1H, C=CCH), 3.08 (d, J = 16.2 Hz, 1H, $ArCH_2$), 3.30 (d, J= 16.2 Hz, 1H, $ArCH_2$), 3.5 (m, 1H, ArCH), 4.00 and 4.12 ({2:3 ratio} q, J = 6.6 Hz, 2H, CO_2CH_2), 5.6-6.2 (m, 2H, C=CH), 7.1-7.6 (m, 4H, ArH); ^{13}C NMR δ 13.78, 13.86, 25.64, 29.61, 29.67, 37.21, 37.85, 40.05, 40.14, 46.07, 52.44, 62.99, 63.05, 63.15, 75.66, 76.79, 126.35, 126.79, 126.95, 128.16, 128.24, 128.48, 128.56, 129.46, 129.58, 129.64, 129.79, 129.95, 130.07, 130.12, 130.24, 130.81, 137.39, 140.11, 168.49, 168.63; IR 3030, 2928, 2868, 2250 (C≡N), 1736 (C=O), 1493, 1466, 1369, 1238, 1096, 760 cm^{-1}; Anal. Calculated for $C_{18}H_{19}NO_2$: C, 76.84%; H, 6.81%. Found: C, 76.55%; H 6.71%.

Compound 42

Compound 42 was isolated in 11% yield from ethyl 2-cyano-3-(2'-iodophenyl)propanoate and 1,3-cyclohexadiene when the reaction was run in the presence of sodium carbonate for 5 days at 80°C. ^{1}H NMR δ 2.63 (t, J = 6.9 Hz, 2H, $ArCH_2$), 2.99 (t, J = 6.9 Hz, 2H, CH_2CN), 6.9-7.4 (m, 4H, ArH).

Compound 43

Compound 43 was isolated as a 4 : 5 mixture of diastereomers in 96% yield from methyl 2-thiophenyl-3-(2'-iodophenyl)propanoate and 1,3-cyclohexadiene when the reaction was run in the presence of sodium acetate at 80°C for 4 days. ^{1}H NMR δ 2.1-2.5 (m, 4H, aliphatic), 3.1-3.3 (m, 3H, aliphatic), 3.54 and 3.57 ((4:5 ratio) s, 3H, CO_2CH_3), 3.7-4.1 (m, 1H, ArCH), 5.8-6.1 (m, 2H, C=CH), 7.0-7.5 (m, 9H, ArH); ^{13}C NMR δ 14.24, 23.14, 28.36, 31.25, 31.45, 34.83, 35.41, 35.52, 36.22, 51.69, 52.08, 52.21, 52.40, 60.39, 123.64, 123.79, 124.54, 124.74, 125.13, 125.28, 125.53, 126.30, 126.95, 127.34, 127.98, 128.21, 128.41, 128.77, 128.95, 130.30, 133.02, 133.14, 133.29, 134.48, 137.81, 143.56, 171.97, 172.14; IR 3034, 2949, 2870, 1738 (C=O), 1481, 1439, 1258, 1225, 1190, 1153, 1024, 750, 690 cm^{-1}; Anal. Calculated for $C_{22}H_{22}O_2S$: C, 75.39%; H, 6.32%. Found: C, 75.43%; H, 6.38%.

Compound 44

Compound 44 was isolated in 95% yield from 2-(2'-iodophenyl)-1-methylsulfinyl-1-thiomethylethane and 1,3-cyclohexadiene when the reaction was run using 5% triphenylphosphine and sodium carbonate as the base for 1 day at 60°C. ^{1}H NMR δ 2.41 (s, 3H, SCH_3), 6.45 (d, J = 15.3 Hz, 1H, -C(SR)H), 6.71 (d, J = 15.3 Hz, 1H, -C(Ar)H), 6.85 (t, J = 7.8 Hz, 1H, ArH), 7.25 (t, J = 7.5 Hz, 1H, ArH), 7.36 (d, J = 7.8 Hz, 1H, ArH), 7.79 (d, J = 8.1 Hz, 1H, ArH).

Compound 45

Compound 45 was isolated in 43% yield from 2-(2'-iodophenyl)-1-methylsulfinyl-1-thiomethylethane and 1,3-cyclohexadiene when the reaction was run using 5% triphenylphosphine and sodium carbonate as the base for 1 day at 80°C. ^{1}H NMR δ 2.42 (s, 3H, SCH_3), 6.67 (d, J = 15.3 Hz, 1H -C(SR)H), 6.72 (d, J = 15.3 Hz, 1H, -C(Ar)H), 7.1-7.4 (m, 5H, ArH).

Compound 46, acetophenone

Acetophenone was isolated in 90% yield from ethyl 3-(iodophenyl)-3-oxopropanoate and 1,3-cyclohexadiene when the reaction was run with sodium carbonate for 3 days at 80°C.

Compound 47

Compound 47 was isolated in 24% yield from ethyl 3-(iodophenyl)-3-oxopropanoate and 1,3-cyclohexadiene when the reaction was run with 5% triphenylphosphine and sodium carbonate for 6 days at 60°C. ^{1}H NMR δ 1.26 (t, J = 7.2 Hz, 3H, CH_3), 4.12 (d of q, J = 9.8 and 7.2 Hz, 1H, CH_2), 2.24 (d of q, J = 9.8 and 7.2 Hz, 1H, CH_2), 7.20 (d of t, J = 1.2 and 6.9 Hz, 1H, ArH), 7.3 (m, 3H); ^{13}C NMR δ 14.31, 42.24, 69.00, 83.41, 101.23, 120.01, 123.45, 123.87, 124.79, 126.83, 171.43; IR 2982, 2930, 2205 (C≡C), 1738 (C=O), 1432, 1390, 1225, 1090, 860 cm^{-1}.

Compound 48, 9-phenanthrol

9-Phenanthrol was isolated in 52% yield from t-butyl 3-(iodophenyl)-3-oxopropanoate and 1,3-cyclohexadiene when the reaction was run with 5% triphenylphosphine and sodium carbonate for 1 days at 80°C.

Compound 49

Compound 49 was isolated in 56% yield from o-iodoacetophenone and 1,3-cyclohexadiene when the reaction was run with 5% triphenylphosphine and potassium acetate for 1 day at 80°C. ^{1}H NMR δ 2.1-2.9 (m, 8H, aliphatic), 5.97 (t of d, J = 3 and 10.2 Hz, 1H, vinyl), 6.05 (d of d, J = 1.8 and 10.2 Hz, 1H, vinyl), 7.29 (d of t, J = 0.9 and 7.2 Hz, 1H, ArH), 7.45 (m, 2H, ArH), 7.61 (d of d, J = 1.2 and 7.5 Hz, 1H, ArH); ^{13}C

NMR δ 22.05, 23.01, 35.57, 45.32, 52.13, 122.15, 124.56, 124.79, 125.25, 126.32, 127.17, 127.65, 144.32, 197.63; IR 2982, 2920, 1680 (C=O), 1423, 1227, 1197, 1025; HRMS calculated for $C_{14}H_{14}O$ 198.10648, found 198.1068.

Compound 50

Compound 50 was isolated in 73% yield from 2-(2'-iodophenyl)-1-nitroethane and 1,3-cyclohexadiene when the reaction was run using lithium carbonate as the base for 7 days at 80°C. ^1H NMR δ 2.13 (m, 1H, aliphatic), 2.44 (d of d of d, J = 1.8, 7.2 and 18 Hz, 1H, aliphatic), 2.62 (m, 1H, aliphatic), 2.74 (d of d, J = 4.5 and 18 Hz, 1H, aliphatic), 3.16 (d of d, J = 9.6 and 17.4 Hz, 1H, $ArCH_2$), 3.40 (m, 1H, $ArCH_2$), 3.49 (d of t, J = 16.5 and 8.7 Hz, 1H, ArCH), 4.59 (d of t, J = 15.9 and 7.5 Hz, 1H, $C=CCHCNO_2$), 4.760 (d of d of d, J = 6.9, 8.7 and 10.5 Hz, 1H, $CHNO_2$), 5.55 (t of d, J = 1.8 and 9.9 Hz, 1H, C=CH), 5.90 (m, 1H, C=CH), 7.2-7.4 (m, 4H, ArH); ^{13}C NMR δ 22.68, 28.94, 30.14, 40.24, 45.25, 69.54, 125.75, 125.82, 126.23, 127.72, 128.77, 130.52, 132.89, 125.01; IR 3026, 2924, 2853, 1549, 1466, 1373, 1358, 1279, 1261, 750 cm^{-1}; Anal. Calculated for $C_{14}H_{15}NO_2$: C, 73.33; H, 6.60; Found: C, 73.43, H, 6.38.

Compound 51

Compound 51 was isolated in 87% yield from the reaction of dimethyl 2-iodophenylmalonate and 1,3-cyclohexadiene when

the reaction was run in the presence of sodium carbonate for 1 day at 60°C. ^{1}H NMR δ 1.8-2.0 (m, 5H, ArCHCH$_2$CH$_2$), 3.53 (q, J = 6.9 Hz, 1H, C-CCH), 3.73 (s, 3H, CO$_2$CH$_3$), 3.75 (s, 3H, CO$_2$CH$_3$), 5.5-5.6 (m, 1H, C-C<u>H</u>CH$_2$), 5.8-5.9 (m, 1H, C-C<u>H</u>CH), 7.2-7.4 (m, 3H, ArH), 7.58 (d, J = 7.8 Hz, 1H, ArH); ^{13}C NMR δ 22.13, 24.51, 41.65, 45.72, 52.28, 52.90, 68.97, 123.49, 124.69, 126.96, 127.40, 128.64, 130.51, 138.34, 146.81, 170.21, 170.44; IR 3051, 2951, 2926, 1736 (C=O), 1477, 1458, 1244, 1229, 1177, 1057, 1032, 743, 673, 617 cm^{-1}; Anal. Calculated for $C_{17}H_{18}O_4$: C, 71.31%; H, 6.34%. Found: C, 71.18%; H, 6.40%.

<u>Compound 52</u>

Compound 52 was isolated in 86% yield from the reaction of diethyl <u>o</u>-iodophenyl malonate and 1,3-cyclooctadiene when the reaction was run in the presence of 5% triphenylphosphine and sodium carbonate at 60°C for 10 days. ^{1}H NMR δ 1.20 (t, J = 7.2 Hz, 3H, CH$_3$), 1.26 (m, 1H, aliphatic), 1.31 (t, J = 7.2 Hz, 3H, CH$_3$), 1.63 (m, 3H, aliphatic), 1.87 (m, 1H, aliphatic), 2.16 (m, 1H, aliphatic), 2.44 (d, d of d, J = 3.3, 10.5 and 13.8 Hz, 2H, C-CCH$_2$), 3.16 (d of t, J = 3.3 and 11.1 Hz, 1H, ArCH), 3.51 (d, d of d, J = 1.2, 7.8 and 11.1 Hz, 1H, C-CCH), 4.15 (q, J = 7.2 Hz, 2H, CO$_2$CH$_2$), 4.29 (q, J = 7.2 Hz, 2 H, CO$_2$CH$_2$), 5.68 (d, d, d of d, J = 1.2, 10.5, 10.5 and 10.5 Hz, 1H, C-C<u>H</u>CH$_2$), 6.03 (d of d, J = 7.8 and 10.5 Hz, 1H, C-C<u>H</u>CH), 7.15-7.35 (m, 4H, ArH); ^{13}C NMR δ

14.15, 23.47, 24.57, 28.38, 30.52, 49.33, 53.80, 61.31, 61.46, 64. 68, 67.02, 123.16, 125.63, 126.76, 128.44, 129.61, 129.68, 139.50, 147.46, 169.59, 170.21; IR 2980, 2930, 1730 (C=O), 1475, 1462, 1298, 1254, 1221, 1123, 1096, 1055, 752 cm^{-1}; Anal. Calculated for $C_{21}H_{26}O_4$: C, 73.66; H, 7.65. Found: C, 73.27, H, 7.60.

Compound 53

Compound 53 was obtained in 73% yield from the reaction of diethyl o-iodophenyl malonate and 1,3-octadiene when the reaction was run in the presence of sodium carbonate for 1 day at 60°C. ^1H NMR δ 0.86 (t, J = 6.9 Hz, CH_3), 1.28 (m, 4H, aliphatic), 1.96 (m, 2H, C=CCH), 2.86 (d of d, J = 5.4 and 15.6 Hz, 1H, $ArCH_2$), 3.27 (d of d, J = 7.5 and 15.6 Hz, 1H, $ArCH_2$), 3.76 (d, d, d of d, J = 1.2, 5.4, 7.5 and 8.7 Hz, 1H, C=CCH), 5.38 (d of d, 8.7 and 15.0 Hz, 1H, C=C<u>H</u>CH), 5.64 (d, d of t, J = 1.2, 15.0 and 7.5 Hz, 1H, C=C<u>H</u>CH_2), 7.24 (m, 3H, ArH), 7.55 (m, 1H, ArH); ^{13}C NMR δ 13.94, 22.19, 31.61, 32.19, 37.46, 49.89, 52.15, 52.71, 69.66, 124.69, 126.70, 126.80, 128.27, 128.60, 133.58, 138.53, 143.60, 169.62, 170.11; IR 3028, 2955, 2854, 1736 (C=O), 1477, 1458, 1265, 1232, 1161, 1103, 1055, 1015, 972 cm^{-1}; Anal. Calculated for $C_{19}H_{26}O_4$: C, 72.13; H, 7.65. Found: C, 69.47; H, 7.18.

Compound 54

Compound 54 was obtained in 82% yield from diethyl o-iodophenylmalonate and isoprene in the presence of 5% triphenylphosphine using sodium carbonate as the base when the reaction was run for 8 days at 60°C. ^{1}H NMR δ 1.22 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 1.23 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 1.55 (br s, 3H, $-CCH_3$), 2.94 (d of d, J = 4.5 and 15.9 Hz, 1H, $ArCH_2$), 3.33 (d of d, J = 7.5 and 15.9 Hz, 1H, $ArCH_2$), 3.96 (d of d, J = 4.5 and 7.5 Hz, 1H, -CCH), 4.1-4.25 (m, 4H, CO_2CH_2), 4.78 (t, J = 1.5 Hz, 1H, C=CH), 4.82 (br, 1H, C=CH), 7.15-7.25 (m, 3H, ArH), 7.54 (d of d, J = 2.1 and 7.5 Hz, 1H, ArH); ^{13}C NMR δ 14.31, 14.34, 21.30, 36.58, 52.67, 61.11, 61.65, 69.65, 113.74, 124.23, 126.51, 126.62, 128.56, 139.34, 143.80, 145.13, 169.15, 169.72; IR 2982, 2937, 1732, 1477, 1460, 1298, 1263, 1232, 1161, 1103, 1045 cm^{-1}; Anal. Calculated for $C_{18}H_{22}O_4$: C, 71.51; H, 7.33. Found: C, 71.35; H, 7.25.

Compound 55

Compound 55 was isolated as a 1.1 : 1 mixture of diastereomers in 85% yield from ethyl 2-iodophenylacetate and 1,3-cyclohexadiene when the reaction was run using potassium acetate as the base for 2 day at 80°C. ^{1}H NMR δ 1.26 (two t (1.1 : 1 ratio), J = 7.5 Hz, 3H, CO_2CCH_3), 2.2-2.6 (m, 2H, aliphatic), 3.5-4.0 (m, 5H, aliphatic), 4.17 (two q (1.1 : 1 ratio), J = 7.5 Hz, 2H, CO_2CH_2), 5.7-6.1 (m, 2H, C=CH), 7.1-

7.4 (m, 4H, ArH); ^{13}C NMR δ 13.25, 14.01, 19.18, 22.13, 24.51, 24.78, 41.65, 42.00, 45.07, 46.11, 52.28, 52.90, 67.13, 68.97, 123.49, 124.69, 126.96, 127.40, 128.64, 130.51, 138.34, 146.81, 170.21, 170.44; IR 3051, 2951, 2926, 1736 (C=O), 1244, 1229, 1177, 1057, 1032, 743, 673, 617 cm^{-1}; Anal. Calculated for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.56; H, 7.56.

Compound 56

Compound 56 was isolated in 51% yield from the reaction of ethyl 2-ethoxycarbonyl-4-(2'-iodophenyl)butanoate and 1,3-cyclohexadiene when the reaction was run in the presence of 5% triphenylphosphine and sodium carbonate for 1 day at 100°C. ^1H NMR δ 1.25 (t, J = 7.2 Hz, 6H, CH_3), 2.0-2.8 (m, 6H, aliphatic), 3.40 (t, J = 7.5 Hz, 1H, $CH(CO_2Et)_2$), 3.89 (m, 1H, ArCHC=C); 4.23 (q, J = 7.2 Hz, 4H, CO_2CH_2), 5.7-6.1 (m, 4H, C=CH); 7.1-7.5 (m, 4H); ^{13}C NMR δ 14.11, 19.54, 22.43, 34.21, 45.23, 56.43, 61.10, 123.01, 123.56, 123.78, 124.67, 125.98, 127.10, 127.65, 128.56, 129.03, 134.53, 171.01; IR 3001, 2926, 1728 (C=O), 1252, 1172, 1057, 1032, 743 cm^{-1}; HRMS calculated for $C_{21}H_{26}O_4$ 342.19718, found 342.1969.

Compound 57

Compound 57 was isolated in 47% yield from the reaction of ethyl 2-ethoxycarbonyl-4-(2'-iodophenyl)butanoate and 1,3-

cyclohexadiene when the reaction was run in the presence of 5% triphenylphosphine and sodium carbonate for 1 day at 100°C. ^{1}H NMR δ 1.28 (t, J = 7.2 Hz, 3H, CH_3), 1.91 (p, J = 7.2 Hz, 2H, aliphatic), 2.4 (m, 4H, aliphatic), 2689(ţ, J = 7.2 Hz, CH_2CO_2Et), 3.80 (m, 1H, ArCHC=C); 4.22 (q, J = 7.2 Hz, 2H, CO_2CH_2), 5.7-6.1 (m, 4H, C=CH); 7.1-7.5 (m, 4H); ^{13}C NMR δ 13.95, 19.46, 23.04, 34.22, 45.28, 56.33, 60.75, 122.56, 123.46, 123.85, 124.52, 125.42, 126.41, 127.48, 128.09, 129.23, 135.28, 169.31; IR 3021, 2932, 1735 (C=O), 1241, 1225, 1054, 743, 628 cm^{-1}; HRMS calculated for $C_{18}H_{22}O_2$ 270.16206, found 270.1628.

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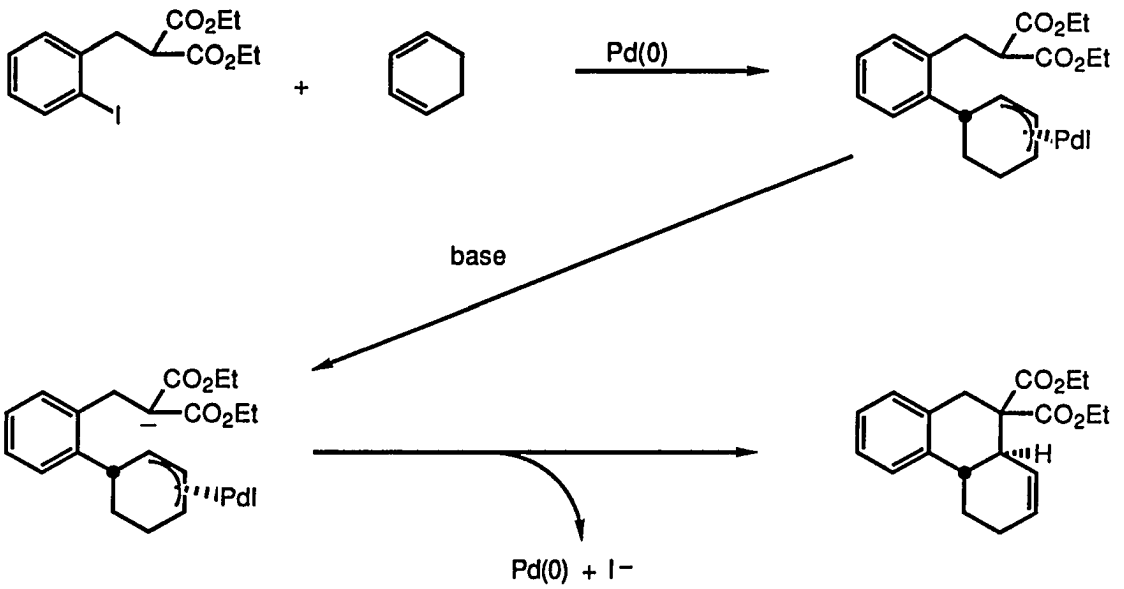
SECTION 3. ARYLANNULATION OF ALLENES AND OTHER NON-CONJUGATED DIENES, ALKYNES AND SIMPLE ALKENES

INTRODUCTION

The development of synthetic methods for the formation of fused carbocycles is a growing area in organic chemistry. Such methods are necessary for the synthesis of complex polycycles, many of which are biologically active. In the previous section, a study of the palladium-catalyzed arylannulation of conjugated dienes was discussed. We thought this procedure could be extended to the use of other unsaturated compounds.

The arylannulation process discussed in section two is thought to proceed through a π-allylpalladium intermediate which is trapped by an internal nucleophile (Scheme I).

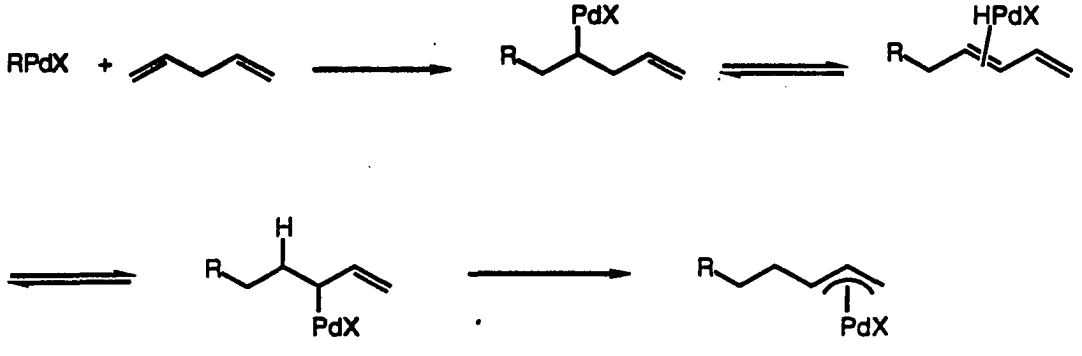
Scheme I



Palladium-mediated additions to conjugated dienes are not the only route to π-allylpalladium compounds. The exploration of other unsaturated compounds in arylannulation should lead to new and interesting chemistry.

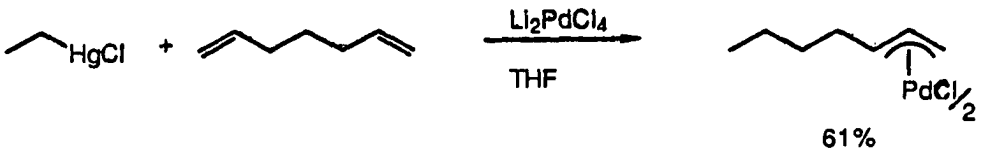
Recent reports have shown that π-allylpalladium compounds can be formed from non-conjugated dienes.[1-3] The formation of a stable π-allylpalladium complex from palladium-mediated addition of aryl and vinylic groups to non-conjugated dienes is thought to result from remote palladium migration (Scheme II). Remarkably, palladium can

Scheme II

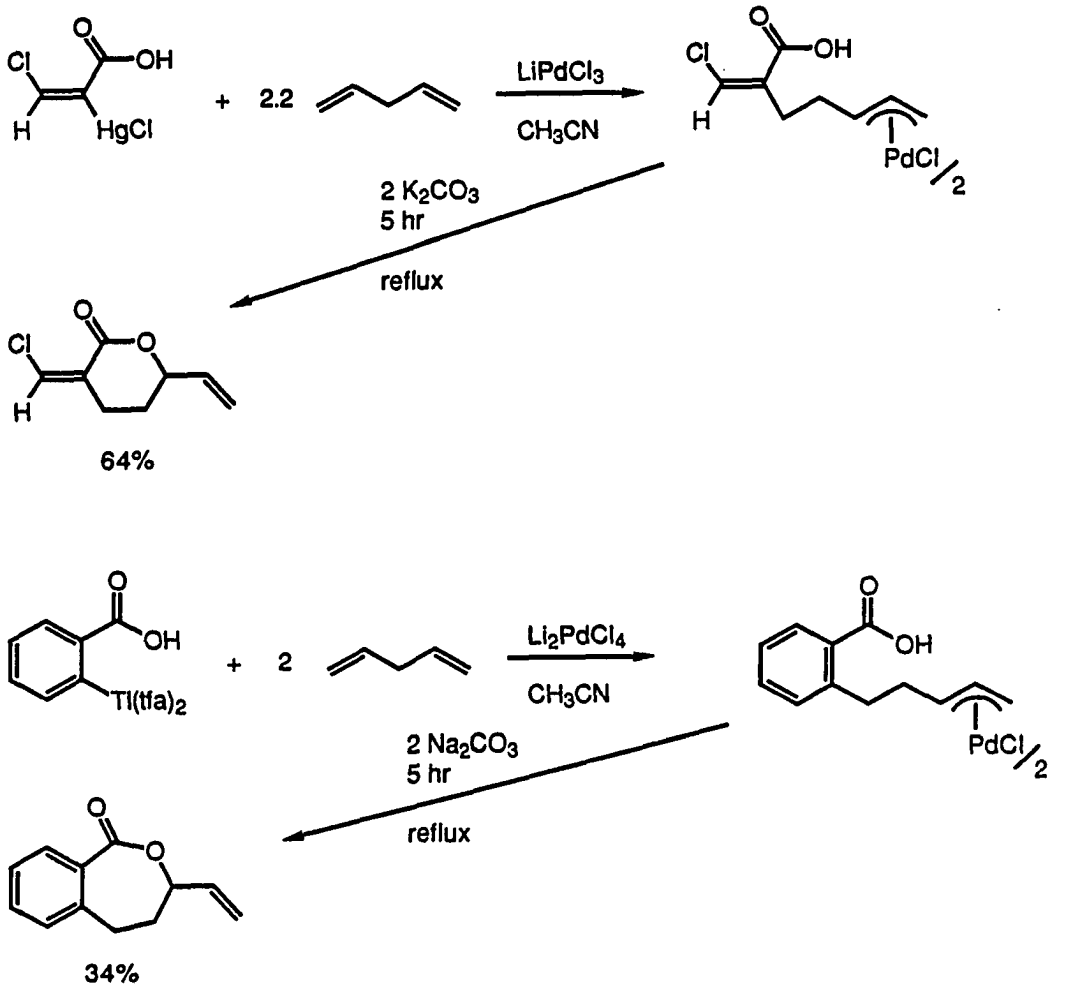


migrate down rather long carbon chains. Larock and Takagi have added organomercurials to 1,4-, 1,5-, 1,6- and 1,7-dienes in the presence of palladium(II) salts to form π-allylpalladium compounds (Scheme III).[2,3] Larock and co-workers have also used non-conjugated dienes in various palladium-mediated heteroannulations that proceed through π-allylpalladium intermediates (Scheme IV).[4,5]

Scheme III



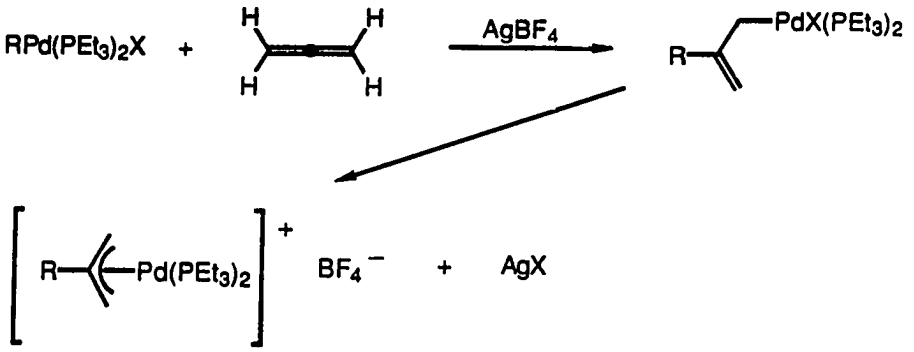
Scheme IV



Allenes have also been used to form π-allylpalladium compounds.[6-10] Stevens and Shier reported the addition of a

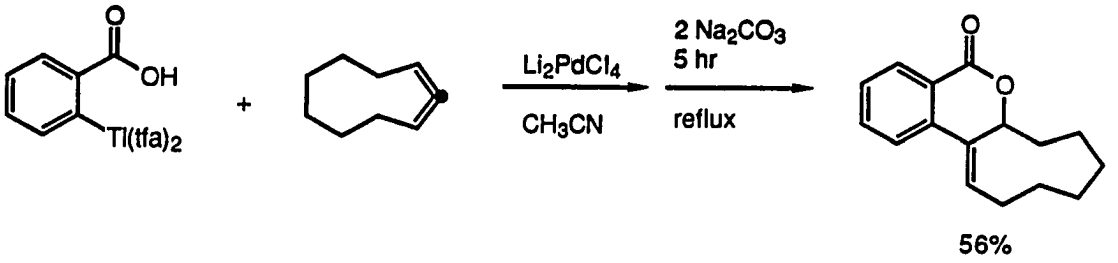
variety of organopalladium compounds to 1,2-propadiene.[10] An assortment of π-allylpalladium compounds were formed from this reaction. The reaction proceeds via addition of the organic group to the central carbon of the allene with the palladium bonding to the terminal end (Scheme V). Larock and

Scheme V



associates have used allenes in the palladium-mediated formation of heterocycles (Scheme VI).[5] Ahmar et al.

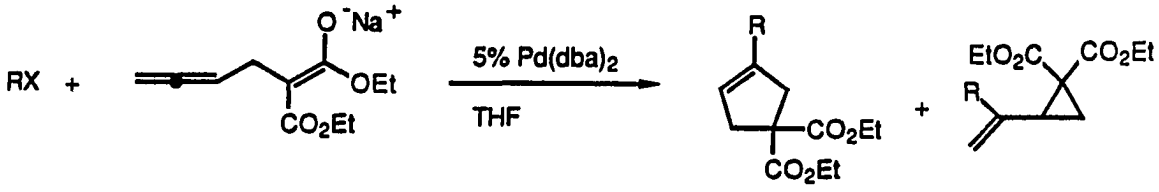
Scheme VI



reported that palladium-catalyzed addition of vinylic or aryl halides to β-allenyl malonate anions furnishes cyclopentenes and cyclopropenes (Scheme VII).[11]

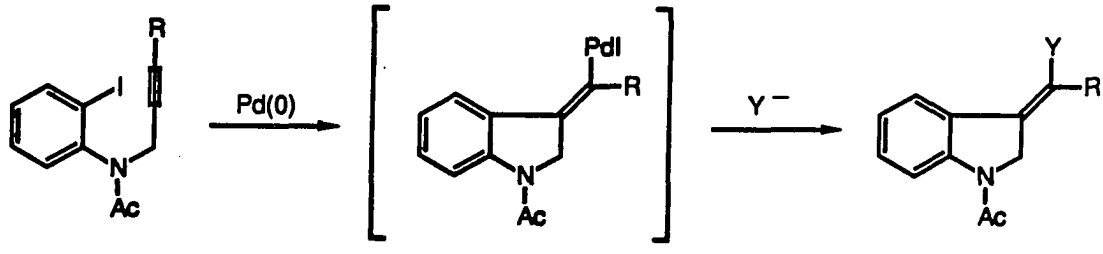
Another possible reactant for arylannulation is an alkyne. Organopalladium compounds are known to undergo cis-

Scheme VII



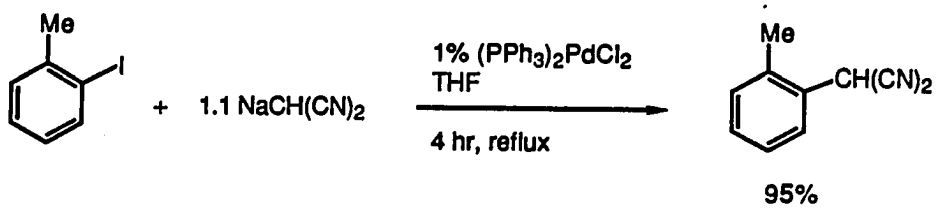
addition to alkynes to form σ-vinylpalladium compounds.[12] Burns and co-workers have recently examined palladium-catalyzed intramolecular coupling of aryl iodides to alkynes.[13-16] The proposed σ-vinylpalladium intermediate was then trapped in situ with hydride sources,[13,14] organotin reagents,[15] organozinc reagents or organoboron reagents[16] (Scheme VIII).

Scheme VIII

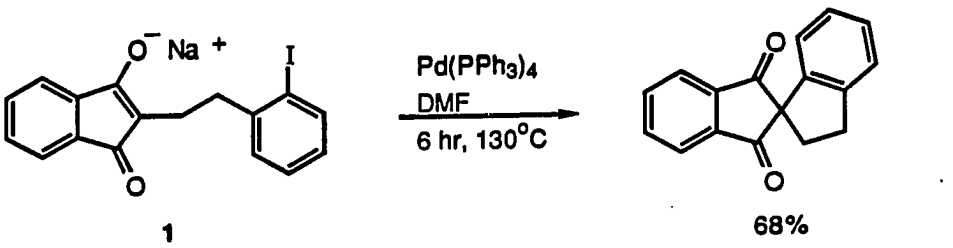


While nothing has been reported in the literature about the trapping of σ-vinylpalladium compounds with stabilized carbanions, the analogous reaction of σ-arylpalladium compounds has been studied.[17,18] Uno and associates examined the intermolecular coupling of aryl iodides with sodiomalononitrile (Scheme IX).[17] Ciufolini and Browne were able to use a similar procedure in the intramolecular cyclization of aryl iodide 1 (Scheme X).[18]

Scheme IX

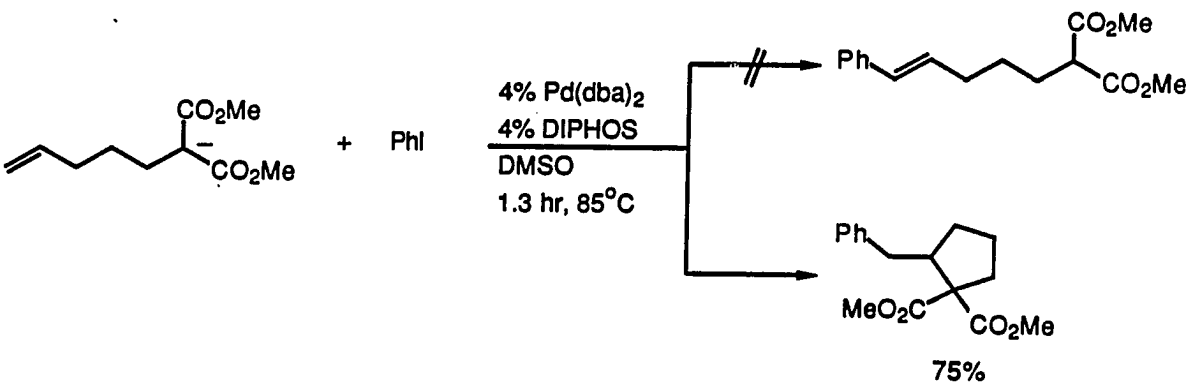


Scheme X



Recently, Fournet et al. reported the intramolecular trapping of a σ-alkylpalladium intermediate (Scheme XI).[19,20]

Scheme XI



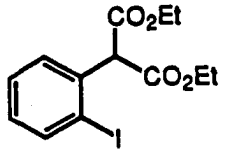
This report suggested that even simple alkenes may be useful reagents in palladium-catalyzed arylannulation.

The work in this section involves an extension of the palladium-catalyzed arylannulation discussed in section two. The use of non-conjugated dienes, allenes, alkynes and simple

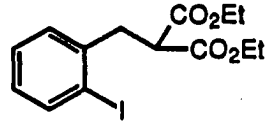
alkenes in the arylannulation process is explored. Prior to initiating this study, there were no reports of a palladium-catalyzed annulation involving an aryl iodide and a non-conjugated diene, an allene, an alkyne or a simple alkene. Our research involves the formation of carbocycles under mild conditions using palladium as the catalyst.

RESULTS AND DISCUSSION

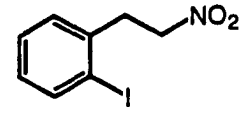
The following aryl iodides 2-4 were considered for the



2



3

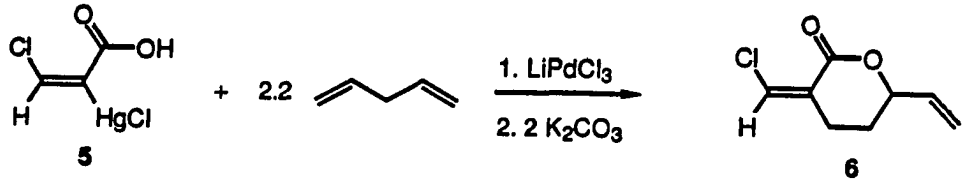


4

carboannulation study. The preparations of 2-4 were discussed in Section two of this dissertation.

The results discussed in the previous section indicate that certain aryl iodides undergo reaction with 1,3-dienes to form polycycles. The proposed mechanism for arylannulation proceeds through a π-allylpalladium compound. Other members of the Larock research group have used non-conjugated dienes in palladium-mediated heteroannulations proceeding through π-allylpalladium intermediates.[4,5] In particular, vinylic mercurial 5 and 1,4-pentadiene underwent reaction to yield lactone 6 (Scheme XII).

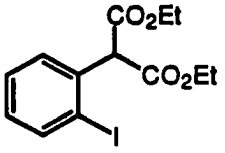
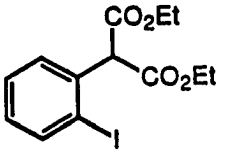
Scheme XII



5 6

Arylannulation of non-conjugated dienes by compounds 2 and 3 was examined. The results of this study are summarized in Table I. Having gained an understanding of what factors

Table I. Arylannulation of Non-conjugated Dienes[a]

Entry	Arene	Diene	Base[b]
1	 **2**		Na_2CO_3
2	 **2**		NaOAc

[a]Actual amounts of reagents used were as follows: 0.25 mmole arene, 1.25 mmole diene, 0.25 mmole (n-Bu)$_4$NCl, 0.0125 mmole palladium acetate, 1 ml DMF, 1.25 mmole base.

[b]In entries where more than one base is listed, results of separate trials using each base gave nearly identical results (± 5% in the yield).

[c]Triphenylphosphine (0.0125 mmole) was occasionally used as part of the catalyst system.

[d]Numbers given are isolated yields of purified products obtained from flash column chromatography.

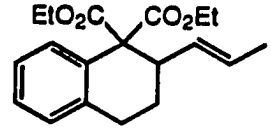
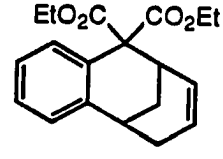
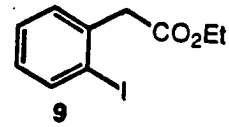
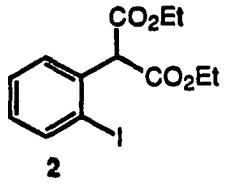
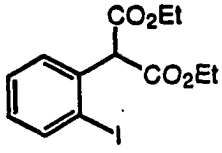
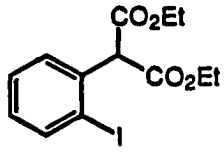
Reaction Conditions[c]	Product(s)	%Yield[d]
5d, 60°C	 7	85
5d, 60°C	 8	64
	 9	12

Table I. (continued)

Entry	Arene	Diene	Base[b]
3[e]	 2		Na_2CO_3
4[f]	 2		KOAc
5[g]	 2		Na_2CO_3

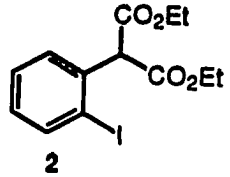
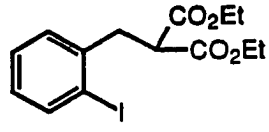
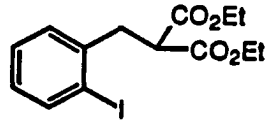
[e]The starting aryl iodide was recovered from the reaction mixture in 83% yield.

[f]Numerous unidentified products were isolated from the reaction mixture.

[g]The starting aryl iodide was recovered from the reaction mixture in 77% yield.

Reaction Conditions[c]	Product(s)	%Yield[d]
5d, 60°C	-	-
5d, 60°C	-	-
5d, 80°C	-	-

Table I. (continued)

Entry	Arene	Diene	Base[b]
6[f,h]	 2		Na_2CO_3
7[i]	 3		Na_2CO_3 or NaOAc
8[f,j]	 3		KOAc

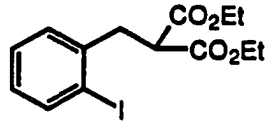
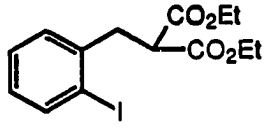
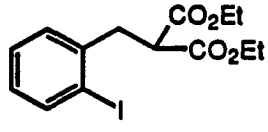
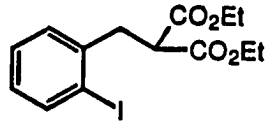
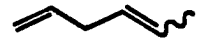
[h]The starting aryl iodide was recovered from the reaction mixture in 36% yield.

[i]The starting aryl iodide was recovered from the reaction mixture in 86% yield.

[j]The starting aryl iodide was recovered from the reaction mixture in 47% yield.

Reaction Conditions[c]	Product(s)	%Yield[d]
5d, 100°C	-	-
5d, 60°C	-	-
2d, 60°C	-	-

Table I. (continued)

Entry	Arene	Diene	Base[b]
9[k,l]	 3		Na_2CO_3
10[f,m]	 3		Na_2CO_3
11[f]	 3		Na_2CO_3
12[f]	 3		Na_2CO_3

[k]Bis(dibenzylideneacetone)palladium was used in place of palladium acetate.

[l]The starting aryl iodide was recovered from the reaction mixture in 69% yield.

[m]The starting aryl iodide was recovered from the reaction mixture in 72% yield.

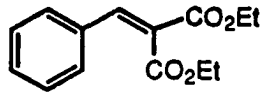
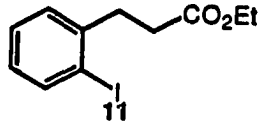
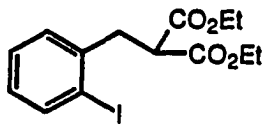
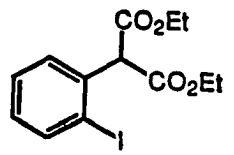
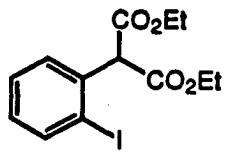
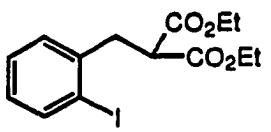
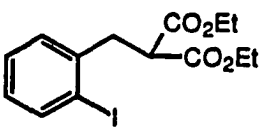
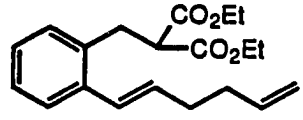
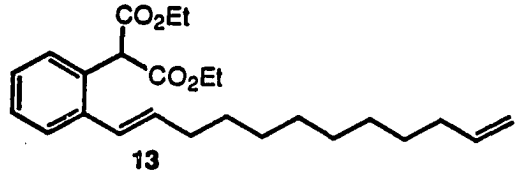
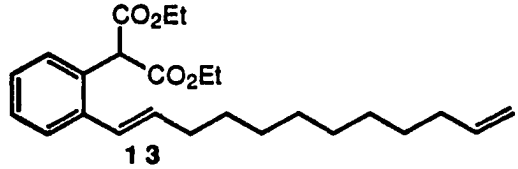
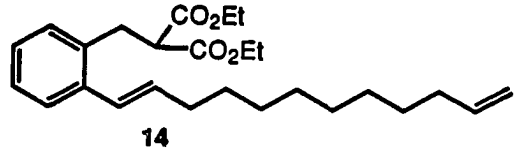
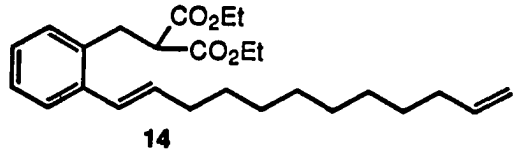
Reaction Conditions[c]	Product(s)	%Yield[d]
5d, 60°C	 **10**	24
5d, 100°C	-	-
PPh_3, 5d, 100°C	-	-
$P(OPh)_3$, 5d, 100°C	 **11**	39

Table I. (continued)

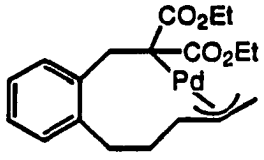
Entry	Arene	Diene	Base[b]
13[h]	 3		Na_2CO_3
14	 2		Na_2CO_3
15	 2		Na_2CO_3
16	 3		Na_2CO_3
17	 3		Na_2CO_3

Reaction Conditions[c]	Product(s)	%Yield[d]
5d, 60°C	 **12**	35
3d, 80°C	 **13**	86
PPh_3, 5d, 80°C	 **13**	89
3d, 80°C	 **14**	72
PPh_3, 5d, 80°C	 **14**	91

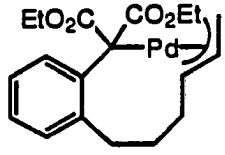
influence the arylannulation of conjugated dienes, we applied this knowledge to the arylannulation of non-conjugated dienes. In each case, carboannulation was initially attempted using three bases (sodium carbonate, sodium acetate and potassium acetate) under palladium(0) conditions (5 mole percent palladium acetate, 1 equivalent of tetra-n-butylammonium chloride, 5 equivalents of base, in DMF at 80°C). Occasionally a phosphorus ligand (triphenylphosphine or triphenylphosphite) was added in an attempt to improve the yield of the desired product.

The formation of six-membered rings via reaction of 2 and 1,4-dienes proceeds readily (Entries 1 and 2). Interestingly, the reaction of diethyl o-iodophenylmalonate and 1,4-cyclohexadiene proceeds to yield the bridged tricyclic compound 8. The synthesis of bridged polycyclic compounds has received considerable attention lately.[21]

Synthesis of larger than six-membered rings has failed uniformly under the reaction conditions employed (Entries 3 - 17). The formation of seven-membered rings was examined using the reaction of diethyl o-iodophenylmalonate and 1,5-hexadiene (Entries 3 - 6), as well as the reaction of diethyl o-iodobenzylmalonate and 1,4-hexadiene (Entries 7 - 12). Reactions at 60°C or 80°C using sodium carbonate as a base lead to high recovery of starting aryl iodide (Entries 3, 5, 7 and 9). A possible explanation for this is the stability of the intermediate π-allylpalladium complexes 15 and 16.

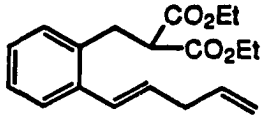


16

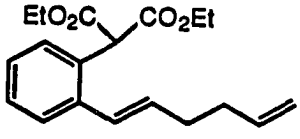


15

Formation of a stable palladium intermediate would explain why significant amounts of the aryl-addition products 17 and 18 are not formed. If the palladium is not being tied up in



18



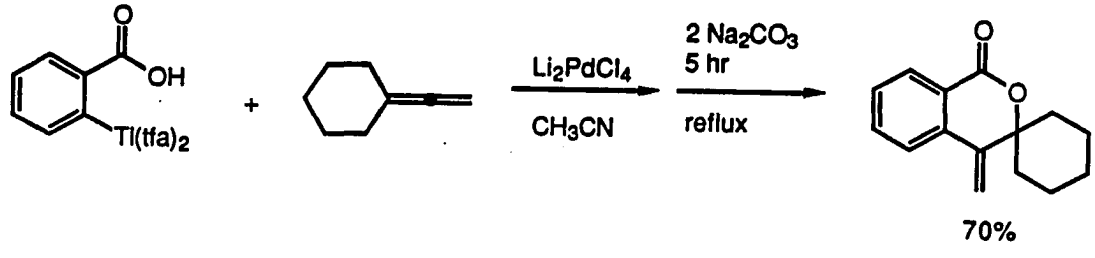
17

some manner, it should catalyze coupling between the aryl iodide and the diene. Complexation by the diene can be ruled out as a possibility because 1,4-hexadiene reacts with aryl iodide 2, and 1,5-hexadiene reacts with aryl iodide 3. When potassium acetate is used as the base, numerous products are formed (Entries 4 and 8). It has been previously noticed that when potassium acetate is used as the base, significant amounts of decomposed starting aryl iodides were isolated. The aryl iodides must decompose before they react with the diene, because none of the products isolated showed both aryl and vinylic protons in the ^{1}H NMR spectrum. Elevation of the reaction temperature to 100°C also results in the formation of numerous undesired products (Entries 6, 10 - 12). When diethyl o-iodobenzylmalonate is reacted with 1,5-hexadiene in

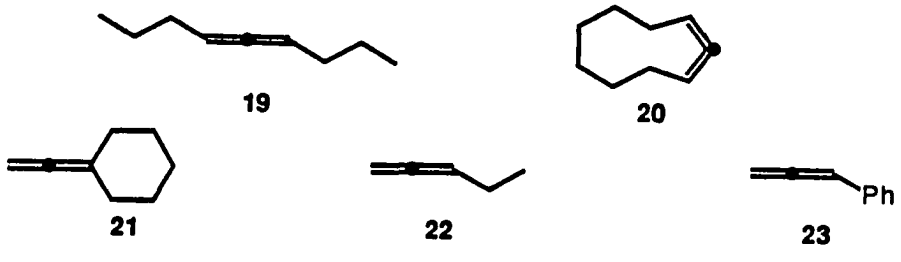
an attempt to form an eight-membered ring, a fair amount of the aryl-addition product 12 is isolated along with a significant amount of starting aryl iodide (Entry 13). Attempts at producing macrocycles failed under the palladium(0) conditions (Entries 14 - 17). The reactions of either 2 or 3 with 1,11-dodecadiene formed aryl-substitution products in high yields.

Allenes have also been used in palladium-mediated heteroannulations (Scheme XIII).[5] Aryl iodides 2 - 4 have

Scheme XIII

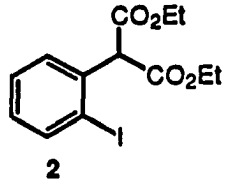
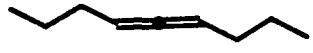
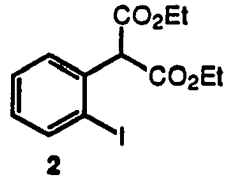
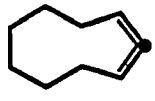
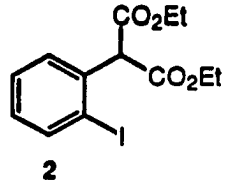
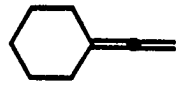
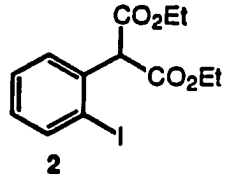


been reacted with various allenes. Five representative allenes, 19-23, were chosen for the arylannulation study.



The results of this study are summarized in Table II. Carboannulation was initially attempted under the conditions which generally gave the highest yields in previous trials (5 mole percent palladium acetate, 5 mole percent triphenylphosphine, 1 equivalent of tetra-n-butylammonium chloride, 5

Table II. Arylannulation of Allenes[a]

Entry	Arene	Allene	Base
1	 2		Na_2CO_3
2	 2		Na_2CO_3
3	 2		Na_2CO_3
4	 2		Na_2CO_3

[a]Actual amounts of reagents used were as follows: 0.25 mmole arene, 1.25 mmole allene, 0.25 mmole $(n\text{-Bu})_4NCl$, 0.0125 mmole $Pd(OAc)_2$, 0.0125 mmole PPh_3, 1 ml DMF, 1.25 mmole base.

[b]Numbers given are isolated yields of purified products.

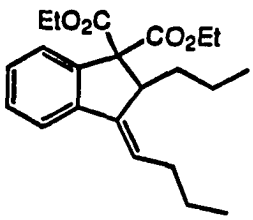
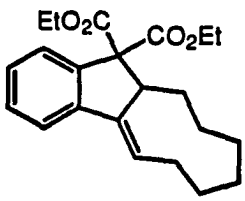
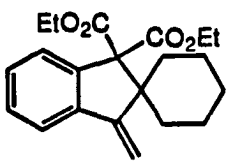
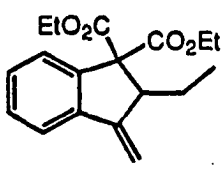
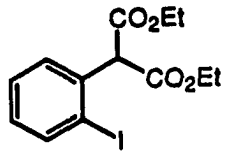
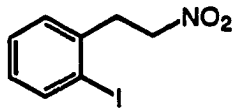
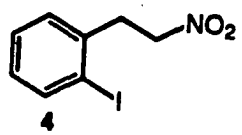
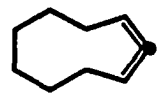
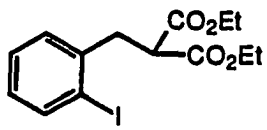
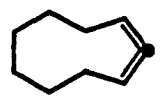
Reaction Conditions	Product(s)	%Yield[b]
2d, 80°C	 **24**	86
8d, 80°C	 **25**	85
2d, 80°C	 **26**	82
4d, 80°C	 **27**	88

Table II. (continued)

Entry	Arene	Allene	Base
5	 2		Na_2CO_3
6	 4		Li_2CO_3
7[c]	 4		Li_2CO_3
8[c]	 3		Na_2CO_3

[c]Numerous unidentified products were isolated.

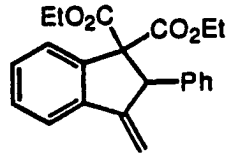
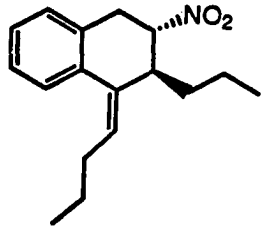
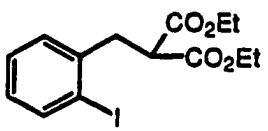
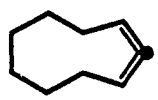
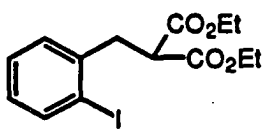
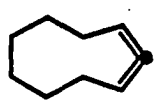
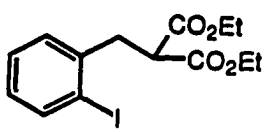
Reaction Conditions	Product(s)	%Yield[b]
5d, 80°C	 **28**	95
2d, 80°C	 **29**	86
2d, 80°C	-	-
6d, 80°C	-	-

Table II. (continued)

Entry	Arene	Allene	Base
9[d]	 3		Na_2CO_3
10[c,e]	 3		Na_2CO_3
11[c,f]	 3		Na_2CO_3

[d]Triphenylphosphine was omitted from the reaction mixture.

[e]Tri(o-tolyl)phosphine was used in place of triphenylphosphine.

[f]DMSO was used in place of DMF.

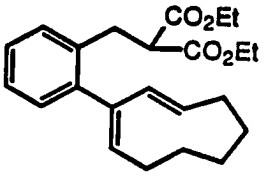
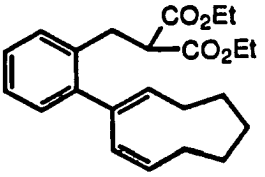
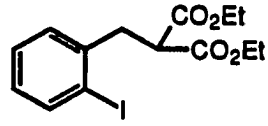
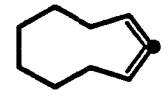
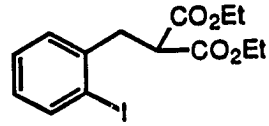
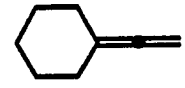
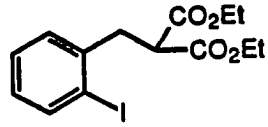
Reaction Conditions	Product(s)	%Yield[b]
3d, 80°C	 **30**	60 (3 : 2)
	 **31**	
4d, 80°C	-	-
5d, 80°C	-	-

Table II. (continued)

Entry	Arene	Allene	Base
12[c,g]	 3		Na_2CO_3
13	 3		Na_2CO_3
14[d]	 3		Na_2CO_3

[g]Triphenylphosphite was used in place of triphenylphosphine.

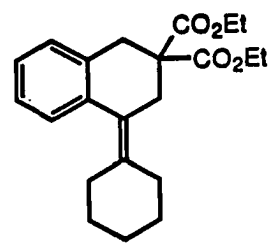
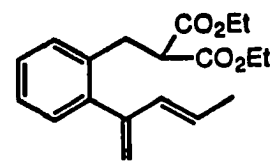
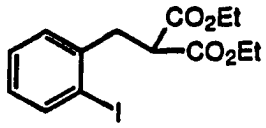
Reaction Conditions	Product(s)	%Yield[b]
2d, 80°C	-	-
2d, 80°C	 **32**	87
5d, 80°C	 **36**	87

Table II. (continued)

Entry	Arene	Allene	Base
15	 3		Na_2CO_3

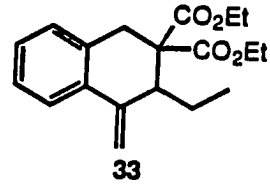
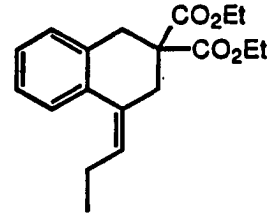
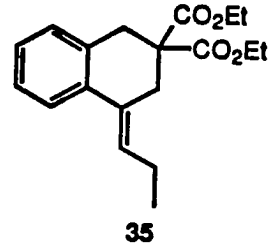
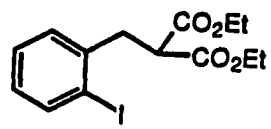
Reaction Conditions	Product(s)	%Yield[b]
4d, 80°C	 **33**	96 (10 : 4 : 1)
	 **34**	
	 **35**	

Table II. (continued)

Entry	Arene	Allene	Base
16	 3		Na_2CO_3

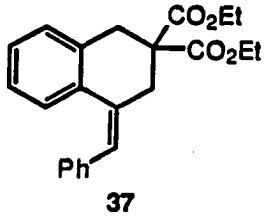
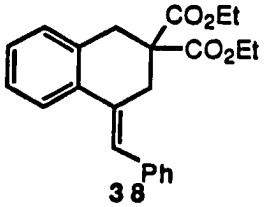
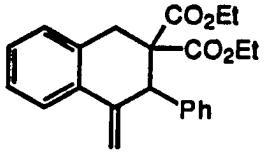
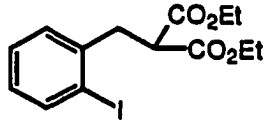
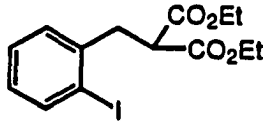
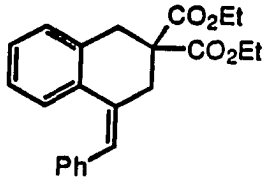
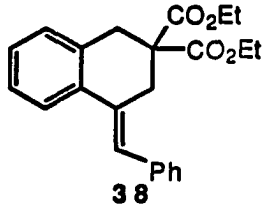
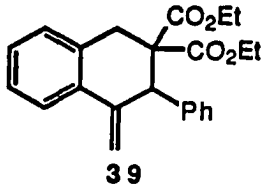
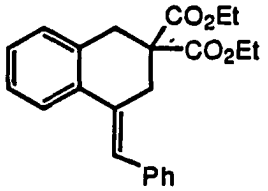
Reaction Conditions	Product(s)	%Yield[b]
6d, 80°C	 **37**	
	 **38**	93 (35 : 54 : 11)
	 **39**	

Table II. (continued)

Entry	Arene	Allene	Base
17[g,h]	 3		Na_2CO_3
18[i]	 3		Na_2CO_3

[h]The starting aryl iodide was recovered from the reaction mixture in a 72% yield.

[i]The starting aryl iodide was recovered from the reaction mixture in a 76% yield.

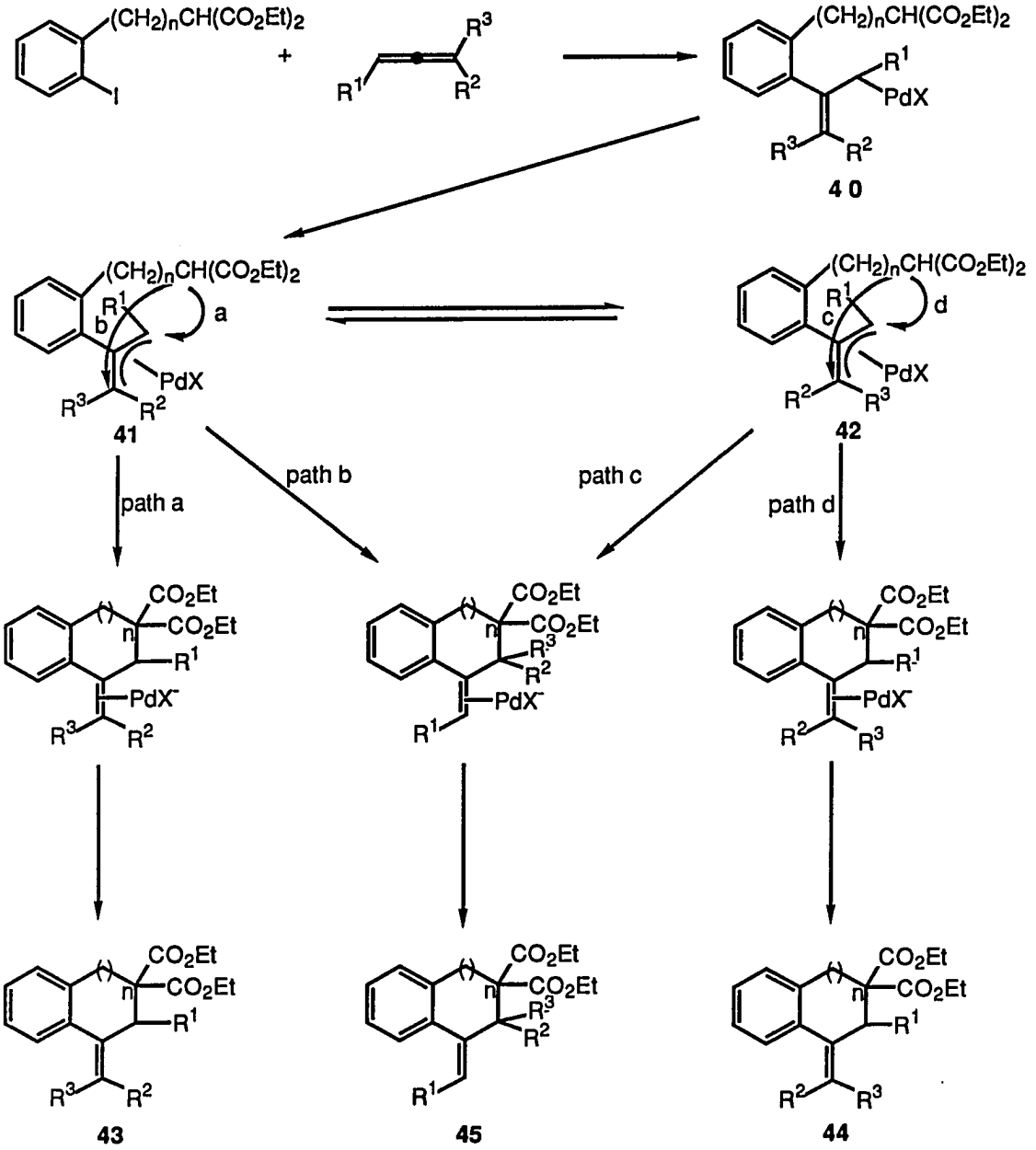
Reaction Conditions	Product(s)	%Yield[b]
14d, 80°C	 **37**	
(1 : 10 : 1)	 **38**	18
	 **39**	
14d, 80°C	 **38**	19

equivalents of sodium carbonate, in DMF at 80°C). When these conditions gave regioisomers or numerous products, the ligand, the solvent or the palladium source was varied to try and improve the reaction.

Palladium-mediated addition of an aryl iodide to an allene proceeds via addition of the aryl group to the internal carbon of the allene with the palladium bonding to the end of the allene to yield a σ-allylpalladium species 40 which rapidly forms a π-allylpalladium intermediate 41 (Scheme XIV). The initially formed π-allylpalladium compound 41 can undergo syn to anti isomerization to yield a new π-allylpalladium compound 42.[22] Three unique products can result from 41 and 42. Nucleophilic attack at the more substituted end in both cases leads to product 45 (paths b and c). However, attack at the least hindered end leads to two different products, 43 and 44, depending on the stereochemistry of the intermediate π-allylpalladium compound (paths a and d). Asymmetrical allenes can yield three separate products.

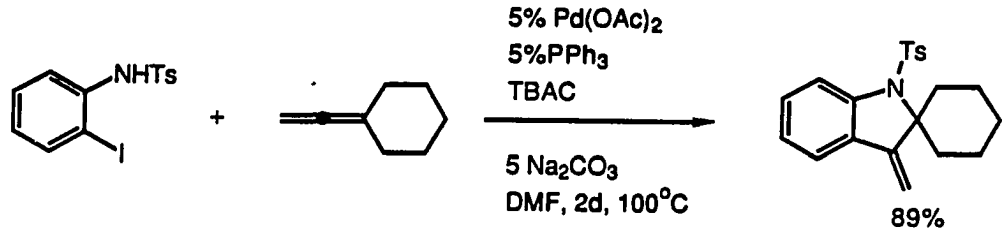
The reactions of diethyl o-iodophenylmalonate and each of the five allenes proceeded readily to furnish the desired annulated product in high yield (Entries 1-5). Allenes which proceed through an unsymmetrical π-allylpalladium intermediate uniformly give the product where nucleophilic attack has occurred at the more substituted end of the allylic unit (Entries 3-5). Norman Berrios-Pena observed

Scheme XIV

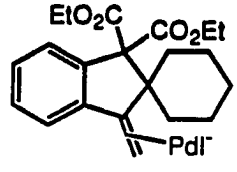

(CH2)nCH(CO2Et)2
I
R3
R1
R2
PdX
40
a
b
c
d
41
42
path a
path b
path c
path d
CO2Et
PdX-
43
45
44

similar regiocontrol in the reaction of N-tosyl-2-iodoaniline and vinylidenecyclohexane (Scheme XV).[23] Nucleophilic attack

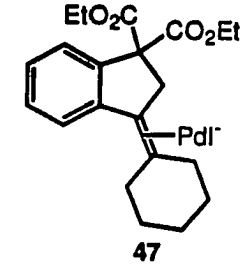
Scheme XV



is presumably occurring at the more substituted end to force the bulky palladium away from the alkyl groups, and to form the least hindered palladium π-complex (46 vs. 47).



46



47

The reaction of aryl iodide 4 with 4,5-nonadiene furnished one stereoisomer in high yield (Entry 6). However, reaction of 4 and 1,2-cyclononadiene afforded a number of products with only a small amount of the desired product seen by ^{1}H NMR spectral analysis of the crude reaction mixture (Entry 7). The reaction of diethyl o-iodobenzylmalonate and 1,2-cyclononadiene produced similar results (Entries 8-12). It is thought that the desired product is not formed, because

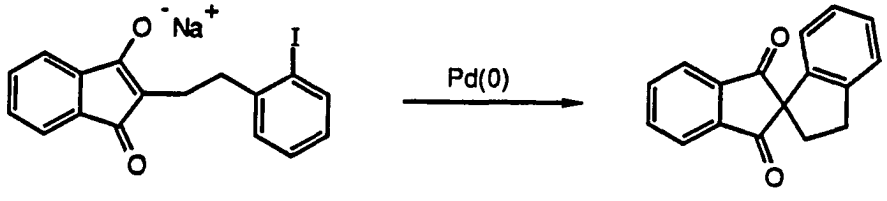
there is too much steric hindrance during carbanion attack on the intermediate π-allylpalladium species. Similar problems were encountered in the reaction of 3 and 1,3-cyclooctadiene (see Section 2 of this dissertation).

The reaction of diethyl o-iodobenzylmalonate and vinylidenecyclohexane proceeded via attack at the least hindered side of the π-allylpalladium intermediate. (Entry 13). This is contrary to the regiochemistry of the attack in entry 3. Most likely, the steric interaction controlling this reaction is between the gem-diester groups and the cyclohexyl ring. The steric bulk of the palladium is not affecting the reaction course. In the formation of six-membered rings with asymmetrical allenes, there is an obvious trend away from regiocontrol by palladium interaction to regiocontrol by carbon-carbon interactions (Entries 13-18). The reaction between diethyl o-iodobenzylmalonate and 1,2-pentadiene produced 33 as the major product when triphenylphosphine was used in the reaction mixture (Entry 15). This is in accordance with forming the least hindered palladium π-complex. When phenylallene is used in the reaction with 3, attack at the least hindered end of the π-allylpalladium intermediate predominates under identical conditions (Entry 16). By changing the bulk around the palladium by removing the ligand, triphenylphosphine, product 39 can be completely eliminated (Entry 18). This trend indicates that as the bulk around the palladium decreases,

interactions between carbons begin to control the regiochemistry of the product.

Alkynes were also tried as substrates in the arylannulation. Work by Uno and co-workers,[17] as well as work by Ciufolini and Browne,[18] indicates that it should be possible to trap σ-vinylpalladium transients with stabilized carbanions (Scheme XVI). Both terminal and symmetrical

Scheme XVI

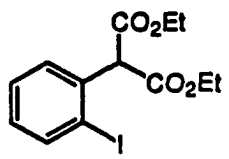
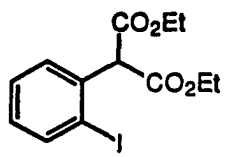
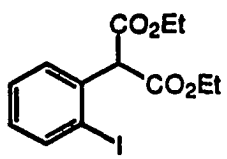


68%

alkynes were tried in the carboannulation procedure. The results of this study are summarized in Table III. Standard palladium(0) conditions (5 mole percent palladium, 1 equivalent of (n-Bu)$_4$NCl, 5 equivalents of base, in DMF at 80°C) were tried initially. If the reaction did not yield the desired product, very little effort was made to improve the reaction.

Arylannulation of terminal alkynes produced only the alkyne substitution product (Entries 1, 5 and 6). Terminal alkynes are known to react with aryl halides to produce aryl alkynes (Scheme XVII).[24-27] This reaction is more efficient than the desired arylannulation.

Table III. Arylannulation of Alkynes[a]

Entry	Arene	Alkyne	Base
1	 2	Ph—C≡C—H	Na_2CO_3
2[d]	 2	Ph—C≡C—Ph	Na_2CO_3
3[d]	 2	Et—C≡C—Et	Na_2CO_3

[a]Actual amounts of reagents used were as follows: 0.25 mmole arene, 1.25 mmole alkyne, 0.25 mmole (n-Bu)$_4$NCl, 0.0125 mmole palladium acetate, 1 ml DMF, 1.25 mmole base.

[b]Triphenylphosphine (0.0125 mmole) was occasionally used as part of the catalyst system.

[c]Numbers given are isolated yields of purified products obtained from flash column chromatography.

[d]Numerous other products seen by TLC, but none were isolated.

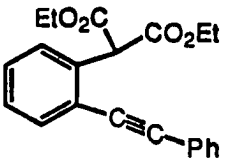
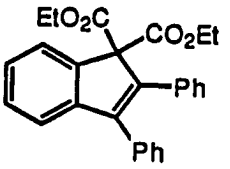
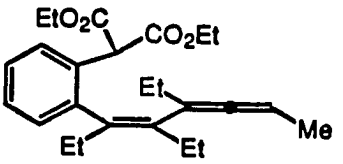
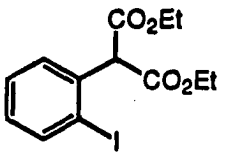
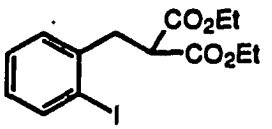
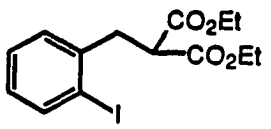
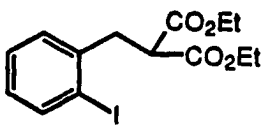
Reaction Conditions[b]	Product(s)	%Yield[c]
PPh_3, 1d, 80°C	 **48**	90
PPh_3, 1d, 80°C	 **49**	61
1d, 80°C	 **50**	65

Table III. (continued)

Entry	Arene	Alkyne	Base
4[d]	 2	Et—C≡C—Et	Na_2CO_3
5	 3	H—C≡C—CH_2CH_2OH	Na_2CO_3
6	 3	H—C≡C—$C(CH_3)_3$	Na_2CO_3
7	 3	Ph—C≡C—Ph	Na_2CO_3

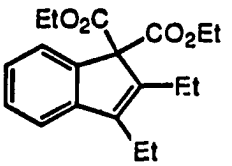
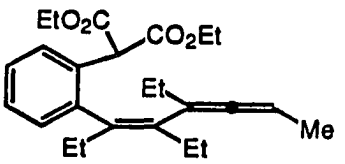
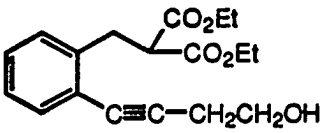
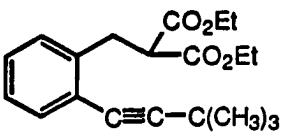
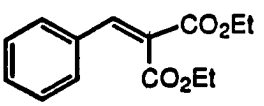
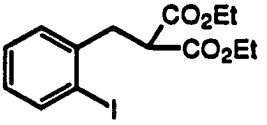
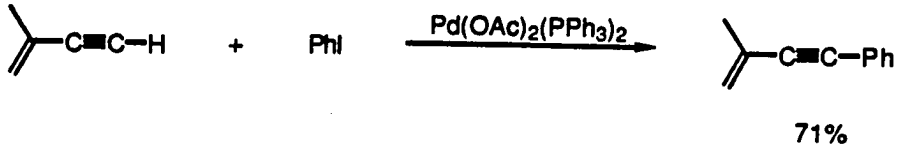
Reaction Conditions[b]	Product(s)	%Yield[c]
PPh_3, 1d, 80°C	 **51**	23
	 **50**	35
1d, 80°C	 **52**	24
1d, 80°C	 **53**	72
PPh_3, 1d, 80°C	 **10**	71

Table III. (continued)

Entry	Arene	Alkyne	Base
8[d]	 3	Et—C≡C—Et	Na_2CO_3

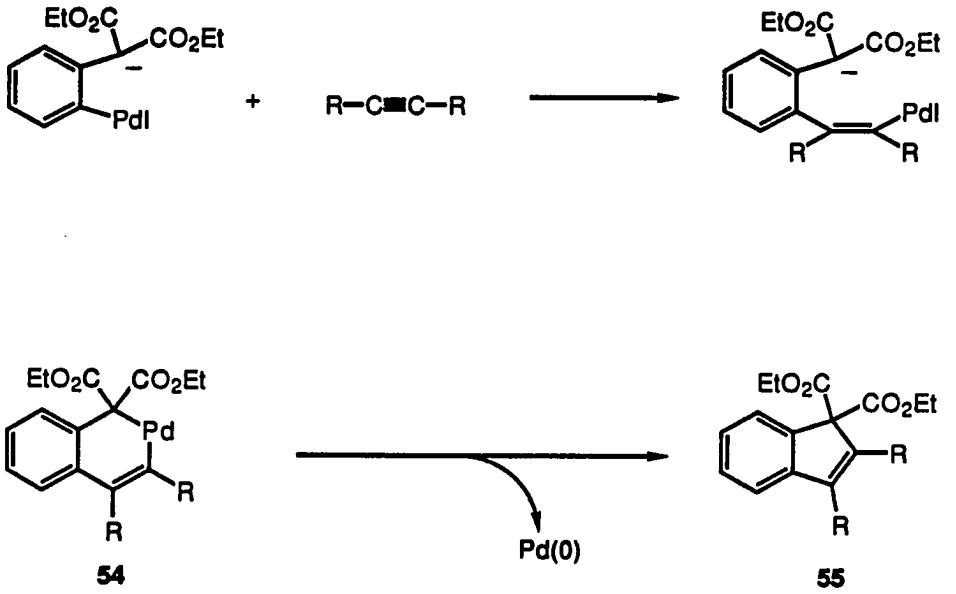
Reaction Conditions[b]	Product(s)	%Yield[c]
5d, 80°C	-	-

Scheme XVII



Symmetrical alkynes yield the desired annulated products when reacted with 2 (Entries 2 and 4). The reaction most likely proceeds by attack on palladium to yield an intermediate metallocycle 54 (Scheme XVIII). Reductive

Scheme XVIII

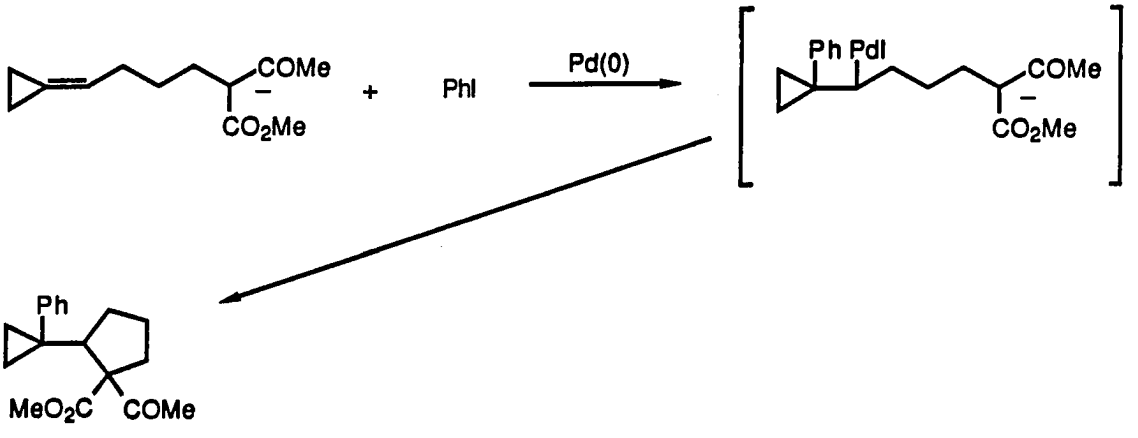


elimination of the palladium furnishes the annulated product 55. The formation of six-membered rings through this mechanism would require an intermediate seven-membered metallocycle. The lack of desired annulated product in the

reactions of 3 and diphenylacetylene or 3-hexyne (Entries 7 and 8) may be due to problems in forming seven-membered metallocycles. Multiple insertion of the alkyne competes with the desired arylannulation. GC-MS of the crude reaction mixtures showed that non-cyclized products had inserted two to four alkynes per arene. Slow addition of the alkyne may be a suitable way to improve this reaction.

The work of Fournet et al. indicates that simple olefins may be useful substrates for carboannulation.[19,20] Members of the Fournet group were able to trap σ-alkylpalladium compounds with stabilized carbanions before they underwent β-hydride elimination or opened neighboring cyclopropanes (Scheme XIX).

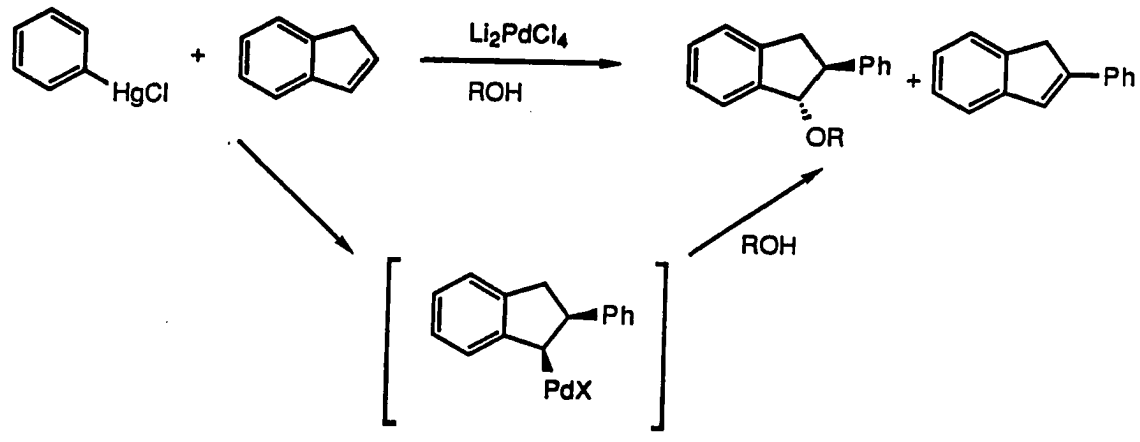
Scheme XIX



Other groups have been able to trap σ-alkylpalladium transients with heteroatom nucleophiles, but these σ-

alkylpalladium species have been unable to undergo syn-β-hydride elimination (Scheme XX).[28]

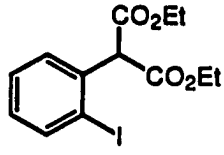
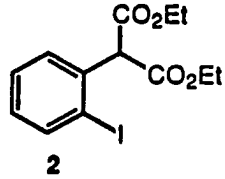
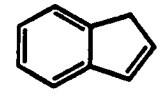
Scheme XX



Arylannulation of mono-olefins was attempted under standard palladium(0) conditions (5 mole percent palladium acetate, 1 equivalent of tetra-n-butylammonium chloride, 5 equivalents of base, in DMF at 80°C). The results of this study are summarized in Table IV. Very few modifications of this procedure were attempted.

The reactions of 2 and 3 with norbornene appeared to yield norbornenyl polymers (Entries 1 and 11). The ^1H NMR spectra of the isolated products were dominated by aliphatic protons. Aryl and ester peaks were very small. GC-MS of these products showed insertions of four to eight norbornenes per arene group. A trial using one equivalent of 3 and one

Table IV. Arylannulation of Alkenes[a]

Entry	Arene	Alkene	Base
1[d]	 2		Na_2CO_3
2	 2		Na_2CO_3

[a]Actual amounts of reagents used were as follows: 0.25 mmole arene, 1.25 mmole alkene, 0.025 mmole (n-Bu)$_4$NCl, 0.0125 mmole palladium acetate, 1 ml DMF, 1.25 mmole base.

[b]Triphenylphosphine (0.0125 mmole) was occasionally used as part of the catalyst system.

[c]Numbers given are isolated yields of purified products obtained from flash column chromatography.

[d]Reaction yielded numerous unidentified products.

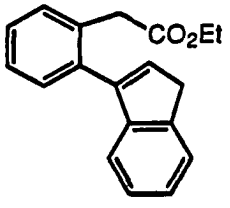
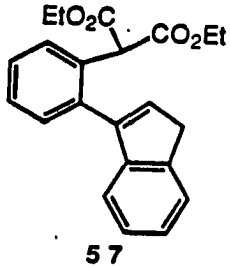
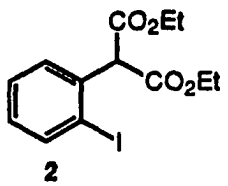
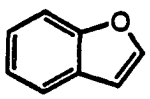
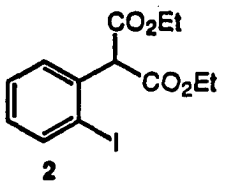
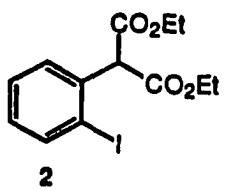
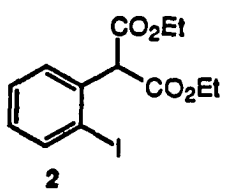
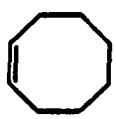
Reaction Conditions[b]	Product(s)	%Yield[c]
PPh_3, 1d, 80°C	-	-
PPh_3, 8d, 80°C	 **56**	32
	 **57**	29

Table IV. (continued)

Entry	Arene	Alkene	Base
3[d]	 2		Na_2CO_3
4	 2		Na_2CO_3
5[d]	 2		Na_2CO_3
6	 2		Na_2CO_3

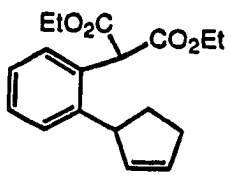
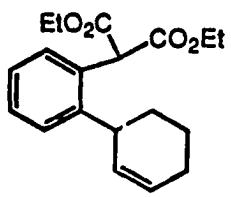
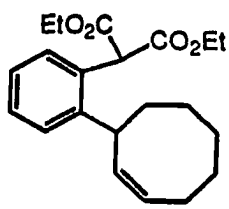
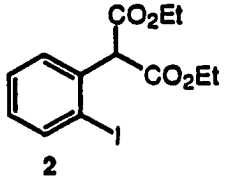
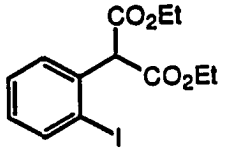
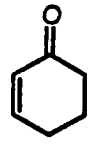
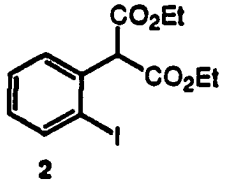
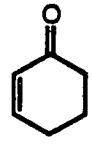
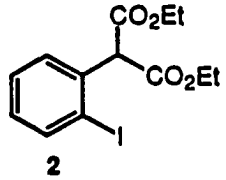
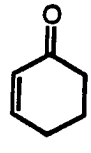
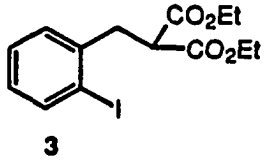
Reaction Conditions[b]	Product(s)	%Yield[c]
PPh_3, 8d, 80°C	-	-
PPh_3, 1d, 80°C	 **58**	82
PPh_3, 6d, 80°C	 **59**	32
PPh_3, 1d, 80°C	 **60**	87

Table IV. (continued)

Entry	Arene	Alkene	Base
7	 **2**		Na_2CO_3
8[d]	 **2**		Na_2CO_3
9[d]	 **2**		Na_2CO_3
10[d]	 **2**		NaOAc
11[d]	 **3**		Na_2CO_3

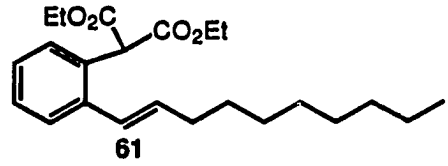
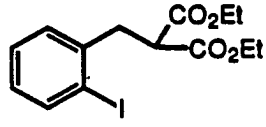
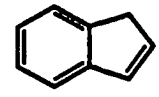
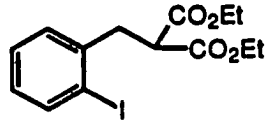
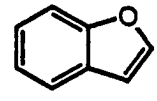
Reaction Conditions[b]	Product(s)	%Yield[c]
PPh_3, 1d, 80°C	 61	93
9d, 80°C	-	-
PPh_3, 9d, 80°C	-	-
9d, 80°C	-	-
3d, 80°C	-	-

Table IV. (continued)

Entry	Arene	Alkene	Base
12	 3		Na_2CO_3
13	 3		Na_2CO_3

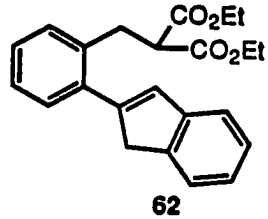
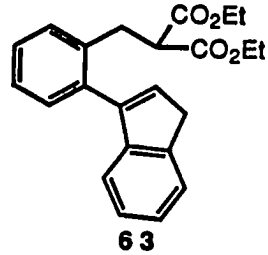
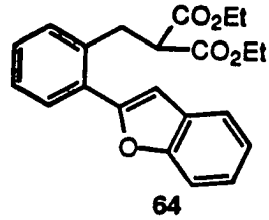
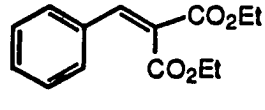
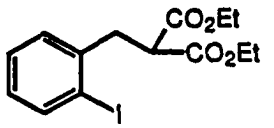
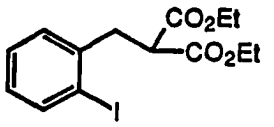
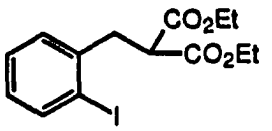
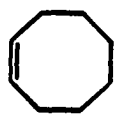
Reaction Conditions[b]	Product(s)	%Yield[c]
1d, 80°C	 **62**	45
	 **63**	51
1d, 80°C	 **64**	20
	 **10**	75

Table IV. (continued)

Entry	Arene	Alkene	Base
14	 **3**		Na_2CO_3
15	 **3**		Na_2CO_3
16	 **3**		Na_2CO_3

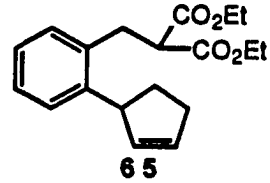
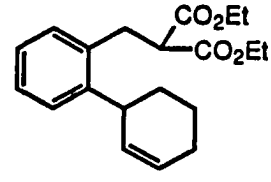
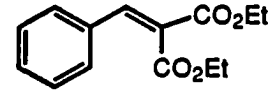
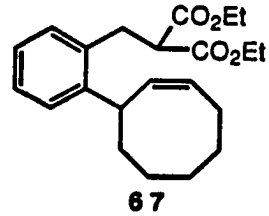
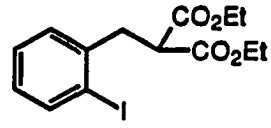
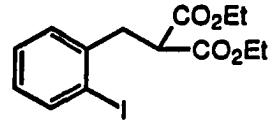
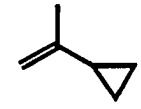
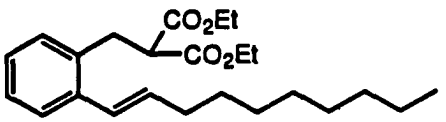
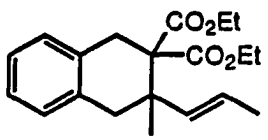
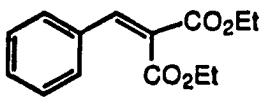
Reaction Conditions[b]	Product(s)	%Yield[c]
PPh_3, 1d, 80°C	 **65**	86
PPh_3, 6d, 80°C	 **66**	46
	 **10**	47
PPh_3, 1d, 80°C	 **67**	86

Table IV. (continued)

Entry	Arene	Alkene	Base
17	 3		Na_2CO_3
18	 3		Na_2CO_3

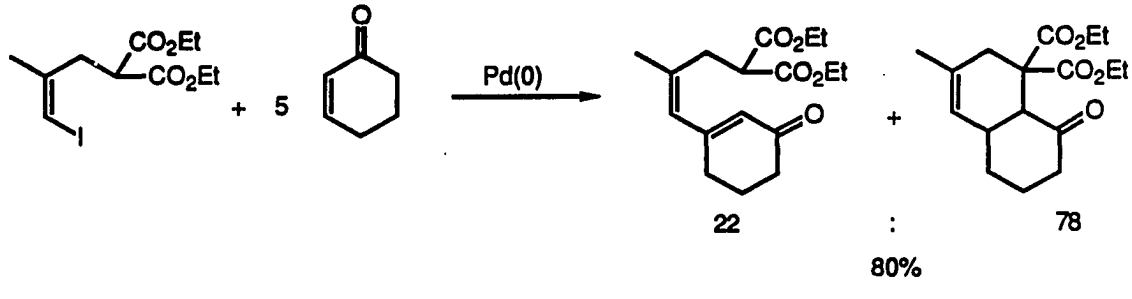
Reaction Conditions[b]	Product(s)	%Yield[c]
PPh_3, 6d, 80°C	 **68**	81
5d, 60°C	 **69**	22
	 **10**	75

equivalent of norbornene was run. Again, polymeric material was obtained as evidenced by ^1H NMR and GC-MS spectra. Starting aryl iodide (65%) was recovered from the reaction mixture.

Benzofuran or indene underwent reaction with 2 or 3, but none of the desired arylannulation products were obtained (Entries 2, 3, 12 and 13). In the arylannulation of indene, compound 2 added exclusively to the benzylic carbon (Entries 2 and 3) while compound 3 added to both the benzylic carbon and the homobenzylic carbon (Entries 12 and 13). The reason for this incongruity is not known. Cyclic alkenes provided allylic-substitution products under the conditions employed (Entries 4-6 and 14-16), while decene provides vinyl-substitution products (Entries 7 and 17).

Dr. William Leong, a member of the Larock research group reported the use of cyclohexenone in a similar carboannulation procedure (Scheme XXI).[29] However, the

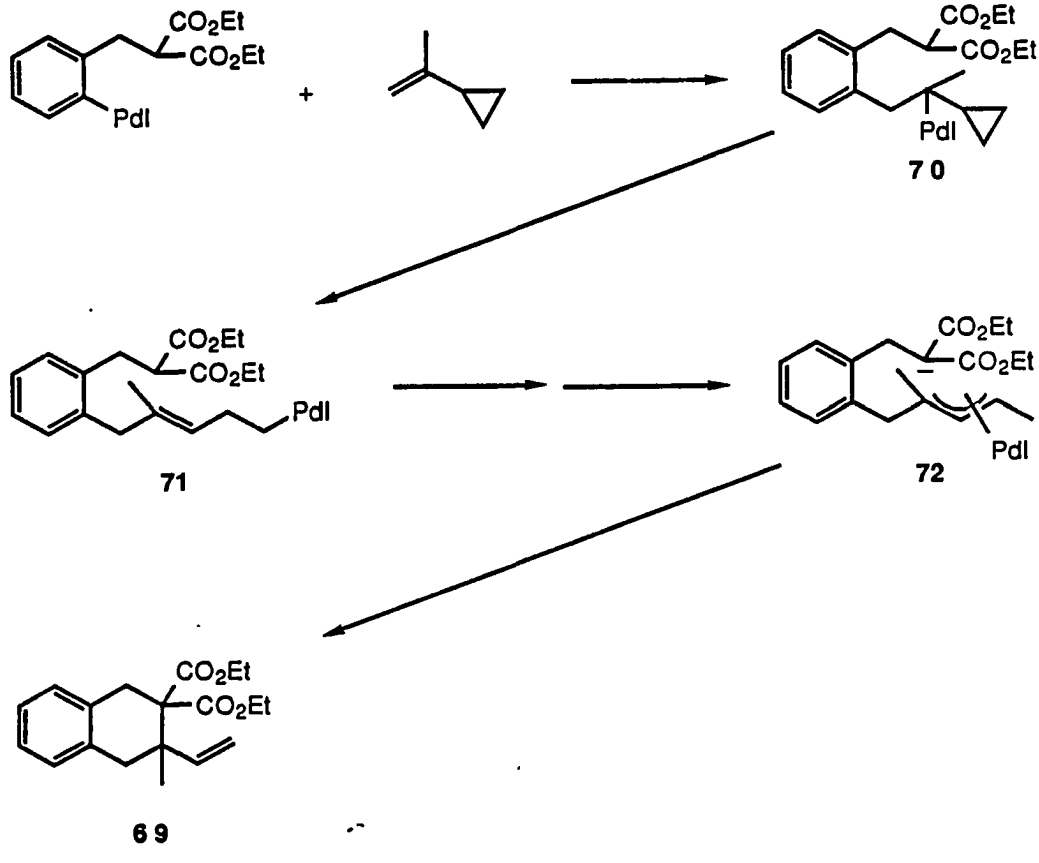
Scheme XXI



reaction of aryl iodide 2 and cyclohexenone provided numerous products, and the desired product was not found.

Finally, the use of isopropenylcyclopropane afforded the desired annulated product in low yield (Entry 18). The reaction to furnish the carboannulated product from 3 and isopropenylcyclopropane most likely proceeds through a π-allylpalladium intermediate (Scheme XXII). Initially, addition of the arylpalladium species across the double bond

Scheme XXII



yields 70. The palladium is situated beta to a strained carbon-carbon bond. Ring opening of the cyclopropane affords a homoallylic palladium compound 71. Palladium-hydride

migration then yields the π-allylpalladium intermediate 72, which in turn yields the annulated product.

CONCLUSION

The extension of the palladium-catalyzed arylannulation process discussed in Section Two of this dissertation to the use of non-conjugated dienes, allenes, alkynes and mono-olefins provided interesting results. Allenes have proven to be valuable substrates in carboannulation, providing polycyclic compounds in high yield. Non-conjugated dienes work well for the formation of six-membered rings, but thus far no larger rings have been formed. A thorough investigation of the mechanism involved should provide the information necessary to make proper modifications of this reaction. Five-membered rings can be formed through the use of internal alkynes, but six-membered rings cannot be formed. Again, a mechanistic investigation should provide clues that will lead to the solution of this problem. Mono-olefins do not undergo the desired arylannulation reaction, but rather yield allylic or vinylic substitution products. The only exception to this is the use of vinylcyclopropanes. Vinylcyclopropanes should provide interesting products in the arylannulation process. Much work is left to be done on extending arylannulation to substrates other than conjugated dienes. The investigation should begin with a complete investigation of the mechanisms involved in the formation of the desired products, as well as the mechanisms involved in the formation of the side products. A good understanding of

the processes connected with these reactions will allow the investigator to make educated decisions on how to eliminate side products and improve the yield of the desired product.

EXPERIMENTAL SECTION

Equipment

NMR spectra were recorded on a Nicolet NT-300 spectrometer (^{1}H NMR, 300 MHz; ^{13}C NMR, 75 MHz), and chemical shifts are reported in ppm relative to TMS (δ 0.00) as an internal standard. IR spectra were obtained on an IBM IR98. High-resolution mass spectra were recorded on a Kratos MS-30 spectrometer.

Reagents

All chemicals were used directly as obtained commercially unless otherwise noted. N,N-Dimethylformamide and dimethyl sulfoxide were distilled from calcium hydride under reduced pressure and stored over 4 Å molecular sieves. Triphenylphosphine was recrystallized from absolute ethanol. Sodium methoxide was obtained from Aldrich or prepared from sodium and methanol.

General procedure for the arylannulation of non-conjugated dienes

Palladium acetate (0.0028 g, 0.0125 mmole), base (1.25 mmole), aryl halide (0.25 mmole) and tetra-n-butylammonium chloride (0.0695 g, 0.25 mmole) were weighed into a 2 dram vial equipped with a magnetic stirring bar and septum inlet. DMF (1 ml) and diene (1.25 mmole) were added sequentially via

syringe. Stirring was continued at the appropriate temperature for the required amount of time. The reaction mixture was diluted with ether (10 ml), washed with saturated ammonium chloride (5 x 10 ml) and dried over sodium sulfate. Following removal of the solvents, the compounds were purified by flash column chromatography. Occasionally other solvents, palladium salts or additives were used, but the general procedure remained the same. The following compounds were obtained from the above procedure.

Compound 7

Compound 7 was isolated in 85% yield from the reaction of diethyl o-iodophenyl malonate and 1,4-hexadiene when the reaction was run in the presence of sodium carbonate for 5 days at 60°C. ^{1}H NMR δ 1.21 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 1.23 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 1.62 (d, J = 4.5 Hz, 3H, $C{=}CCH_3$), 1.91 (d, d, d of d, J = 6.6, 6.9, 7.8 and 13.2 Hz, 1H, $ArCCH_2$), 2.22 (d, d, d of d, J = 3.3, 6.3, 9.6 and 13.2 Hz, 1H, $ArCCH_2$), 2.78 (d, d of d, J = 6.3, 6.6 and 17.1 Hz, 1H, $ArCH_2$), 2.91 (d, d of d,6.9, 9.6 and 17.1 Hz, 1H, $ArCH_2$), 3.20 (d, d of d, J = 3.3, 4.5, and 7.8 Hz, 1H, C=CCH), 4.14 (q, J = 7.2 Hz, 2H, CO_2CH_2), 4.15 (q, J = 7.2 Hz, 2H, CO_2CH_2), 5.53 (q of d, J = 4.5 and 15.3 Hz, 1H, $C{=}C\underline{H}CH_3$), 5.59 (d of d, J = 4.5 and 15.3 Hz, 1H, $C{=}C\underline{H}CH$), 7.05-7.25 (m, 3H, ArH), 7.48 (d of d, J = 1.5 and 7.8 Hz, 1H, ArH); ^{13}C NMR δ 13.95, 14.06, 17.90, 25.96, 26.52, 43.72, 61.14, 61.40,

62.18, 125.24, 127.29, 127.36, 128.89, 130.04, 131.68, 132.10, 137.06, 170.27, 170.30; IR 2982, 2937, 1732 (C=O), 1447, 1366, 1298, 1246, 1215, 1178, 1119, 1059, 972, 750 cm^{-1}; Anal. Calculated for $C_{19}H_{24}O_4$: C, 72.13; H, 7.65. Found: C, 72.30; H, 7.86.

Compound 8

Compound 8 was isolated in 64% yield from the reaction of diethyl o-iodophenyl malonate and 1,4-cyclohexadiene when the reaction was run in the presence of sodium acetate for 5 days at 60°C. ^1H NMR δ 1.20 (t, J = 7.2 Hz, 3H, CH_3), 1.23 (t, J = 7.2 Hz, 3H, CH_3), 1.62 (d of t, J = 14.1 and 4.8 Hz, 1H, $CHCH_2CH$), 2.62 (br s, 2H, $C{=}CCH_2$), 2.80 (d of t, J = 14.1 and 7.2 Hz, 1H, $CHCH_2CH$), 4.12 (q, J = 7.2 Hz, 2H, CO_2CH_2), 4.13 (q, J = 7.2 Hz, 2H, CO_2CH_2), 4.72 (d of d, J = 4.8 and 7.2 Hz, 1H, C=CCH), 5.45 (d of d, J = 4.8 and 7.2 Hz, 1H, C=CCH), 5.59 (d of t, J = 5.7 and 1.5 Hz, 1H, C=CH), 5.89 (d of t, J = 5.7 and 1.5 Hz, 1H, C=CH), 7.3-7.5 (m, 4H, ArH); ^{13}C NMR δ 13.87, 14.01, 25.90, 31.48, 41.12, 52.84, 53.00, 57.52, 74.80, 128.29, 128.63, 129.21, 129.66, 129.86, 130.98, 139.60, 168.10, 171.93; IR 2990, 2932, 1732 (C=O), 1445, 1362, 1298, 1250, 1212, 1175, 1120, 1058, 972, 750 cm^{-1}; Anal. Calculated for $C_{19}H_{22}O_4$: C, 72.59; H, 7.05. Found: C, 72.34; H, 7.12.

Compound 9. Ethyl 2-iodophenylacetate

Ethyl 2-iodophenylacetate was isolated in 12% yield from the reaction of diethyl o-iodophenyl malonate and 1,4-cyclohexadiene when the reaction was run in the presence of sodium acetate for 5 days at 60°C.

Compound 10

Compound 10 was isolated in 24% yield from the reaction of diethyl o-iodobenzyl malonate and 1,4-hexadiene when the reaction was run in the presence of sodium carbonate using bis(dibenzylideneacetone)palladium as the catalyst source for 5 days at 60°C. Spectral data are reported in Section 2 this dissertation.

Compound 11

Compound 11 was isolated in 39% yield from the reaction of diethyl o-iodobenzyl malonate and 1,4-hexadiene when the reaction was run in the presence of 5% triphenylphosphite and sodium carbonate for 5 days at 100°C. ^{1}H NMR δ 1.23 (t, J = 7.2 Hz, 3H, CH_3), 2.63 (t, J = 7.5 Hz, 2H, $ArCH_2$), 3.14 (t, J = 7.5 Hz, 2H, CH_2CO_2Et), 4.18 (q, J = 7.2 Hz, 2H, CO_2CH_2), 6.91 (d of t, J = 1.8 and 7.5 Hz, 1H, ArH), 7.2 (m, 2H, ArH), 7.82 (d of d, J = 0.9 and 7.5 Hz, ArH).

Compound 12

Compound 12 was isolated in 35% yield from the reaction of diethyl o-iodobenzyl malonate and 1,5-hexadiene when the reaction was run in the presence of sodium carbonate for 5 days at 60°C. ^{1}H NMR δ 1.22 (t, J = 7.2 Hz, 4H, CH_3), 2.3 (m, 4H, C-CCH_2), 3.25 (d, J = 7.5 Hz, 2H, $ArCH_2$), 3.64 (t, J = 7.5 Hz, 1H, $CH(CO_2Et)_2$), 4.18 (q, J = 7.2 Hz, 4H, CO_2CH_2), 5.01(d of d, J = 1.2 and 10.2 Hz, 1H, cis-C-CH_2), 5.08 (d of d, J = 1.2 and 16.8 Hz, 1H, trans-C-CH_2), 5.88 (d, d of t, J = 10.2, 16.8 and 6.9 Hz, 1H C$\underline{H}$-CH_2), 6.12 (d of t, J = 17.1 and 7.2 Hz, 1H, ArC-CH), 6.65 (d, J = 17.1 Hz, 1H, ArCH-C), 7.2-7.3 (m, 4H, ArH); ^{13}C NMR δ 13.98, 25.72, 28.72, 29.10, 45.68, 55.72, 114.52, 124.35, 125.48, 126.54, 127.01, 128.52, 129.68, 130.10, 130.92, 134.24, 168.92; IR 3002, 2928, 1732 (C=O), 1452, 1360, 1295, 1248, 1210, 1172, 1125, 1052, 968, 752 cm^{-1}.

Compound 13

Compound 13 was obtained in 89% yield from the reaction of diethyl o-iodophenyl malonate and 1,11-dodecadiene when the reaction was run in the presence of 5% triphenylphosphine and sodium carbonate for 5 days at 80°C. ^{1}H NMR δ 1.24 (t, J = 7.2 Hz, 6H, CH_3), 1.28 (m, 8H, aliphatic), 2.04 (m, 4H, C-$CCCH_2$), 2.11 (q, J = 6.6 Hz, 2H, C-CCH_2), 2.61 (d, d of t, J = 0.9, 6.9 and 7.2 Hz, 2H, ArC-CCH_2), 3.67 (s, 1H, $CH(CO_2Et)_2$), 4.14 (q, J = 7.2 Hz, 4H, CO_2CH_2), 4.93 (d of d,

J = 1.8 and 10.2 Hz, 1H, cis-C-CH_2), 4.98 (d of d, J = 1.8 and 17.2 Hz, 1H, trans-C-CH_2), 5.81 (t, d of d, J = 6.6, 10.2, 17.2 Hz, 1H, C$\underline{H}$-CH_2), 6.08 (t of d, J = 6.9 and 15.6 Hz, 1H, ArC-CH), 6.57 (d, J = 15.6 Hz, 1H, ArCH-C, 7.2 (m, 4H, ArH); ^{13}C NMR δ 14.10, 28.96, 29.08, 29.22, 29.27, 29.41, 29.56, 29.68, 33.86, 39.30, 60.82, 114.14, 126.28, 126.99, 127.05, 127.48, 129.36, 130.48, 134.04, 134.15, 139.25, 176.39; IR 2964, 2928, 1738 (C=O), 1466, 1447, 1367, 1302, 1261, 1213, 1144, 1086, 1032, 800, 752 cm^{-1}; HRMS calculated for $C_{25}H_{36}O_4$ 400.26148, found 400.26081.

Compound 14

Compound 14 was isolated in 91% yield from the reaction of diethyl o-iodobenzyl malonate and 1,11-dodecadiene when the reaction was run in the presence of 5% triphenylphosphine and sodium carbonate for 5 days at 80°C. ^1H NMR δ 1.20 (t, J = 7.2 Hz, 4H, CH_3), 1.31 (m, 8H, aliphatic), 2.04 (p, J = 7.2 Hz, 4H, C-CCH_2), 2.23 (q, J = 7.2 Hz, 2H, C-CH_2), 2.62 (q, J = 7.8 Hz, 2H, ArC-CH_2), 3.26 (d of d, J = 7.8 and 10.5 Hz, 2H, ArCH_2), 3.64 (t, J = 7.8 Hz, 1H, CH($CO_2Et)_2$), 4.14 9q, J = 7.2 Hz, 4H, CO_2CH_2), 4.92 (d of d, 1.5 and 10.5 Hz, 1H, cis-C-CH_2), 4.98 (d of d, J = 1.5 and 17.4 Hz, 1H, trans-C-CH_2), 5.81 (d, d of t, J = 10.5, 17.4 and 6.6 Hz, C$\underline{H}$-CH_2), 6.11 (d of t, J = 15.3 and 6.9 Hz, 1H, ArC-CH), 6.52 (d, J = 15.3 Hz, 1H, ArCH-C), 7.1 (m, 4H); ^{13}C NMR δ 14.07, 28.98, 29.20, 29.28, 29.34, 29.40, 29.51, 32.18, 32.58, 33.38,

33.85, 52.73, 53.08, 61.44, 114.21, 126.20, 126.72, 126.82, 126.86, 127.10, 129.38, 130.02, 133.90, 139.21, 168.93, 168.998; IR 2980, 2928, 2854, 1736 (C=O), 1464, 1447, 1369, 1335, 1227, 1178, 1151, 1096, 1034, 752 cm^{-1}; HRMS calculated for $C_{26}H_{40}O_4$ 414.27702, found 414.27629.

General procedure for the arylannulation of allenes

Palladium acetate (0.0028 g, 0.0125 mmole), triphenylphosphine (0.0033 g, 0.0125 mmole), base (1.25 mmole), aryl halide (0.25 mmole) and tetra-n-butylammonium chloride (0.0695 g, 0.25 mmole) were weighed into a 2 dram vial equipped with a magnetic stirring bar and septum inlet. DMF (1 ml) and allene (1.25 mmole) were added sequentially via syringe. Stirring was continued at the appropriate temperature for the required amount of time. The reaction mixture was diluted with ether (10 ml), washed with saturated ammonium chloride (5 x 10 ml) and dried over sodium sulfate. Following removal of the solvents, the compounds were purified by flash column chromatography. Occasionally other solvents or phosphorus ligands were used, but the general procedure remained the same. The following compounds were obtained from the above procedure.

Compound 24

Compound 24 was isolated in 86% yield from the reaction of diethyl o-iodophenyl malonate and 4,5-nonadiene when the

reaction was run in the presence of sodium carbonate for 2 days at 80°C. ^{1}H NMR δ 0.86 (t, J = 6.9 Hz, 3H, CCCCH$_3$), 0.98 (t, J = 7.5 Hz, C-CCCCH$_3$), 1.14 (p, J = 7.5 Hz, 4H, aliphatic), 1.19 (t, J = 7.2 Hz, 3H, CO$_2$CCH$_3$), 1.28 (t, J = 7.2 Hz, 3H, CO$_2$CCH$_3$), 2.41 (h, J = 7.8 Hz, 2H, C-CCCH$_2$), 3.55 (t of d, J = 4.8 and 9.0 Hz, 1H, C-CCH$_2$), 4.03 (t of d, J = 7.2 and 10.2 Hz, 1H, C-CCH$_2$), 4.19 (d, d of d, J = 1.2, 3.6 and 10.8 Hz, 1H, ArCCH), 4.24 (q, J = 7.2 Hz, 2H, CO$_2$CH$_2$), 4.30 (q, J = 7.2 Hz, 2H, CO$_2$CH$_2$), 5.59 (d, d of d, J = 1.2, 9.0 and 10.2 Hz, 1H, C-CH), 7.27 (d of p, J = 1.5 and 7.2 Hz, 2H, ArH), 7.51 (d of d, J = 1.5 and 7.2 Hz, 1H, ArH), 7.63 (d of d, J = 1/5 and 7.2 Hz, 1H, ArH); ^{13}C NMR δ 13.92, 14.14, 14.32, 20.04, 23.25, 30.62, 32.90, 47.85, 52.25, 61.14, 61.49, 67.55, 124.56, 125.71, 127.28, 127.90, 128.30, 139.84, 140.28, 141.06, 169.29, 170.25; IR 2959, 2934, 1736 (C=O), 1466, 1240, 1209, 1173, 1101, 1045, 752, 737 cm^{-1}; Anal. Calculated for $C_{22}H_{30}O_4$: C, 73.71; H, 8.43.

Compound 25

Compound 25 was isolated in 85% yield from the reaction of diethyl o-iodophenyl malonate and 1,2-cyclononadiene when the reaction was run in the presence of sodium carbonate for 8 days at 80°C. ^{1}H NMR δ 1.15 (t, J = 7.2 Hz, 3H, CH$_3$), 1.24 (t, J = 7.2 Hz, 3H, CH$_3$), 1.4-1.8 (m, 8H, aliphatic), 2.2-2.6 (m, 2H, C-CCCH$_2$), 3.90 (d of d, J = 2.7 and 11.4 Hz, 1H, ArCCH), 4.0 (m, 2H, C-CCH$_2$), 4.12 (q, J = 7.2 Hz, 2H,

CO_2CH_2), 4.29 (q, J = 7.2 Hz, 2H, CO_2CH_2), 6.06 (d of d, J = 6.9 and 10.5 Hz, 1H, C=CH), 7.25 (m, 2H, ArH), 7.41 (d of d, J = 1.8 and 6.9 Hz, 1H, ArH); 7.60 (d of d, J = 2.4 and 6.3 Hz, 1H, ArH); ^{13}C NMR δ 13.87, 14.20, 24.08, 24.95, 25.78, 26.09, 27.21, 28.36, 48.38, 61.18, 61.53, 69.01, 120.19, 121.87, 127.48, 128.16, 128.64, 138.70, 141.42, 142.44, 169.39, 169.44; IR 2980, 2926, 2853, 1736 (C=O), 1464, 1240, 1221, 1177, 1096, 1085, 756, 671 cm^{-1}; Anal. Calculated for $C_{22}H_{28}O_4$: C, 74.13; H, 7.92.

Compound 26

Compound 26 was isolated in 82% yield from the reaction of o-iodophenyl malonate and vinylidenecyclohexane when the reaction was run in the presence of sodium carbonate for 2 days at 80°C. ^1H NMR δ 1.24 (t, J = 7.2 Hz, 6H, CH_3),1.4-2.2 (m, 10H, aliphatic),4.18 (q, J = 7.2 Hz, 4H, CO_2CH_2), 5.38 (s, 1H, C=CH), 5.61 (s, 1H, C=CH), 7.2-7.6 (m, 4H, ArH); ^{13}C NMR δ 14.09, 22.45, 25.98, 30.55, 54.22, 61.11, 72.66, 106.01, 120.99, 127.54, 128.51, 129.19, 139.37, 141.68, 153.91, 168.81; IR 2980, 2932, 2854, 1734 (C=O), 1470, 1448, 1367, 1288, 1240, 1209, 1161, 1094, 1043, 727^{-1}; Anal Calculated for $C_{21}H_{26}O_4$: C, 73.66; H, 7.65.

Compound 27

Compound 27 was isolated in 88% yield from the reaction of o-iodophenyl malonate and 1,2-pentadiene when the reaction

was run in the presence of sodium carbonate for 4 days at 80°C. ^{1}H NMR δ 0.98 (t, J = 7.2 Hz, 3H, CH_3), 1.21 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 1.28 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 1.37 (m, 1H, $ArCCCH_2$), 1.53 (m, 1H, $ArCCCH_2$), 3.60 (d of d, J = 4.8 and 9.3 Hz, 1H, C-CCH). 4.1 (m, 4H, CO_2CH_2), 5.12 (d, J = 1.5 Hz, 1H, C-CH), 5.54 (d, J = 1.5 Hz, 1H, C-CH), 7.3-7.7 (m, 4H, ArH); ^{13}C NMR δ 11.75, 14.17, 23.45, 52.25, 61.35, 61.71, 61.78, 62.05, 105.18, 120.74, 127.47, 128.25, 128.56, 128.74, 140.28, 140.76, 168.68, 170.06; IR 2995, 2928, 2852, 1732 (C-O), 1470, 1452, 1364, 1281, 1236, 1209, 1165, 1089, 1035, 727^{-1}; Anal. Calculated for $C_{18}H_{22}O_4$: C, 71.50; H, 7.33.

Compound 28

Compound 28 was isolated in 95% yield from the reaction of o-iodophenyl malonate and phenylallene when the reaction was run in the presence of sodium carbonate for 5 days at 80°C. ^{1}H NMR δ 0.81 (t, J = 7.2 Hz, 3H, CH_3), 1.25 (t, J = 7.2 Hz, 3H, CH_3), 3.49 (d of q, J = 10.8 and 7.2 Hz, 1H, CO_2CH_2), 3.74 (d of q, J = 10.8 and 7.2 Hz, 1H, CO_2CH_2), 4.17 (d of q, J = 10.8 and 7.2 Hz, 1H, CO_2CH_2), 4.27 (d of q, J = 10.8 and 7.2 Hz, 1H, CO_2CH_2), 4.98 (d, J = 2.1 Hz, 1H, C-CH), 5.15 (t, J = 2.1 Hz, 1H, C-CH), 5.67 (d, J = 2.1 Hz, 1H, ArCHC-C), 7.1-7.7 (m, 9H, ArH); ^{13}C NMR δ 13.50, 14.01, 56.29, 61.19, 62.05, 70.12, 106.72, 120.70, 127.16, 127.65, 127.98, 128.36, 129.08, 129.30, 140.27, 140.71, 141.299,

150.74, 168.71, 169.52, IR 2985, 2932, 1732 (C=O), 1468, 1448, 1350, 1282, 1230, 1211, 1155, 1075, 1032, 748^{-1}; MS m/e 350 (M^+), 276 (M^+-HCO_2Et), 203 (M^+-(HCO_2Et + CO_2Et)); Anal. Calculated for $C_{22}H_{22}O_4$: C, 75.41; H, 6.33. Found: C, 75.25; H, 6.54.

Compound 29

Compound 29 was isolated in 86% yield from the reaction of compound 4 and 4,5-nonadiene when the reaction was run in the presence of lithium carbonate for 2 days at 80°C. ^1H NMR δ 0.86 (t, J = 7.2 Hz, 3H, CH_3), 0.87 (t, J = 7.2 Hz, 3H, CH_3), 1.2-1.5 (m, 6H, aliphatic), 2.2-2.4 (m, 2H, C=CCH_2), 3.07 (q, J = 4.2 Hz, 1H, C=CCH), 3.13 (d of d, J = 5.7 and 17.4 Hz, 1H, ;$ArCH_2$), 3.47 (d of d, J = 4.2 and 17.4 Hz, 1H, $ArCH_2$), 4.69 (d, d of d, J = 4.2, 4.2 and 5.7 Hz, $CHNO_2$), 5.46 (d of d, J = 6.0 and 8.4 Hz, 1H, C=CH), 7.15-7.35 (m, 4H, ArH); ^{13}C NMR δ 13.76, 13.83, 20.25, 23.41, 30.38, 31.09, 34.68, 49.05, 86.77, 126.05, 127.40, 127.99, 128.71, 131.77, 132.35, 132.64, 133.68; IR 3020, 2961, 2872, 1551 (NO_2), 1487, 1456, 1470, 1369, 968, 852, 770, 744, 702 cm^{-1}; Anal. Calculated for $C_{17}H_{23}NO_2$: C, 74.69; H, 8.48. Found: C, 74.25; H, 8.32.

Compound 30 and 31

Compounds 30 and 31 were isolated in a 60% yield as a (3 : 2) mixture from the reaction of diethyl o-iodobenzyl

malonate and 1,2-cyclononadiene when the reaction was run omitting triphenylphosphine and using sodium carbonate as the base for 3 days at 80°C. ^{1}H NMR (of the mixture) δ 1.3 (m, CH_3), 1.4-2.5 (m, aliphatic and allylic), 3.21 and 3.34 (2:3 ratio) (d, J = 7.5 Hz, $ArCH_2$), 3.72 (m, $CH(CO_2Et)_2$), 4.85 (d, d of d, J = 1.2, 7.8 and 17.2 Hz, trans-C=CH), 4.98 (d, d of d, J = 1.5 and 7.8 and 10.2 Hz, cis-C=CH), 5.24 (d of d, J = 1.2 and 7.8 Hz, ArC=CH), 5.38 (d of d, J = 1.2 and 7.5 Hz, ArC=CH); 5.52 (d, J = 17.2 Hz, trans-C=CCH=C); 5.74 (d, J = 10.2 Hz, cis-C=CCH=C); 7.2 (m, ArH); IR (mixture) 3020, 2928, 1732 (C=O), 1452, 1326, 1278, 1245, 1200, 1158, 1082, 1015, 732^{-1}; MS m/e 370 (M^+), 296 (M^+-HCO_2Et), 223 (M^+-(HCO_2Et + CO_2Et).

Compound 32

Compound 32 was isolated in 87% yield from the reaction of diethyl o-iodobenzyl malonate and vinylidenecyclohexane when the reaction was run in the presence of sodium carbonate for 2 days at 80°C. ^{1}H NMR δ 1.18 (t, J = 7.2 Hz, 3H, CH_3), 1.19 (t, J = 7.2 Hz, 3H, CH_3), 1.55-1.65 (m, 6H, aliphatic), 2.35 (m, 2H, C=CCH_2), 2.41 (m, 2H, C=CCH_2), 3.00 (s, 2H, ArC(=C)CH_2), 3.16 (s, 2H, $ArCH_2$), 4.0-4.2 (m, 4H, CO_2CH_2), 7.10-7.25 (m, 4H, ArH); ^{13}C NMR δ 13.95, 14.05, 14.12, 26.82, 28.17, 28.70, 31.29, 32.122, 33.71, 35.45, 55.64, 61.43, 125.54, 125.65, 126.28, 128.08, 128.48, 135.30, 137.63, 138.24, 170.02, 171.50; IR 2978, 2928, 1734 (C=O), 1447,

1367, 1300, 1259, 1221, 1180, 1096, 1061, 860, 800, 760 cm^{-1}; Anal. Calculated for $C_{22}H_{28}O_4$: C, 74.13; H, 7.92. Found: C, 74.32; H, 7.84.

Compound 36

Compound 36 was isolated in 87% yield from the reaction of diethyl o-iodobenzyl malonate and 1,2-pentadiene when triphenylphosphine was omitted from the reaction mixture and sodium carbonate was used as the base for 5 days at 80°C. ^1H NMR δ 1.24 (t, J = 7.2 Hz, 6H, CO_2CCH_3), 1.87 (d, J = 7.5 Hz, 3H, $C{=}CCH_3$), 2.98 (d, J = 7.5 Hz, 2H, $ArCH_2$), 3.82 (t, J = 7.5 Hz, 1H, $CH(CO_2Et)_2$), 4.21 (q, J = 7.2 Hz, 4H, CO_2CH_2), 5.14 (d, J = 0.9 Hz, 1H, $C{=}CH_2$), 5.59 (d, J = 0.9 Hz, 1H, $C{=}CH_2$), 6.28 (t of d, J = 7.5 and 16.5 Hz, 1H, ArC(=C)C=CH), 6.74 (d, J = 16.5 Hz, 1H, ArC(=C)CH=C), 7.2-7.5 (m, 4H); ^{13}C NMR δ 14.25, 25.34, 30.52, 40.27, 52.34, 126.14, 126.75, 127.13, 127.23, 127.64, 128.84, 134.10, 134.52, 136.71, 140.01, 169.78; IR 3001, 2942, 1728 (C=O), 1450, 1365, 1287, 1250, 1184, 1084, 1075, 865, 798, 732 cm^{-1}; HRMS calculated for $C_{19}H_{24}O_4$ 316.16752, found 316.1669.

Compound 33, 34 and 35

Compounds 33, 34 and 35 were isolated in 96% yield as a 10 : 4 : 1 mixture from the reaction of diethyl o-iodobenzyl malonate and 1,2-pentadiene when the reaction was run in the presence of sodium carbonate for 4 days at 80°C. ^1H NMR

(mixture) δ 0.84 (t, J = 7.5 Hz, CH_3), 1.08 (t, J = 7.5 Hz, CH_3), 1.18 (t, J = 7.5 Hz, CH_3), 1.2-1.3 (m, CO_2CCH_3 and $C\underline{H}_2CH_3$), 2.25 (p, J = 7.8 Hz, $C{=}CCH_2$), 2.34 (p, J = 7.8 Hz, $C{=}CCH_2$), 2.92 (br s, $ArC(=C)CH_2$), 3.05 (br s, $ArC(=C)CH_2$), 3.1-3.3 (m, $ArCH_2$), 3.52 (t, J = 7.5 Hz, $AeC(=C)CH$), 4.1-4.3 (m, CO_2CH_2), 5.08 (d, J = 0.9 Hz, $C{=}CH_2$, from compound 33, integrates to 10), 5.48 (t, J = 7.8 Hz, C=CH, from compound 34, integrates to 4), 5.98 (d, J = 0.9 Hz, $C{=}CH_2$, from compound 33, integrates to 10), 6.09 (t, J = 7.8 Hz, C=CH, from compound 35, integrates to 1), 7.2 (m, ArH).

Compounds 37, 38 and 39

Compounds 37, 38 and 39 were isolated in 93% yield in a 35 : 54: 11 ratio from the reaction of diethyl o-iodobenzyl malonate and phenylallene when the reaction is run in the presence of sodium carbonate for 6 days at 80°C. ^1H NMR δ 1.2 (m, CH_3), 3.02 (br s, $ArCCH_2$), 3.3-3.4 (m, $ArCH_2$), 3.92 (s, ArCHC=C), 4.0-4.4 (m, CO_2CH_2), 4.74 (d, J = 0.9 Hz, $C{=}CH_2$, from compound 39, integrates to 11), 5.15 (d, J = 0.9 Hz, $C{=}CH_2$, from compound 39, integrates to 11), 5.85 (s, C=CHPh, from compound 37, integrates to 35), 6.50 (s, C=CHPh, from compound 38, integrates to 54), 7.0-7.4 (m, ArH).

General procedure for the arylannulation of alkynes

Palladium acetate (0.0028 g, 0.0125 mmole), base (1.25 mmole), aryl halide (0.25 mmole) and tetra-n-butylammonium

chloride (0.0695 g, 0.25 mmole) were weighed into a 2 dram vial equipped with a magnetic stirring bar and septum inlet. DMF (1 ml) and alkyne (1.25 mmole) were added sequentially via syringe. Stirring was continued at the appropriate temperature for the required amount of time. The reaction mixture was diluted with ether (10 ml), washed with saturated ammonium chloride (5 x 10 ml) and dried over sodium sulfate. Following removal of the solvents, the compounds were purified by flash column chromatography. Occasionally other solvents or phosphorus ligands were used, but the general procedure remained the same. The following compounds were obtained from the above procedure.

Compound 48

Compound 48 was isolated in 90% yield from the reaction of diethyl o-iodophenyl malonate and phenylacetylene when the reaction was run in the presence of 5% triphenylphosphine and sodium carbonate for 1 day at 80°C. ^{1}H NMR δ 1.22 (t, J = 7.2 Hz, 6H, CH_3), 4.18 (q, J = 7.2 Hz, 4H, CO_2CH_2), 5.28 (s, 1H, $CH(CO_2Et)_2$), 7.1-7.5 (m, 9H, ArH); ^{13}C NMR δ 14.04, 47.46, 54.01, 80.01, 83.25, 124.53, 124.89, 125.52, 126.01, 126.46, 126.67, 127.43, 128.21, 128.56, 130.19; IR 3011, 2928, 1735 (C=O), 1442, 1357, 1262, 1232, 1152, 1072, 1001, 863, 789, 730 cm^{-1}; HRMS calculated for $C_{21}H_{20}O_4$ 336.1356, found 336.1348.

Compound 49

Compound 49 was isolated in 61% yield from the reaction of diethyl o-iodophenyl malonate and diphenylacetylene when the reaction was run in the presence of 5% triphenylphosphine and sodium carbonate for 1 day at 80°C. ^{1}H NMR δ 1.07 (t, J = 7.2 Hz, 6H, CH_3), 4.13 (q, J = 7.2 Hz, 4H, CH_2), 7.1-7.6 (m, 14H, ArH); ^{13}C NMR δ 13.75, 61.88, 72.69, 121.17, 124.48, 126.57, 127.18, 127.48, 127.66, 128.37, 128.62, 129.48, 130.22, 134.19, 134.94, 140.50, 140.86, 144.70, 144.96, 168.16; IR 3053, 2980, 2934, 1724 (C=O), 1443, 1248, 1213, 1190, 1115, 1038, 764, 741, 700 cm^{-1}; Anal. Calculated for $C_{27}H_{24}O_4$: C, 78.62; H, 5.86. Found: C, 78.48; H, 5.92.

Compound 50

Compound 50 was isolated in 65% yield from the reaction of diethyl o-iodophenyl malonate and 3-hexyne when the reaction was run in the presence of sodium carbonate for 1 day at 80°C. ^{1}H NMR δ 0.85 (t, J = 7.2 Hz, 3H, C-CCCH$_3$), 1.01 (t, J = 7.2 Hz, 3H, C-CCCH$_3$), 1.07 (t, J = 7.2 Hz, 3H, C-CCCH$_3$), 1.22 (t, J = 7.2 Hz, 6H, CO_2CCH_3), 1.52 (d, J = 6.9 Hz, 3H, C-CCH$_3$), 1.85 (q, J = 7.2 Hz, 2H, C-CCH$_2$), 2.29 (q, J = 7.2 Hz, 2H, C-CCH$_2$), 2.58 (q, J = 7.2 Hz, 2H, C-CCH$_2$), 4.22 (q, J = 7.2 Hz, 4H, CO_2CH_2), 4.91 (s, 1H, CH(CO_2Et)$_2$), 5.62 (q, J = 6.9 Hz, 1H, C-CH), 7.3 (m, 4H, ArH); ^{13}C NMR δ 12.87, 12.45, 13.01, 14.25, 19.75, 26.25, 26.75, 27.01, 58.42, 62.01, 87.05, 88.45, 124.35, 125.63, 125.78, 127.14, 128.63,

129.01, 134.10, 137.92, 170.23, 205.18; IR 3023, 2985, 2928, 1975 (C=C=C), 1738 (C=O), 1432, 1225, 1203, 1185, 1119, 1046, 763 cm^{-1}; MS m/e 398 (M^+), 323 (M^+-(CO_2Et + H_2)).

Compound 51

Compound 51 was isolated in 23% yield from the reaction of diethyl o-iodophenyl malonate and 3-hexyne when the reaction was run in the presence of 5% triphenylphosphine and sodium carbonate for 1 day at 80°C. ^1H NMR δ 0.87 (t, J = 7.2 Hz, 3H, C=CCCH$_3$), 1.04 (t, J = 7.2 Hz, 3H, C=CCCH$_3$), 1.24 (t, J = 7.2 Hz, 6H, CO_2CCH_3), 4.24 (q, J = 7.2 Hz, 4H, CO_2CH_2), 7.1-7.4 (m, 4H, ArH); ^{13}C NMR δ 12.26, 12.67, 14.13, 26.29, 27.13, 59.02, 61.97, 124.35, 125.05, 125.53, 127.07, 128.76, 128.83, 134.53, 137.27, 170.57; IR 2985, 2928, 1722 (C=O), 1428, 1232, 1213, 1163, 1126, 1058, 752, 711 cm^{-1}; MS m/e 316 (M^+), 270 (M^+-EtOH), 242 (M^+-(EtOH + CO)), 196 (M^+-(EtOH + CO + EtOH)).

Compound 52

Compound 52 was isolated in 24% yield from the reaction of diethyl o-iodobenzyl malonate and 3-butyn-1-ol when the reaction was run in the presence of sodium carbonate for 1 day at 80°C. ^1H NMR δ 1.20 (t, J = 7.2 Hz, 6H, CH_3), 2.72 (t, J = 6.0 Hz, 2H, C≡CCH_2), 3.37 (d, J = 7.5 Hz, 2H, ArCH_2), 3.84 (t, J = 6.0 Hz, 2H, CH_2OH), 3.86 (t, J = 7.5 Hz, 1H, $CH(CO_2Et)_2$), 4.16 (q, J = 7.2 Hz, 4H, CO_2CH_2), 7.1-7.4 (m,

4H, ArH); IR 3500 (O-H), 3063, 2980, 2073 (C≡C), 1730 (C=O), 1466, 1447, 1369, 1300, 1227, 1153, 1096, 1043, 756 cm^{-1}.

Compound 53

Compound 53 was isolated in 72% yield from the reaction of diethyl o-iodobenzyl malonate and 3,3-dimethyl-1-butyne when the reaction was run in the presence of sodium carbonate for 1 day at 80°C. ^1H NMR δ 1.20 (t, J = 7.2 Hz, 6H, CO_2CCH_3), 1.33 (s, 9H, $C(CH_3)_3$), 3.33 (d, J = 7.8 Hz, 2H, $ArCH_2$), 3.91 (t, J = 7.8 Hz, 1H, $CH(CO_2Et)_2$), 4.15 (q, J = 7.2 Hz, 4H, CO_2CH_2), 7.1-7.3 (m, 4H, ArH).

General procedure for the arylannulation of alkenes

Palladium acetate (0.0028 g, 0.0125 mmole), base (1.25 mmole), aryl halide (0.25 mmole) and tetra-n-butylammonium chloride (0.0695 g, 0.25 mmole) were weighed into a 2 dram vial equipped with a magnetic stirring bar and septum inlet. DMF (1 ml) and alkene (1.25 mmole) were added sequentially via syringe. Stirring was continued at the appropriate temperature for the required amount of time. The reaction mixture was diluted with ether (10 ml), washed with saturated ammonium chloride (5 x 10 ml) and dried over sodium sulfate. Following removal of the solvents, the compounds were purified by flash column chromatography. Occasionally other solvents or phosphorus ligands were used, but the general

procedure remained the same. The following compounds were obtained from the above procedure.

Compound 56

Compound 56 was isolated in 32% yield from the reaction of diethyl o-iodophenyl malonate and indene when the reaction was run in the presence of 5% triphenylphosphine and sodium carbonate for 8 days at 80°C. ^{1}H NMR δ 1.18 (t, J = 7.2 Hz, 3H, CH_3), 3.55 (m, 2H, $ArCH_2C{=}C$), 3.62 (s, 2H, $ArCH_2$), 4.22 (q, J = 7.2 Hz, 2H, CO_2CH_2), 6.48 (t, J = 1.8 Hz, 1H, C=CH), 7.0-7.5 (m, 8H, ArH); ^{13}C NMR δ 15.23, 35.24, 55.01, 57.43, 122.61, 124.87, 125.32, 125.67, 125.98, 126.23, 126.54, 126.68, 126.98, 127.10, 127.64, 128.22, 134.21, 135.62, 168.73, IR 3001, 2980, 2921, 1742 (C=O), 1452, 1410, 1375, 1328, 1220, 1098 1028, 692 cm^{-1}; HRMS calculated for $C_{19}H_{18}O_2$ 278.13074, found 278.1299.

Compound 57

Compound 57 was isolated in 29% yield from the reaction of diethyl o-iodophenyl malonate and indene when the reaction was run in the presence of 5% triphenylphosphine and sodium carbonate for 8 days at 80°C. ^{1}H NMR δ 1.21 (t, J = 7.2 Hz, 6H, CH_3), 3.54 (m, 2H, $ArCH_2C{=}C$), 4.28 (q, J = 7.2 Hz, 4H, CO_2CH_2), 4.89 (s, ArCH), 6.47 (t, J = 1.8 Hz, 1H, C=CH), 7.0-7.5 (m, 8H, ArH); ^{13}C NMR δ 14.98, 33.62, 54.43, 61.23, 119.32, 124.75, 125.12, 125.59, 125.85, 126.17, 126.49,

126.74, 126.99, 127.34, 127.72, 128.17, 133.89, 134.03, 169.12, IR 3001, 2980, 2934 1740 (C=O), 1448, 1409, 1368, 1332, 1217, 1082, 1031, 714 cm^{-1}; HRMS calculated for $C_{22}H_{22}O_4$ 350.15186, found 350.1488.

Compound 58

Compound 58 was isolated in 82% yield from the reaction of diethyl o-iodophenyl malonate and cyclopentene when the reaction was run in the presence of 5% triphenylphosphine and sodium carbonate for 1 day at 80°C. ^1H NMR δ 1.26 (t, J = 7.2 Hz, 6H, CO_2CCH_3), 1.6-1.7 (m, 1H, $ArCCH_2$), 2.3-2.6 (m, 3H, $ArCCH_2$ and $C{=}CCH_2$), 4.09 (d, d of d, J = 2.1, 3.9 and 8.7 Hz, 1H, ArCHC=C), 4.22 (q, J = 7.2 Hz, 4H, CO_2CH_2), 5.07 (s, 1H, $CH(CO_2Et)_2$), 5.75 (d, d of d, J = 1.5, 3.9 and 5.4 Hz, 1H, C=CH), 5.88 (d of d, J = 2.1 and 5.4 Hz, 1H, C=CH), 7.1-7.4 (m, 4H). ^{13}C NMR δ 14.04, 32.41, 47.46, 53.72, 54.19, 61.77, 126.25, 127.12, 128.34, 129.25, 130.64, 132.53, 133.42, 144.52, 168.56; IR 2982, 2939, 1753 (C=O), 1494, 1464, 1367, 1302, 1263, 1217, 1146, 1096, 1034, 754 cm^{-1}; HRMS calculated for $C_{18}H_{22}O_4$ 302.15181, found 302.15208.

Compound 59

Compound 59 was isolated in 32% yield from the reaction of diethyl o-iodophenyl malonate and cyclohexene when the reaction was run in the presence of 5% triphenylphosphine and sodium carbonate for 6 days at 80°C. ^1H NMR δ 1.24 (t, J =

7.2 Hz, 6H, CO_2CCH_3), 1.5-1.8 (m, 3H, $ArCCH_2CH_2$), 2.3-2.6 (m, 3H, $ArCCH_2$ and $C{=}CCH_2$), 4.15 (d, d of d, J = 2.1, 3.9 and 8.7 Hz, 1H, ArCHC=C), 4.24 (q, J = 7.2 Hz, 4H, CO_2CH_2), 5.11 (s, 1H, $CH(CO_2Et)_2$), 5.68 (d, d of d, J = 1.5, 3.9 and 6.6 Hz, 1H, C=CH), 5.92 (d of d, J = 2.1 and 6.6 Hz, 1H, C=CH), 7.1-7.4 (m, 4H). ^{13}C NMR δ 13.78, 24.32, 31.76, 48.02, 53.54, 54.23, 62.15, 124.75, 125.89, 127.37, 129.02, 131.15, 132.48, 132.99, 140.14, 169.36; IR 2999, 2932, 1734 (C=O), 1482, 1462, 1375, 1297, 1257, 1212, 1156, 1088, 1015, 732 cm^{-1}; HRMS calculated for $C_{19}H_{24}O_4$ 316.16747, found 316.1632.

Compound 60

Compound 60 was isolated in 87% yield from the reaction of diethyl o-iodophenyl malonate and cyclooctene when the reaction was run in the presence of 5% triphenylphosphine and sodium carbonate for 1 day at 80°C. ^1H NMR δ 1.26 (t, J = 7.2 Hz, 6H, CH_3), 1.4-2.5 (m, 10H, aliphatic), 3.87 (m, 1H, ArCHC=C), 4.22 (q, J = 7.2 Hz, 4H, CO_2CH_2), 4.97 (s, 1H, $CH(CO_2Et)_2$), 5.7 (m, 2H, C=CH), 7.1-7.4 (m, 4H, ArH); ^{13}C NMR δ 14.14, 25.31, 25.38, 32.71, 41.54, 53.97, 54.09, 61.68, 61.80, 125.66, 125.98, 128.47, 128.63, 129.47, 129.79, 130.67, 130.95, 168.71; IR 2980, 2928, 2853, 1735 (C=O), 1447, 1367, 1302, 1258, 1215, 1144, 1096, 1025, 750, 671 cm^{-1}.

Compound 61

Compound 61 was isolated in 93% yield from the reaction of diethyl o-iodophenyl malonate and decene when the reaction was run in the presence of 5% triphenylphosphine and sodium carbonate for 1 day at 80°C. ^{1}H NMR δ 0.89 (t, J = 7.2 Hz, 3H, CH_3), 1.2-1.4 (m, 18H, aliphatic and CO_2CCH_3), 2.22 (q, J = 7.2 Hz, 2H, $C-CCH_2$), 4.22 (q, J = 7.2 Hz, 4H, CO_2CH_2), 4.98 (s, 1H, $CH(CO_2Et)_2$), 6.04 (t of d, J = 6.9 and 15.6 Hz, 1H, C=CH), 6.56 (d, J = 15.6 Hz, 1H, ArCH=C), 7.2-7.5 (m, 4H, ArH); ^{13}C NMR δ 14.12, 14.33, 23.56, 29.33, 29.53, 29.62, 31.93, 33.35, 53.54, 54.45, 61.76, 126.66, 127.07, 128.09, 128.15, 129.00, 129.25, 130.05, 135.65, 168.43; IR 2957, 2928, 1757 (C=O), 1466, 1367, 1302, 1259, 1209, 1146, 1096, 1034, 968, 750 cm^{-1}.

Compound 62

Compound 62 was isolated in 45% yield from the reaction of diethyl o-iodobenzyl malonate and indene when the reaction was run in the presence of sodium carbonate for 1 day at 80°C. ^{1}H NMR δ 1.14 (t, J = 7.2 Hz, 6H, CH_3), 3.43 (d, J = 7.5 Hz, 2H, $ArCH_2$), 3.65 (t, J = 7.5 Hz, 1H, $CH(CO_2Et)_2$), 3.78 (br s, 2H, $ArCH_2C=C$), 4.08 (q, J = 7.2 Hz, 4H, CO_2CH_2), 6.94 (br s, ArC=CHAr), 7.2-7.4 (m, 8H, ArH); ^{13}C NMR δ 13.98, 32.54, 52.54, 52.38, 61.26, 120.31, 121.08, 122.98, 123.51, 123.82, 124.90, 126.17, 126.24, 126.82, 127.89, 129.96, 132.02, 135.30, 136.26, 168.88; IR 2982, 2928, 1751 (C=O),

1453, 1374, 1298, 1248, 1212, 1154, 1086, 1026, 972, 734 cm^{-1}.

Compound 63

Compound 63 was isolated in 51% yield from the reaction of diethyl o-iodobenzyl malonate and indene when the reaction was run in the presence of sodium carbonate for 1 day at 80°C. ^1H NMR δ 1.14 (t, J = 7.2 Hz, 6H, CH_3), 3.44 (d, J = 7.5 Hz, 2H, $ArCH_2$), 3.66 (t, J = 7.5 Hz, 1H, $CH(CO_2Et)_2$), 3.78 (br s, 2H, $ArCH_2C{=}C$), 4.07 (q, J = 7.2 Hz, 4H, CO_2CH_2), 6.18 (br s, $ArC{=}CHAr$), 7.2-7.4 (m, 8H, ArH); ^{13}C NMR δ 14.01, 38.52, 52.51, 52.97, 61.44, 120.28, 121.118 122.98, 123.49, 124.95, 126.13, 126.30, 126.85, 127.76, 129.99, 132.12, 135.31, 136.26, 144.21, 168.72; IR 2982, 2928, 1752 (C=O), 1451, 1374, 1298, 1248, 1209, 1154, 1086, 1026, 976, 724 cm^{-1}.

Compound 64

Compound 64 was isolated in 20% yield from the reaction of diethyl o-iodobenzyl malonate and benzofuran when the reaction was run in the presence of sodium carbonate for 1 day at 80°C. ^1H NMR δ 1.29 (t, J = 7.2 Hz, 6H, CH_3), 3.56 (d, J = 7.5 Hz, 2H, $ArCH_2$), 3.78 (t, J = 7.5 Hz, 1H, $CH(CO_2Et)_2$), 4.13 (q, J = 7.2 Hz, 4H, CO_2CH_2), 6.97 (s, 1H, C=CH), 7.3-7.7 (m, 8H, ArH); ^{13}C NMR δ 14.32, 32.18, 45.16, 56.12, 109.57, 118.52, 120.12, 123.15, 123.45, 123.69,

124.57, 125.46, 125.97, 126.15, 126.87, 127.45, 129.32, 140.03, 167.54; IR 2976, 2932, 1743 (C=O), 1447, 1374, 1252, 1209, 1145, 1092, 1019, 968, 732 cm^{-1}.

Compound 65

Compound 65 was isolated in 86% yield from the reaction of diethyl o-iodobenzyl malonate and cyclopentene when the reaction was run in the presence of 5% triphenylphosphine and sodium carbonate for 1 day at 80°C. ^1H NMR δ 1.26 (t, J = 7.2 Hz, 6H, CO_2CCH_3), 1.6-1.7 (m, 1H, $ArCCH_2$), 2.3-2.6 (m, 3H, $ArCCH_2$ and $C=CCH_2$), 3.24 (d, J = 7.8 Hz, 2H, $ArCH_2$), 3.76 (t, J = 7.8 Hz, 1H, $CH(CO_2CH_2)$, 4.09 (d, d of d, J = 2.1, 3.9 and 8.7 Hz, 1H, ArCHC=C), 4.22 (q, J = 7.2 Hz, 4H, CO_2CH_2), 5.75 (d, d of d, J = 1.5, 3.9 and 5.4 Hz, 1H, C=CH), 5.88 (d of d, J = 2.1 and 5.4 Hz, 1H, C=CH), 7.1-7.4 (m, 4H).

Compound 66

Compound 66 was isolated in 46% yield from the reaction of diethyl o-iodobenzyl malonate and cyclohexene when the reaction was run in the presence of 5% triphenylphosphine and sodium carbonate for 6 days at 80°C. ^1H NMR δ 1.20 (t, J = 7.2 Hz, 6H, CH_3), 1.2-1.4 (m, 2H, aliphatic), 1.81 (q, J = 5.4 Hz, 2H, $ArCCH_2$), 2.2-2.3 (m, 2H, $C=CCH_2$), 3.02 (h, J = 5.1 Hz, 1H, ArCHC=C), 3.28 (d, J = 7.8 Hz, 2H, $ArCH_2$), 3.58 (t, J = 7.8 Hz, 1H, $CH(CO_2Et)_2$), 4.14 (q, J = 7.2 Hz, 4H, CO_2CH_2), 5.8 (m, 2H, C=CH), 7.1-7.4 (m, 2H, ArH); ^{13}C NMR δ

14.04, 26.30, 30.03, 31.60, 33.45, 35.21, 53.46, 61.50, 125.80, 126.39, 126.95, 127.00, 127.34, 129.78, 134.81, 145.56, 168.91; IR 3002, 2930, 1749 (C=O), 1491, 1447, 1369, 1333, 1298, 1225, 1150, 1097, 1051, 1032, 756 cm^{-1}.

Compound 67

Compound 67 was isolated in 86% yield from the reaction of diethyl o-iodobenzyl malonate and cyclooctene when the reaction was run in the presence of 5% triphenylphosphine and sodium carbonate for 1 day at 80°C. ^1H NMR δ 1.24 (t, J = 7.2 Hz, 6H, CH_3), 1.4-2.6 (m, 10H, aliphatic), 2.94 (m, 1H, ArCHC=C), 3.27 (d, J = 7.8 Hz, 2H, $ArCH_2$), 3.54 (t, J = 7.8 Hz, 1H, $CH(CO_2Et)_2$), 4.16 (q, J = 7.2 Hz, 4H, CO_2CH_2), 5.74 (m, 2H, C=CH), 7.0-7.2 (m, 4H, ArH); ^{13}C NMR δ 14.04, 25.22, 26.01, 31.67, 32.00, 32.92, 35.23, 38.18, 40.88, 53.24, 125.19, 126.34, 127.02, 128.70, 129.31, 129.88, 130.54, 134.39, 168.86; IR 2982, 2930, 1751 (C=O), 1447, 1369, 1298, 1269, 1223, 1175, 1096, 1049, 752 cm^{-1}.

Compound 68

Compound 68 was isolated in 81% yield from the reaction of diethyl o-iodobenzyl malonate and decene when the reaction was run in the presence of 5% triphenylphosphine and sodium carbonate for 6 days at 80°C. ^1H NMR δ 0.86 (t, J = 6.9 Hz, 3H, CH_3), 1.23 (t, J = 7.2 Hz, 6H, CO_2CCH_3), 1.3-1.6 (m, 12H, aliphatic), 1.9 (m, 1H, $C=CCH_2$), 2.23 (q, J = 7.2 Hz, 1H,

C-CCH_2), 3.28 (d, J = 7.5 Hz, 2H, $ArCH_2$), 3.64 (t, J = 7.5 Hz, 1H, $CH(CO_2Et)_2$), 4.13 (q, J = 7.2 Hz, 4H, CO_2CH_2), 6.11 (t of d, J = 7.2 and 15.6 Hz, 1H, ArC-CH), 6.62 (d, J = 15.6 Hz, 1H, ArCH-C), 7.1-7.3 (m, 3H, ArH), 7.55 (d of d, J = 0.9 and 7.2 Hz, 1H, ArH); ^{13}C NMR δ 14.01, 22.69, 29.19, 29.29, 29.37, 29.52, 31.90, 32.16, 33.35, 52.70, 53.04, 61.38, 126.18, 126.70, 126.79, 127.07, 129.98, 133.87, 134.52, 137.08, 168.89; IR 2957, 2928, 1751 (C=O), 1454, 1369, 1300, 1269, 1227, 1177, 1096, 1034, 752 cm^{-1}.

Compound 69

Compound 69 was isolated in 22% yield from the reaction of diethyl o-iodobenzyl malonate and isopropenylcyclopropane when the reaction was run in the presence of sodium carbonate for 5 days at 60°C. ^1H NMR δ 1.16 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 1.22 (t, J = 7.2 Hz, 3H, CO_2CCH_3), 1.32 (s, 3H, CH_3), 1.63 (d of d, J = 1.5 and 6.3 Hz, 3H, C-CCH_3), 3.00 (d, J = 17.4 Hz, 1H, $ArCH_2$), 3.09 (d, J = 17.4 Hz, 1H, $ArCH_2$), 3.30 (d, J = 17.1 Hz, 1H, $ArCH_2$), 3.38 (d, J = 17.1 Hz, 1H, $ArCH_2$), 4.1 (m, 4H, CO_2CH_2), 5.83 (q of d, J = 6.3 and 15.6 Hz, 1H, C-CH), 5.84 (q of d, J = 1.5 and 15.6 Hz, 1H, C-CH); 7.1 (m, 4H, ArH); ^{13}C NMR δ 13.98, 14.21, 14.25, 19.65, 32.12, 34.12, 45.57, 46.12, 48.32, 59.87, 119.10, 120.32, 124.56, 125.67, 127.01, 127.85, 132.12, 140.25, 168.79, 170.10; IR 2987, 2934, 1737 (C=O), 1352, 1275, 1225, 1165, 1075, 1034, 752 cm^{-1}.

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GENERAL SUMMARY

The work in this dissertation demonstrated the versatility and the tolerance of palladium-based methodoloqy. The first section discussed the exploration of a single reaction. From this reaction two unique σ-vinylpalladium compounds were isolated. The reactivity of these compounds was explored. The last two sections examined a series of reactions leading to the formation of two carbon-carbon bonds in a single step. Section 2 discussed the arylannulation of conjugated dienes, whereas Section 3 discussed the arylannulation of non-conjugated dienes, allenes, alkynes and olefins.

The reactivity of the two σ-vinylpalladium compounds isolated in Section 1 needs further exploration to enhance our understanding of certain palladium-catalyzed reactions. Additional studies of the arylannulation discussed in Sections 2 and 3 could lead to new ring systems which may be important in the synthesis of natural products.

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