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Photostimulated tert-butylations of a,b-unsaturated nitriles, cyclizations of 1,6-dienes and olefinic nitriles, and homolytic aromatic alkylations

Ping Chen
Iowa State University

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Photostimulated *tert*-butylations of α,β–unsaturated nitriles, cyclizations of 1,6-dienes and olefinic nitriles, and homolytic aromatic alkylations

by

Ping Chen

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Graduate College
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This is to certify that the Doctoral dissertation of

Ping Chen

has met dissertation requirements of Iowa State University

Signature was redacted for privacy.

Major Professor

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For the Major Program

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For the Graduate College

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ABSTRACT

α,β–Unsaturated nitriles undergo radical chain addition reactions with *tert*-butylmercury halides in the presence of iodide ions. The mercury adduct products are formed in high yields and can be converted to the reductive alkylation products with NH_4^+ or by $NaBH_4$. The addition reaction involves the attack of the adduct radical upon the ate complex, *t*-$BuHgI_2^-$. Proton donors also promote the reactions by protonating the adduct radicals to form keteniminyl radicals cations which accept an electron from *t*-$BuHgI_2^-$ to produce the alkylation products. Acrylonitrile, crotononitrile and fumaronitrile give nearly quantitative yields of the products in DMSO via photolysis or even in the dark at room temperature. Three-component condensation reactions occur for mixtures of acrylonitrile/*t*-BuHgI and reagents such as CH_2=$CHCH_2Br$ or CH_2=$CHCH_2SPh$ or upon further reaction of the mercury adducts with I_2, NBS, PhCH=CHI, PhSeSePh, or iminium ions.

Cyclization reactions of 1,6-dienes with *t*-BuHgX have been investigated. A radical chain process provides the cyclized organomercurials via 5-exo mode cyclization. *Cis* and *trans* isomeric cyclized mercury compounds are obtained with the *cis*-isomers preferred. The measured initial kinetic chain length for the substrates are 3-10. Photolysis of the mercury compounds with PhSSPh leads to the corresponding sulfides. Allyl vinylphosphonates react with *t*-BuHgX very readily. However, the *cis/trans* product ratio is 1:1.

Alkylmercury halides are very suitable reagents for alkylation of electron-deficient aromatics. In the presence of Dabco (1,4-diazabicyclo[2.2.2]octane), the disubstituted benzenes undergo a regioselective radical alkylation reaction. For 1,3-dicyanobenzene, the initial kinetic chain length is 22 and not only the mono-alkylated but also the dialkylated product is produced in high yield. With larger groups *meta* or *para* to a cyano group such

as -CHO and -CO_2Et, the second alkylation is inhibited. Dabco promotes the chain reaction by removing a proton from adduct cyclohexadienyl radical. The radical anion formed is oxidized by *t*-BuHgX to afford the product and regenerate *t*-Bu•.

GENERAL INTRODUCTION

Free radical chemistry has undergone rapid development within the last two decades. During earlier years, free radicals had been known to be intermediates involved in a large number of chemical reactions. Although the fundamental concepts about reactivity and selectivity and knowledge of mechanistic and kinetic aspects were well established,[1] radical chemistry, as a whole, remained a limited area, especially for synthesis. Now, however, radical chemistry has evolved to such a stage that chemists can easily design and perform the preparation or synthesis of molecules of interest via a radical approach by control of radical processes based on radical properties, such as electrophilic, nucleophilic or capto-dative properties, etc.[2] The majority of free radical reactions which are of interest to synthetic organic chemists are chain processes and they involve three steps: (1) initiation; (2) propagation; (3) termination. (Non-chain reactions often deal with redox processes. For example, manganese(III)-based method[3] uses a stochiometric amount of oxidant to generate radicals.)

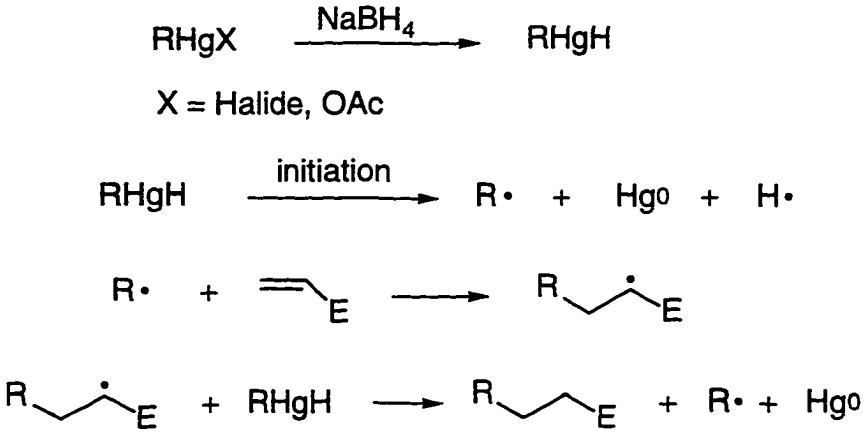
Azo compounds or peroxides are the most frequently used initiators to start a chain process, whereas thermal and photolytic initiation are alternative choices, depending on the nature of the reactions. The propagation step can be radical addition, elimination, direct substitution or electron transfer reaction in which a new radical is formed. The termination step includes radical coupling or disproportionation leading to stable products.

Organomercury compounds are among the oldest organometallic compounds known and can be useful in organic synthsis. Due to their stability and availability, organomercury compounds are often used as reagents or intermediates, for example in the mercuration of aromatic compounds and solvomercuration of alkenes.[4] On the other hand, the weakness of the C-Hg bond and the Hg-H bond, and the ease of oxidation or reduction of Hg(II) species, renders organomercury chemistry an important field for radical and radical ion processes.[5]

Over the last decade, Russell developed a series of radical reactions in which RHgX or R_2Hg participates in the propagation step of a chain process.[6-10] It has been shown that RHgX can react by mechanisms involving neutral radicals, radical cations or radical anions, depending on the demand of the substrates.

The metal hydride method, developed by Giese for mercury compounds, [11] is one of the best studied radical chain processes. In the metal hydride method, the rate of addition of an alkyl radical to the substrate must match the rate of hydrogen transfer from the metal hydride. In the mercury method, the mercury hydride generated by the reaction of an alkylmercury halide with borohydride, decomposes to give an alkyl radical which adds to activated alkenes, such as acrylonitrile, vinyl ketones, acrylates, fumaronitrile or maleic anhydrides (Scheme 1).[12] For those alkenes with lower reactivities, such as styrene, vinylidene chloride and crotonic ester, low yields of alkylation will be obtained because the mercury hydrides are so reactive that the alkylation can not compete with the direct reduction of the alkyl radicals. The advantage of tin hydrides is that they are about ten times less reactive than mercury hydride as hydrogen donor. Therefore tin hydride nearly always gives better results.[13]

Scheme 1



The Russell group has developed a number of new radical chain processes involving alkylmercury halides. There are basically four different types of processes several of which involve electron transfer either to RHgX or from $RHgI_2^-$.

(A) Homolytic substitution reactions (S_H2)[6]

$$R^\bullet + Y\text{-}Q \longrightarrow R\text{-}Y + Q^\bullet$$

$$Q^\bullet + RHgX \longrightarrow QHgX + R^\bullet$$

Y-Q = RSSR, PhSeSePh, PhTeTePh, $PhSeSO_2Ph$, $PhSO_2Cl$, etc.

Under photolytic conditions, or with initiation by AIBN at 80 °C, direct homolytic substitution can occur at a heteroatom Y in compounds YQ as listed above.

(B) $S_{RN}1$ type reactions[7]

One of the important properties of RHgX is that it can undergo $S_{NR}1$ type reaction with nucleophiles such as $(Me)_2C{=}NO_2^-$ and Ph_2P^- (Scheme II). As a propagation step, $RNu^{\bullet -}$ readily transfers an electron to the alkylmercury halide to regenerate the alkyl radical.

Scheme 2

$$R^\bullet + Nu^- \longrightarrow RNu^{\bullet -}$$

$$RNu^{\bullet -} + RHgX \longrightarrow RNu + R^\bullet + Hg^0 + X^-$$

(C) Addition-elimination[8]

If the alkene carries a suitable substitute Q (e.g., Bu_3Sn, HgCl, I, SO_2Ph), the addition of the alkyl radical can be followed by a geminal elimination of that substitutent, resulting in overall substitution.

$$R'CH{=}CHQ + RHgX \longrightarrow R'CH{=}CHR + QHgX \text{ (or } QX + Hg^0 \text{)}$$

Another type of elimination occurs when addition of alkyl radicals to allyl or propargyl derivatives forms adduct radicals which undergo β–elimination with substituents such as halogen, PhS, $PhSO_2$, Bu_3Sn, HgCl, O_2CR, O_3SAr, OPh, $OSiMe_3$, or OH to form propene or allene (Scheme 3).[8h]

Scheme 3

$$R\bullet + CH_2{=}CHCH_2A \longrightarrow RCH_2\dot{C}HCH_2A$$

$$RCH_2\dot{C}HCH_2A \longrightarrow RCH_2CH{=}CH_2 + A\bullet$$

$$A\bullet + RHgCl \longrightarrow AHgCl + R\bullet$$

(D) Addition followed by electron transfer

An electron transfer process is also involved in other chain reactions. RHgX acts as either an electron donor or acceptor, depending on the structures of the substrates.

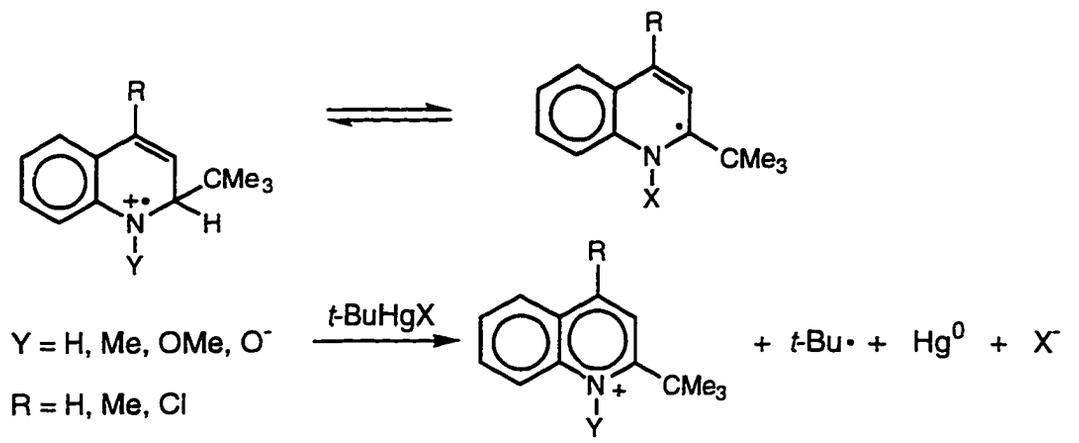
1. Electron transfer to RHgX[9]

This process occurs with α,β-unsaturated carbonyl compounds under basic condition. The radical anion, generated from deprotonation of the radical adduct by a base, such as Dabco, transfers an electron to RHgX to regenerate the alkyl radical (Scheme 4). Another example is the reaction of quinoline cations with *tert*-butylmercury halides or the oxidation of 1,1-di-(*p*-anisyl)ethyl radicals.

Scheme 4

$$YC(O)CH(R)\dot{C}HC(O)Y \xrightarrow[-H+]{\text{Dabco}} [YC(O)C(R){=}CHC(O)Y]^{\bullet-} \xrightarrow{RHgX}$$

$$YC(O)C(R){=}CHC(O)Y + R\bullet + Hg^0 + I^-$$



$$t\text{-BuCH}_2\dot{C}(C_6H_4OMe\text{-}p)_2 \xrightarrow{t\text{-BuHgCl}} t\text{-BuCH}_2\overset{+}{C}(C_6H_4OMe\text{-}p)_2 + R + Hg^0 + Cl^-$$

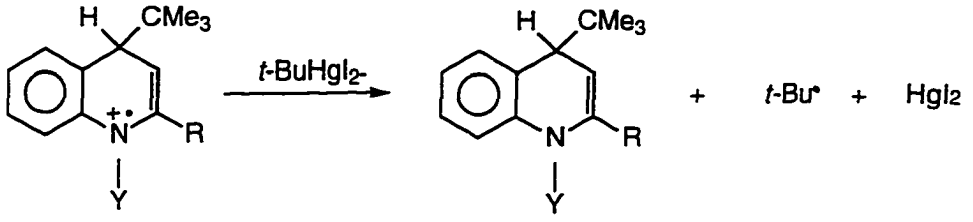
$$t\text{-BuCH}_2\overset{+}{C}(C_6H_4OMe\text{-}p)_2 \xrightarrow{-H^+} t\text{-BuCH=C}(C_6H_4OMe\text{-}p)_2$$

2. An electron transfer from RHgX (or from $RHgI_2^-$)[10]

This process often involves nitrogen centered radical cations. Strong promotion of the reaction by an acid is often observed in this case. For example, reduction of the amine radical cations which are produced from addition of *tert*-butyl radical and protonation occurs readily by *t*-$BuHgI_2^-$, the ate complex.

$$R^1CH{=}NR^2 \xrightarrow{H^+} R^1CH{=}\overset{+}{N}HR^2 \xrightarrow{R\bullet} R^1CH(R)\overset{+\bullet}{N}HR^2 \xrightarrow{RHgI_2^-}$$

$$R^1CH(R)NHR^2 + R\bullet + HgI_2$$

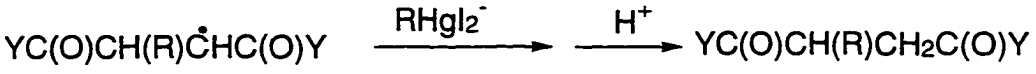


Y = H, Me, OMe, O-

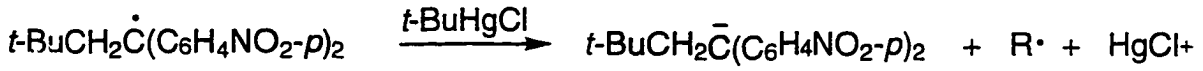
R = H, Me, Cl

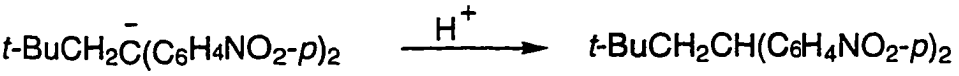
RHgX or $RHgI_2^-$ can also transfer an electron to a neutral acceptor radicals to produce a carbanion which is protonataed to form reductive product (Scheme 5).

Scheme 5



Another example of this type of reaction is shown below:



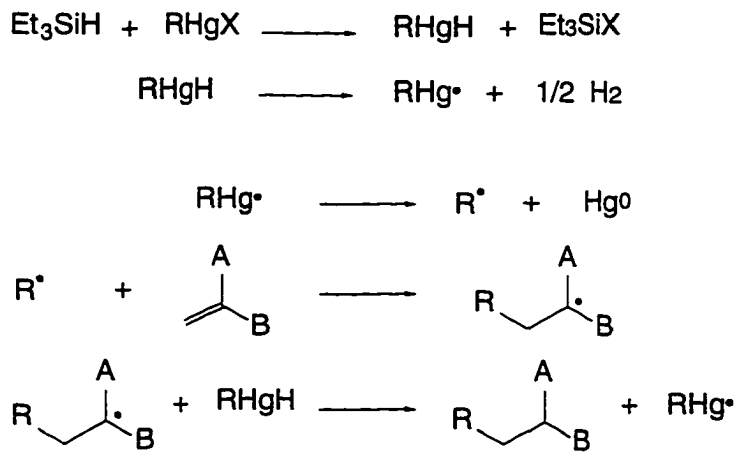


0CHAPTER I. *TERT*-BUTYLATIONS OF α,β-UNSATURATED NITRILES BY *TERT*-BUTYLMERCURY HALIDES AND THREE-COMPONENT CONDENSATION REACTIONS

Introduction

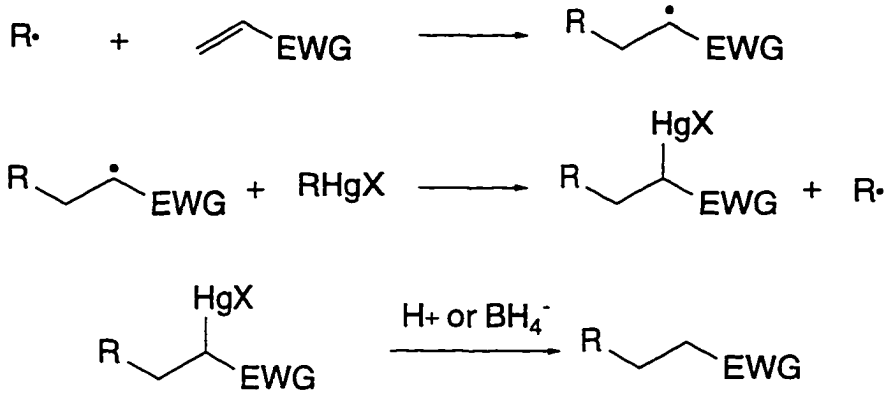
The addition of a radical to a π-bond, to form a carbon-carbon single bond, is a fundamental reaction of organic radicals. However, application in synthesis of non-polymer molecules evolved slowly.[14,15] Giese developed the metal hydride method (Bu_3SnH and RHgH) which can be employed in alkylation of alkenes.[11] Because of the high reactivity of Bu_3SnH and RHgH, a serious side reaction is the trapping of R• to form RH. This kind of drawback has been largely overcome by the use of silyl hydrides in place of $NaBH_4$ to convert RHgCl slowly into RHgH.[16,17] The combination of RHgX and silyl hydrides such as Et_3SiH or $PhSiH_3$ in DMSO solution is an excellent system for the reductive alkylation of many alkenes substituted with electron withdrawing groups such as CO_2Et, CN, COPh, $(EtO)_2P(O)$ and SO_2Ph (Scheme 6). In this case, the adduct radical is trapped by RHgH to form the reductive product and regenerate R•.

Scheme 6



For some substrates (EWG = SO_2Ph, $(EtO)_2P(O)$), radical chain reaction occurs without a hydride (Scheme 7). The intermediate *t*-$BuCH_2CHP(O)(OEt)_2$• is an acceptor radical which reacts readily with *t*-BuHgCl with $k>10^5$ $M^{-1}s^{-1}$.[10b] The kinetic chain length measured in DMSO by the $(t\text{-Bu})_2NO$• method is 116, suggesting it is good chain reaction.[9a] The resulting mercurial can be reduced by $NaBH_4$ or cleaved by I_2 in high overall yields.

Scheme 7



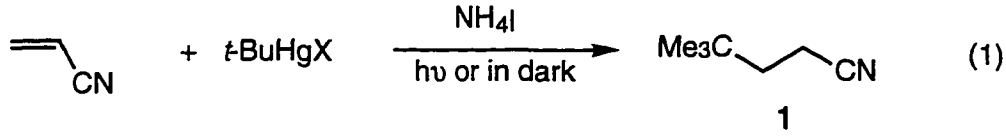
Iodide ion has been shown to promote the reactions of alkenes CH_2=CH(EWG) with RHgX.[9c] It was initially assumed that an electron transfer from *t*-$BuHgI_2^-$ to the adduct radical was involved. With EWG = $(EtO)_2P(O)$, the kinetic chain length increased to as large as 500. Telomerization is not observed when a proton donor, such as NH_4I or MeOH, is present. As shown in Scheme 7, the mercurial can also be cleaved ionically by a proton.

Results and Discussion

tert-Butylations of α,β–Unsaturated Nitriles by *tert*-Butylmercury Halides Promoted by Iodide Ion

Acrylonitrile

Acrylonitrile reacts readily with *t*-BuHgX in the presence of KI with sunlamp irradiation or in the dark. In the presence of NH_4I, the *t*-butylation product **1** was obtained in high yield. Preliminary work shows that iodide ion has a significant effect on promotion of the reaction (Table 1) while the absence of a proton donor dramatically reduced the yield of the alkylation product (**1**).



When NH_4Cl is used in place of NH_4I, the yield of **1** is only 26% with sunlamp irradiation for 1 h. In contrast. the yield of 61% is obtained with NH_4I in the same conditions. A large excess of NH_4I and long reaction time can give a very high yield, e.g. 95% with 4 equivalent of *t*-BuHgI and 20 equivalent of NH_4I in 12 h of photolysis. Other protons donor such as PTSA (*p*-toluene sulfonic acid), causes a decrease in yield due to side reactions. Reactions in dark are also observed for acrylonitrile with *t*-BuHgX/NH_4I or *t*-BuHgX/KI.

Workup of the reaction mixture of acrylonitrile with *t*-BuHgX/KI by $NaBH_4$ also gives the *tert*- butylation product **1**. Thus, the reaction of acrylonitrile with 2 eq of *t*-BuHgX/KI and 4 eq of KI in dark for 3 h followed by treatment with $NaBH_4$ affords **1** in 65%. Therefore, an intermediate must be formed and it is believed to be *t*-$BuCH_2CH(HgI)CN$ (**2**). In the absence of proton or hydride donors, **2** should be stable. To get a conclusive result, ^1H NMR monitoring was utilized to follow the reactions in DMSO-d_6 solution.

Table 1. *t*-Butylation of CH=CHCN with *t*-BuHgCl in DMSO[a]

Entry	*t*-BuHgCl	Additive	Conditions	Yield of **1**[b]
1	4	NH_4Cl (8)	hυ, 1 h	26
2	4	NH_4I(8)	hυ, 1 h	61
3	2	NH_4I(4)	hυ, 1 h	39
4	4	NH_4I(8)	hυ, 4 h	82
5	4	NH_4I(8)	dark, 1 h	78
6	4	NH_4I(8), H_2O(22)	hυ, 5 h	83
7	4	NH_4I(8), D_2O(22)	hυ, 5 h	89[c]
8	4	NH_4I(20)	hυ, 12 h	95
9	4	KI(8), PTSA(10)	hυ, 12 h	42
10	4	KI(8)	hυ, 40 min	21
11	4	KI(8)	dark, 40 min	72[d]
12	2	KI(4)	dark, 3 h	65[e]

a. Reaction of 0.1 mmol acrylonitrile with *t*-BuHgCl in 4 mL of DMSO with 275W sunlamp irradiation at 35-40 °C.

b. By ^1H NMR with toluene(0.1 mmol) as internal standard. After workup with aqueous $Na_2S_2O_3$.

c. *t*-$BuCH_2CH(D)CN$

d. Workup by NH_4I for 1 h before treatment with aqueous $Na_2S_2O_3$ and extraction.

e Workup with $NaBH_4$

In all cases, the ^1H NMR spectra are clean and are interpreted easily. For the *t*-BuHgX/KI system, two new peaks for the *t*-butyl group at δ=0.92 and 0.94 are observed in dark reactions. At first, the peak at δ=0.92 appears as soon as the reactants are mixed and initially increases with time. The second peak δ=0.94 then shows up while the first peak gets to its climax, decreases slowly, and fades finally. The details of other signals of interest are not easily recognized because of the presence of more than one species and the overlapping of

peaks. The molar ratio of the reactants can be adjusted in such a way (acrylonitrile : *t*-BuHgI : KI = 2 : 1 : 2) that the first peak is persistant and the appearance of the second peak is slowed

t-$BuCH_2CH(HgI)CN$ ($(t\text{-}BuCH_2CHCN)_2Hg$)

2 **3**

$$\mathbf{2, 3} \xrightarrow[\text{or } H^+]{NaBH_4} t\text{-}BuCH_2CH_2CN \qquad (2)$$

down. The mercurial intermediate **2** (δ for *t*-Bu = 0.92) as a stable species is confirmed by ^1H NMR interpretation of the three groups of ^1H NMR peaks each of which is a doublet of doublet. The mercurial **3** is quite stable and can be isolated in nearly quantitative yield by the reaction with *t*-BuHgI/KI with sunlamp irradiation in DMSO and fully characterized. Treatment of **3** by $NaBH_4$ gives an essentially quantitative yield of **1**.

Iodide ion is critical for the chain reaction.[18] No reaction is observed without KI in the dark. With 2 equiv. of *t*-BuHgI and 2 equiv. of KI, 10% of acrylonitrile remains unreacted in 2 h while it is all consumed in only 10 min with 8 eq of KI at room temperature. ^1H NMR monitoring was also conducted for the *t*-$BuHgX/NH_4I$ reaction system. In this case, besides **2** and **3**, the reduction product **1** was also detected (Table 2). The reactions are typically inhibited by 10 mol % of $(t\text{-}Bu)_2NO\bullet$ for more than 12 h with either the *t*-BuHgI/KI or the *t*-$BuHgI/NH_4I$ system, proving that the dark reactions proceed by a chain initiated by the thermal production of *t*-Bu•. The chain propagation reactions leading to **1** are formulated in Scheme 8.

Scheme 8

$$CH_2{=}CHCN + t\text{-}Bu\bullet \longrightarrow t\text{-}BuCH_2\dot{C}HCN$$

$$t\text{-}BuCH_2\dot{C}HCN + t\text{-}BuHgI_2^- \longrightarrow t\text{-}BuCH_2CH(HgI_2^-)CN + t\text{-}Bu\bullet$$

The conversion of mercurial **2** to **3** is faster either with sunlamp irradiation or at higher temperature (40 °C). A radical process may be responsible for the conversion as illustrated in Scheme 9.

Scheme 9

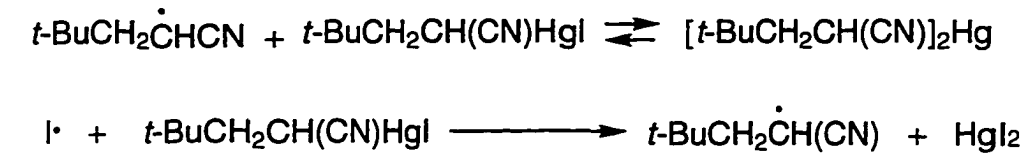


Table 2. Reaction of CH_2=CHCN(AN) with *t*-BuHgX in Me_2SO-d_6[a]

	Mol equiv.			%Yield[b]			
AN(M)	*t*-BuHgI	M^+I^-	Conditions	RH	RHgI	R_2Hg	AN
0.1	2	KI(2)	5 min, dark	0	17	0	23
0.1	2	KI(2)	15 min, dark	0	32	<2	64
0.1	2	KI(2)	55 min, dark	0	28	34	35
0.1	2	KI(2)	2 h, dark	0	10	80	10
0.1	2	KI(2)	5 h, dark	0	0	100	0
0.1	2	KI(8)	10 min, dark	0	95	5	0
0.1	2	KI(8)	40 min, dark	0	77	23	0
0.1	2	NH_4I(8)	5 min, dark	38	49	13	0
0.1	2	NH_4I(8)	30 min, dark	70	14	16	0
0.1	2	NH_4I(8)	8 h, dark	92	0	8	0
0.1	2	NH_4I(8),D_2O(60)	50 min, dark	80[c]	5	12	0
0.1	4	KI(4)	20 min, dark	0	2	98	0
0.2	2	KI(4)	5 min, dark	0	98	0	10
0.2	2	KI(4)	30 min, dark	0	70	30	0
0.2	2	KI(4)	3.5 h, dark	0	5	95	0
0.2	2	NH_4I(2), KI(6)	5 mni, dark	24	67	9	0
0.2	2	NH_4I(2), KI(6)	10 min, dark	27	61	11	0

Table 2. (continued)

0.2	2	NH_4I(2), KI(6)	15 min, dark	32	53	15	0
0.2	2	NH_4I(2), KI(6)	30 min, dark	45	37	18	0
0.2	2	NH_4I(4), KI(4)	5 min, dark	22	40	8	30
0.2	2	NH_4I(4), KI(4)	10 min, dark	30	51	9	10
0.2	2	NH_4I(4), KI(4)	15 min, dark	38	48	14	0
0.2	2	NH_4I(4), KI(4)	30 min, dark	53	32	14	0
0.2	2	NH_4I(8)	5 min, dark	39	41	10	10
0.2	2	NH_4I(8)	10 min, dark	55	38	7	0
0.2	2	NH_4I(8)	15 min, dark	63	29	8	0
0.2	2	NH_4I(8)	30 min, dark	74	16	10	0
0.2	1.1	KI(2 or 8)	10 min, hυ	0	2	98	0
0.2	1.1	KI(8)	10 min, dark, 40 °C	78	17	5	0
0.2	1.1	KI(8)	30 min, dark, 40 °C	0	18	82	0
0.2	1.1	NH_4I(8)	10 or 20 min, hυ	95	0	5	0
0.2	1.1	NH_4I(8)	10 min, dark, 40 °C	78	17	5	0
0.2	1.1	NH_4I(8)	30 min, dark, 40 °C	92	4	4	0

[a] At 25 °C for dark reaction, 35-40 °C for reaction irradiated with a 275W sunlamp.
[b] ^{1}H NMR yield with toluene as an internal standard on a 0.1-0.2 mmol scale; R=*t*-$BuCH_2CH(CN)$. [c] *t*-$BuCH_2CHDCN$.

It is worthwhile to note that from ^{1}H NMR monitoring, **1** is formed rather soon in the presence of NH_4I. It had been found [10c,19] that proton donors such as PTSA increase the yield of **1** and decrease the dimerization or oligomerization products in the *t*-BuHgX/KI system by following Scheme 10. The ketenimine intermediate *t*-$BuCH_2CH{=}C{=}NH$ had been trapped by EtOH to form ethyl 4,4-dimethylpentanoate.[19] In the present work it was found that for *t*-BuHgI/NH_4I, Scheme 10 is followed, although NH_4^+ is a weaker proton donor than PTSA. The protonation effect by NH_4^+ via Scheme 10 is verified by plotting of the ratio of **1/2** against the concentration of NH_4^+.[20] Extrapolation of the curves of Figure 1 to $t = 0$

Scheme 10

$$t\text{-BuCH}_2\dot{C}\text{HCN} + H^+ \rightleftharpoons t\text{-BuCH}_2\text{CH=C=NH}^{\bullet+}$$

$$t\text{-BuCH}_2\text{CH=C=NH}^{\bullet+} + t\text{-BuHgI}_2^- \rightarrow t\text{-BuCH}_2\text{CH=C=NH} + \text{HgI}_2 + t\text{-Bu}\bullet$$

$$t\text{-BuCH}_2\text{CH=C=NH} \longrightarrow t\text{-BuCH}_2\text{CH}_2\text{CN}$$

clearly demonstrates that the concentration of NH_4^+ controls the competition between the processes leading to **1** and **2**. As expected, the ratio of **1/2** increases as the concentration of NH_4^+ increases. Compound **1** is formed as the initial reaction product via Scheme 10 and formed by the protonolysis of **2** formed by Scheme 8.

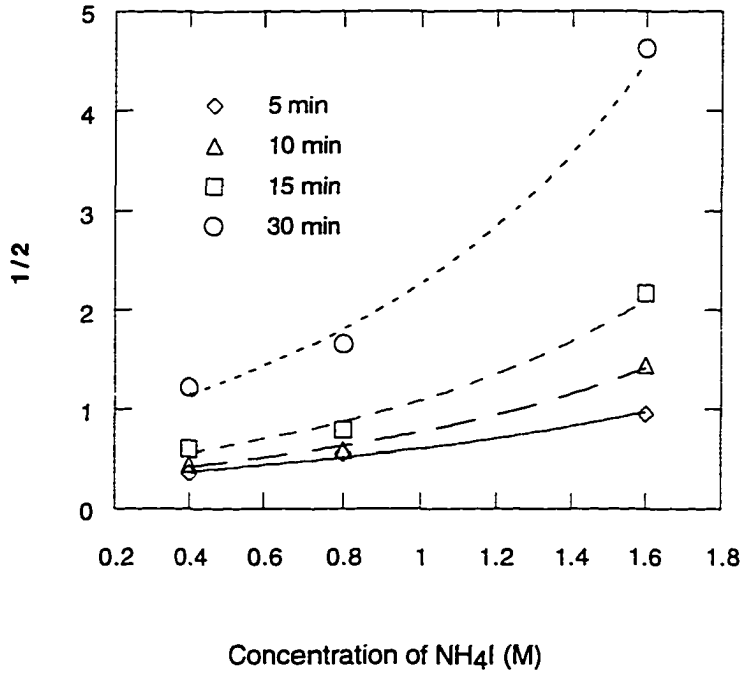
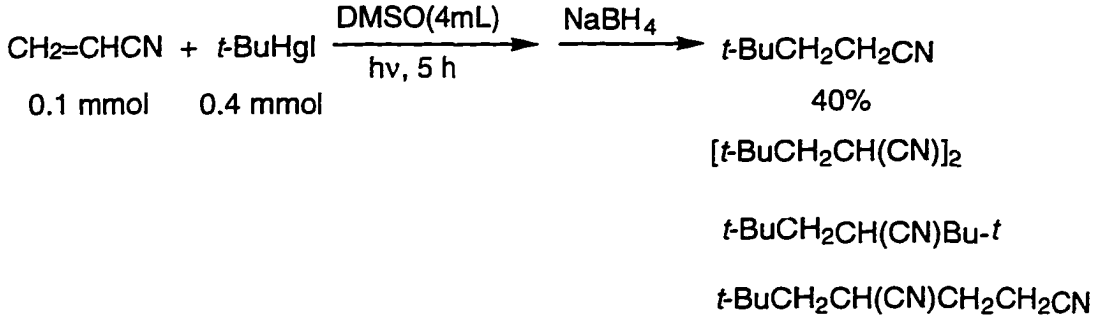


Figure 1. Reaction of 2 equiv. of *t*-BuHgI with 0.2 M acrylonitrile in the presence of 8 equiv. (1.6 M) of M^+I^- at room temperature in the dark: $[NH_4^+]$ is 0.4, 0.8, and 1.6 M; $[K^+]$ is 1.2, 0.8, and 0 M.

The promotion effect by KI and by NH_4^+ is very important in the alkylation of acrylonitrile. In absence of KI and a proton donor, photolysis of acrylonitrile with 4 equivalent of *t*-BuHgI in DMSO-d_6 at 35-40 °C for 5 h gives a mixture of at least eight different products containing a *tert*-butyl group bound to carbon by ^{1}H NMR monitoring. Workup of the mixture with NH_4I/H_2O or $NaBH_4$ gives **1** in 40% yield as the major product. Other products detected by GCMS are *t*-$BuCH_2CH(CN)CH(CN)CH_2Bu$-*t* (**4**, two isomers), *t*-$BuCH_2CH(CN)Bu$-*t* (**5**), and the telomer *t*-$BuCH_2CH(CN)CH_2CH_2CN$ (**6**). The mechanism is illustrated in Scheme 11. The product **1** is formed by hydrogen atom abstraction by *t*-$BuCH_2CH(CN)\bullet$.

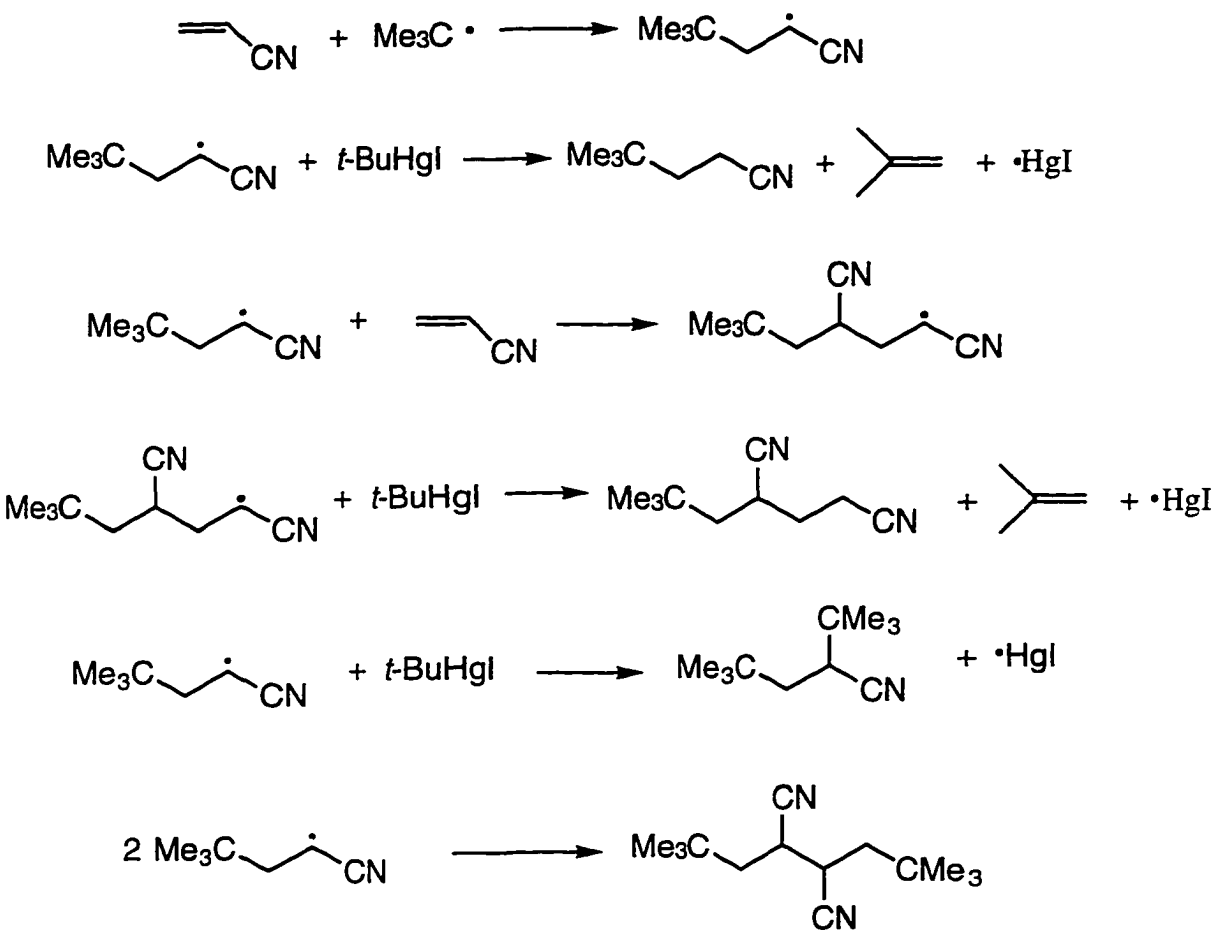


In the absence of a proton donor, photolysis of **3**, prepared by the reaction of acrylonitrile with *t*-BuHgI/KI is a slow process. After 8 h of irradiation with a sunlamp in DMSO, the dimer **4** is found as the major product with only 5% of **1** and 20% of **3** recovered. All three products are detected after workup with aqueous $Na_2S_2O_3$. In this case without the presence of CH_2=CHCN and excess *t*-BuHgI, *t*-$BuCH_2CH(CN)\bullet$ undergoes radical coupling with very little disproportionation as evidenced by very low yield of **1** (Scheme 11).

Crotononitrile

A mixture of *E*- and *Z*-isomers of crotononitrile was allowed to react with *t*-BuHgI/KI in DMSO in the dark at room temperature to give the mercurial RHgI and R_2Hg by ^{1}H NMR monitoring (R = *t*-$BuCH(CH_3)CH(CN)$). Reaction with 2 equiv. of *t*-BuHgI and 8 equiv. of NH_4I for 4 h at room temperature gave a 95% yield of the reductive alkylation product **7** with

Scheme 11



CH_2=CHCN + *t*-BuHgI + KI $\xrightarrow[h\nu,\ 8\ h]{DMSO}$ [*t*-BuCH_2CH(CN)]$_2$ **4** 33%

0.1 mmol 1.1eq 2eq

[*t*-BuCH_2CH(CN)]$_2$Hg 20%

t-BuCH_2CH_2CN 5%

5% of RHgI and R_2Hg (Table 3). Crotononitrile follows the general mechanism proposed for α,β-unsaturated nitriles in radical chain processes in DMSO (Scheme 8, 9 and 10) and its reactions had been shown to be greatly promoted by KI and PTSA.[10c]

Table 3. Reaction of Crotononitrile with *t*-BuHgI in Me_2SO-d_6[a]

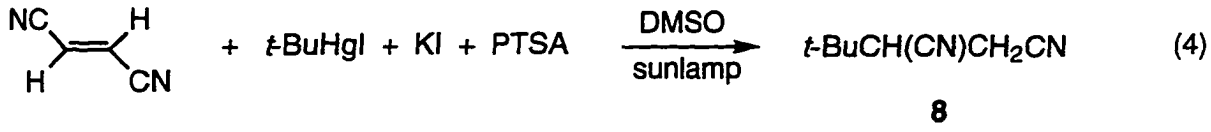
(*E*)- and (*Z*)-$CH_3CH{=}CHCN$ + [ ] ⟶ *t*-$BuCH(CH_3)CH_2CN$ (3)
7

Mol equiv.				%Yield[b]	
t-BuHgI	NH_4I	Condition	**7**	$RHgI+R_2Hg$	S.M.
2	4	10 min, dark	7	10	83
2	4	40 min, dark	19	15	66
2	4	220 min, dark	59	29	12
2	4	18 h, dark	73	25	0
2	8	100 min, dark	71	14	15
2	8	4 h, dark	95	5	0

[a] Reaction of crotononitrile (0.1 mmol) in 0.6 mL of DMSO-d_6.
[b] ^1H NMR yield with toluene as an internal standard.

Fumaronitrile

Previous work demonstrated that fumaronitrile is very reactive toward alkyl radicals. Competitive study shows that it is about 20 times as reactive as acrylonitrile.[10b] In the absence of KI and proton donors, little product was detected. However, good reactions were observed with KI present and a 95% yield of *tert*-butylation product **8** was obtained when 2 equiv of KI and 3 equiv of PTSA were present (eq 4), implying a remarkable promotion effect by KI. Table 4 demonstrates a similar promotion by NH_4I.[10c] Fumaronitrile also undergoes oxidative alkylation reactions when a base such as Dabco is present (Scheme 12).[18,19]



The reaction of fumaronitrile with *t*-BuHgI/KI was monitored by ^{1}H NMR in DMSO-*d*6. As expected, no reaction was observed with *t*-BuHgI even with sunlamp irradiation. With KI present no reaction occurs in the dark either. However, a fast reaction is observed upon sunlamp irradiation in the presence of I^- to give the mercurials RHgI and R_2Hg which are not recognized easily due to the ^{1}H NMR signal overlap of the several diastereomers but are confirmed by the formation of the reductive alkylation product upon protonolysis by NH_4I. For *t*-BuHgI/NH_4I, the dark reaction occurs rapidly, indicating a strong promotion by the proton donor NH_4^+ (Table 4).

Table 4. Reaction of fumaronitrile with *t*-BuHgI/KI in DMSO-*d*6

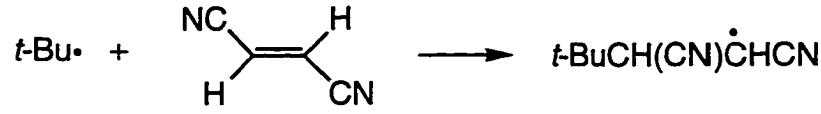
Mol equiv.			Yield[a]	
t-BuHgI	NH_4I	Condition	**8**	RHgI+R_2Hg
2	2(KI)	5 min, hυ	<5	90
2	8	25min, dark	94	-
1.1	8	5 min, hυ	95	-
1.1	8	10min hυ, 30min dark	99	-
2	2	24 h, dark	70	-
4[b]	8	100 min, hυ	99[c]	-

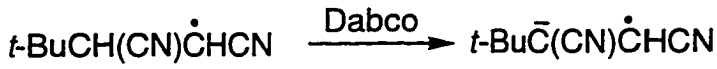
[a] ^{1}H NMR yield with toluene as an internal standard.

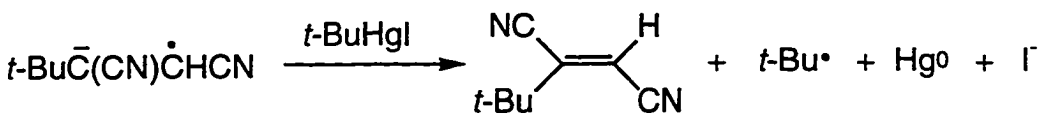
[b] *t*-BuHgCl used

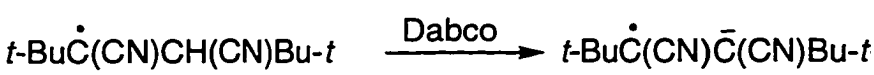
[c] workup with $Na_2S_2O_3$.

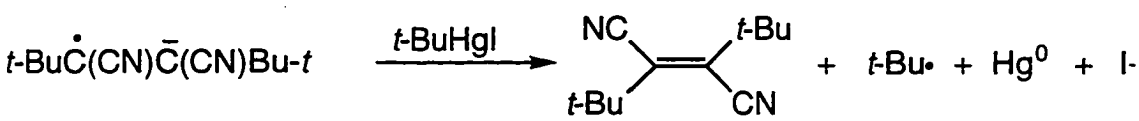
Scheme 12

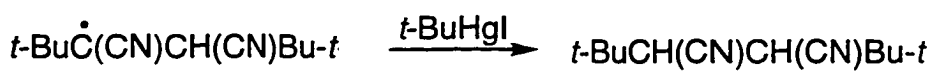




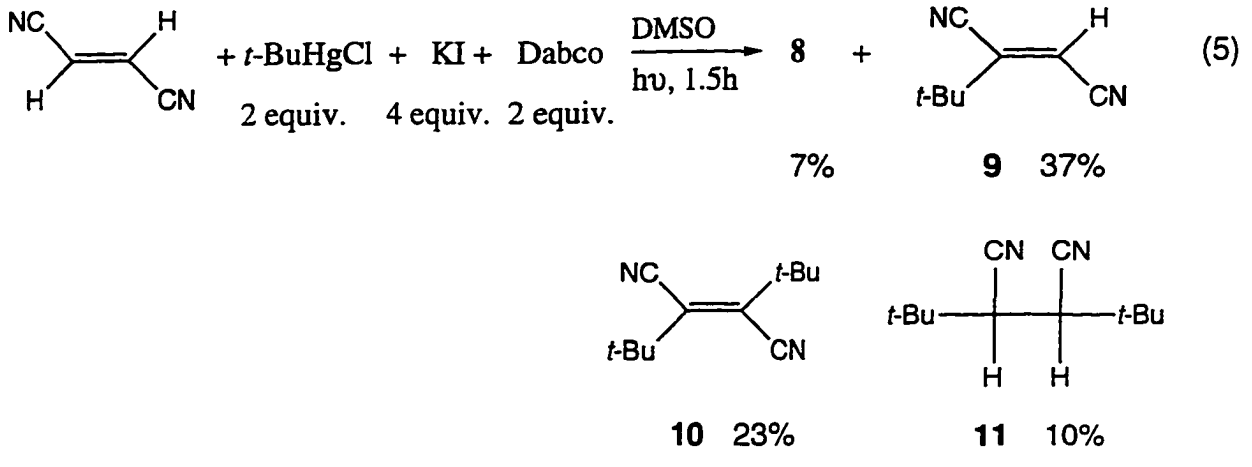








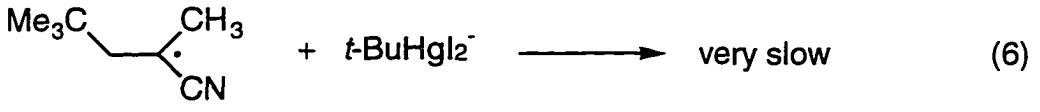
The oxidative alkylation product is produced as the major product with Dabco which deprotonates the adduct redical to form the radical anion (eq 5). *t*-BuHgX readily accepts an electron from the radical anion to give the product and *t*-butyl radical, forming a chain process.



(5)

Methacrylonitrile

Methacrylonitrile reacts with *t*-BuHgCl/Et_3SiH to give a satisfactory yield of the reductive alkylation product.[10b] However, no reaction is observed with *t*-BuHgI/KI or even with *t*-BuHgI/NH_4I in the dark. Photolysis gives messy results. The problem is that the tertiary adduct radical fails to react with *t*-$BuHgI_2^-$ to propagate the chain process.

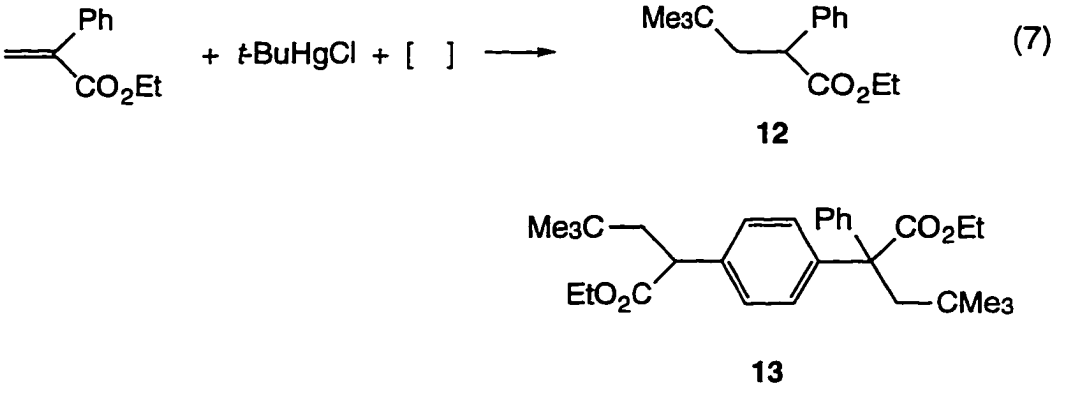


(6)

Ethyl α-phenylacrylate

No reaction was observed for a mixture of ethyl α-phenylacrylate and *t*-BuHgCl/NH_4I for 48 h in the dark. However, a 39% yield of the reductive alkylation product was obtained with *t*-BuHgCl (4equiv.)/KI(8equiv.). Photolysis increased the yield to 61% (Table 5). Proton donors do not promote the reactions since the adduct radical is not easily protonated. In the presence of a base, the dimer **13** is produced in high yield as the major product. The adduct radical *t*-$BuCH_2C(Ph)(CO_2Et)$• undergoes coupling preferentialy instead of hydrogen abstraction leading to the reductive alkylation product (Scheme 13). The coupling occurs at the

Table 5. Reaction of ethyl α-phenylacrylate with *t*-BuHgCl[a]



(7)

Mol equiv.				%Yield[b]	
t-BuHgCl	KI	Dabco	Condition	**12**	**13**
4	8	-	dark, 48 h	39	6[c]
4	-	-	hν, 10 h	22	48
4	4	-	hν, 10 h	56	29
4	-	10	hν, 10 h	tr	62
4	4	10	hν, 10 h	7	83
4	8	-	hν, 16 h	61	14

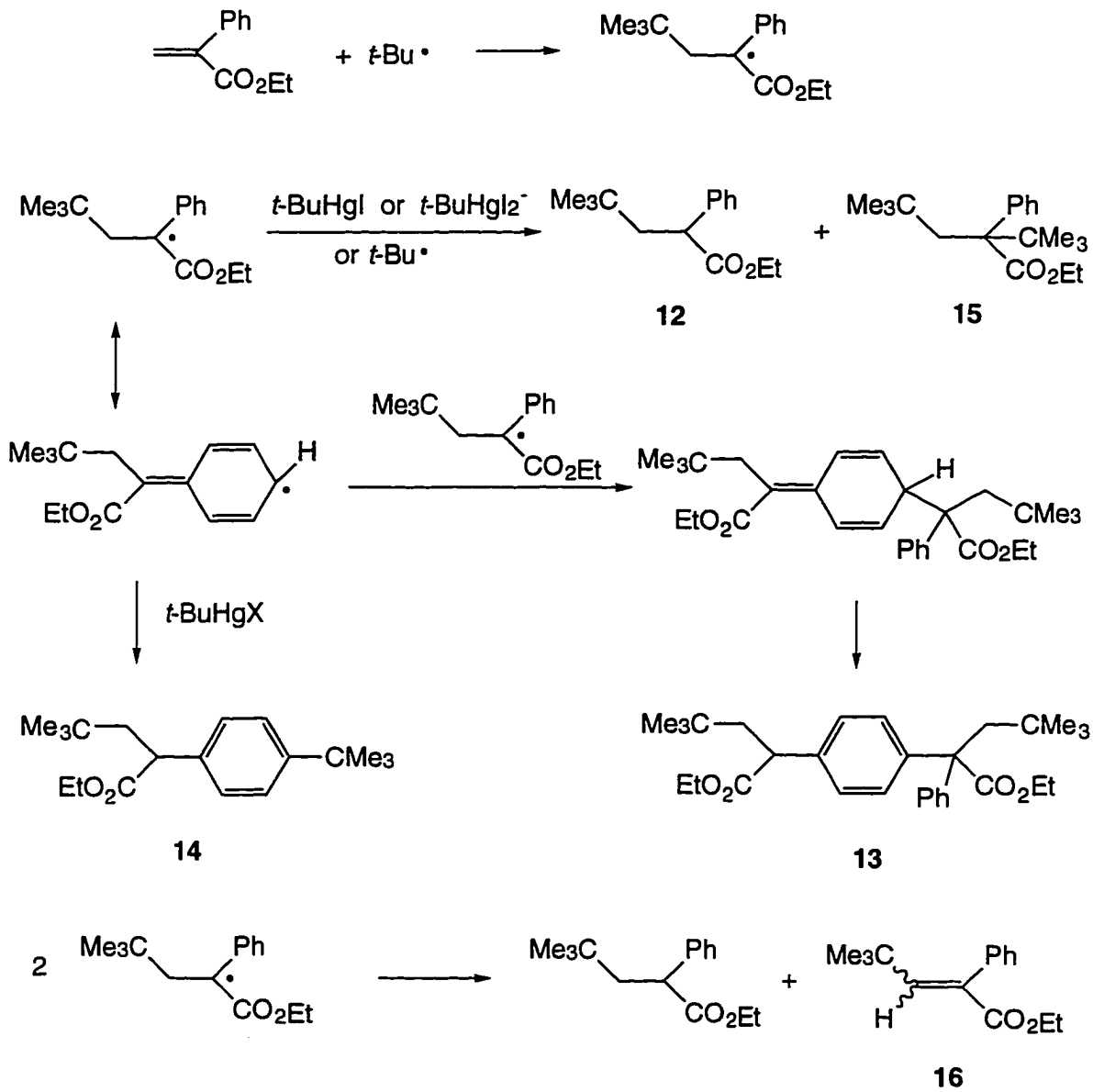
a Reaction of ethyl α-phenylacrylate(0.1 mmol) in 4 mL of DMSO with sunlamp at 40 °C followed by workup with aqueous $Na_2S_2O_3$.

b ^{1}H NMR yield with toluene as an internal standard.

c In 0.6 mL of DMSO-d_6 in the dark.

para posiion of the benzene ring to yield two diasteromers that could not be separated. The structure of these 1,4 disubstituted benzene was assigned by ^{1}H NMR and ^{13}C NMR. The effect of Dabco is not understood. It appears to increase the steady state concentration of the adduct radical and thus favors the bimolecular coupling reaction. Possibly Dabco promotes the

Scheme 13



comproportionation of *t*-BuHgX to the labile $(t\text{-Bu})_2Hg$ which readily forms *t*-Bu•.

More by-products including **14** and **15** are found in the reaction mixtures by ^1H NMR and GCMS. In the absence of KI the dimer is the major product. With small amounts of KI (~2-4 equiv.) **14** and **15** are comparable in yield with **12** but with excess of KI they decrease significantly (9% and 5% with 4 equiv. of *t*-BuHgCl and 8 equiv of KI). The oxidative alkylation product **16** (*(E)*- and*(Z)*-forms) is also observed in small quantity (5-10%) by GCMS, indicating disproportionation occurs to some extent.

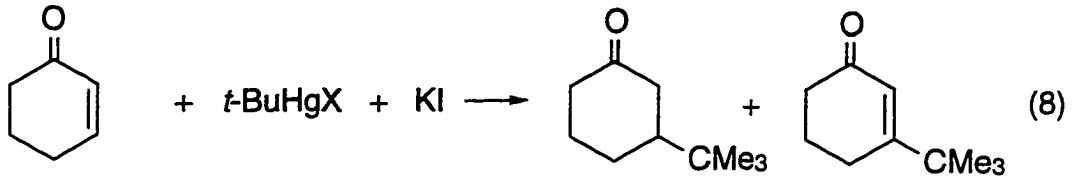
It is quite obvious that ethyl α-phenylacrylate is different from acrylonitrile in the *tert*-butylation reaction. For the former the adduct radical is tertiary which does not react readily with $t\text{-BuHgI}_2^-$. On the other hand, the benzene ring makes the adduct radical stable and some radical reactions take place on the aromatic ring through the resonance structures (Scheme 13). Thus, the reactions are more complicated for ethyl α-phenylacrylate.

2-Cyclohexenone

Photolysis of 2-cyclohexenone with *t*-BuHgX with or without KI in DMSO gives the 1,4-addition product (**17**). A Promotion effect by KI is observed. Table 6 lists the results for a series of the reactions with different combinations of *t*-BuHgX and KI. At the same time, a little unsaturated alkylated product (**18**) is found. The ratio of **18/17** seems to decreases with increasing KI.

Previous work on alkylation of enones with alkylmercury halides has been interpreted as an electron transfer process in which the enolate is formed as an intermediate. With the intent to trap the anion, CH_3I was added. However, The reaction fails to give the trapping product. Also, the addition of D_2O does not give a conclusive result. This study does not exclude the electron transfer process but suggests that the adduct radical abstracts a hydrogen atom from *t*-BuHgX or $t\text{-BuHgI}_2^-$ because **17** is produced in 45% with 2 equivalent of *t*-BuHgCl in the absence of iodide ion (Scheme 14). The unsaturated product **18** is probably formed from

Table 6. 1,4-Addition of *t*-BuHgX to 2-cyclohexenone in DMSO[a]



(8)

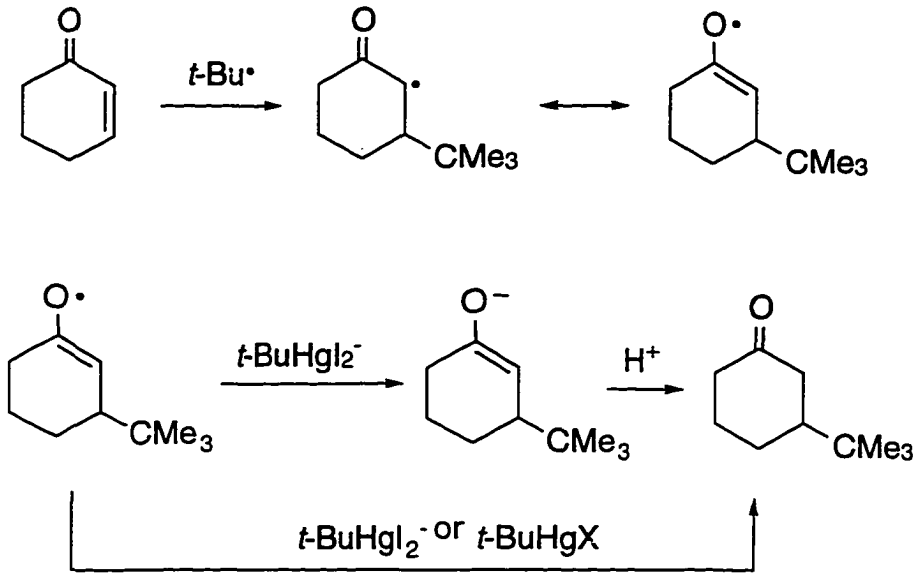
17 **18**

Mol equiv.			%Yield[b]		
t-BuHgX	KI	Condition	**17**	**18**	**18/17**
Cl(1)	-	hν, 23 h	20	4	0.2
Cl(2)	-	hν, 23 h	45	5	0.11
I(4)	-	hν, 5 h	31	3	0.10
Cl(1)	2	hν, 4 h	34	4	0.12
Cl(2)	4	hν, 5 h	78	8	0.10
I(1.1)	-	D_2O(20), hν, 5 h	12	<1	0.08
I(1.1)	4	hν, 160 min	41	2.4	0.06
I(4)	8	hν, 5 h	66	1.7	0.03
I(2)	4	CH_3I(10), hν, 5 h	50	15	0.3

a Reaction of 2-cyclohexenone (0.1 mmol) with reagents in 0.6 mL of DMSO-d_6 with sunlamp at 35-40 °C.

b ^{1}H NMR yield with toluene as an internal standard.

Scheme 14



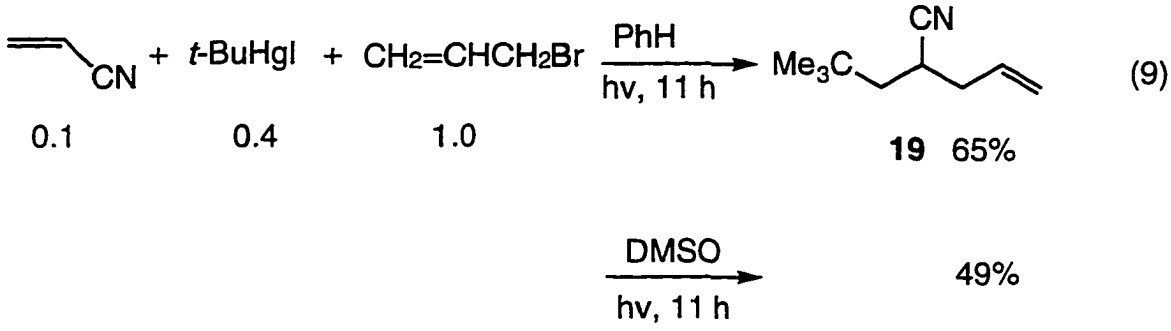
disproportionation of the adduct radical but this cannot be the major route to **17** since with 4 equiv. of KI the yields of **17** and **18** are 78 and 8%, respectively.

Three-Component Condensation Reaction involving Acrylonitrile

Radical trapping is one of the carbon-carbon bond and carbon-heteroatom bond forming methods in radical processes and has been applied in organic synthesis. The trapping step often involves radical substitution, radical addition and other processes. There have been many examples of trapping of nucleophilic radicals with electron-deficient alkenes. Electrophilic radicals such as carbonyl-substituted radicals can be trapped with electron-rich alkenes to generate nucleophilic radicals which are trapped with PhSSPh, giving the three-component condensation product.[21] This study shows that three-compoent condensation reactions involving acrylonitrile can be also realized.

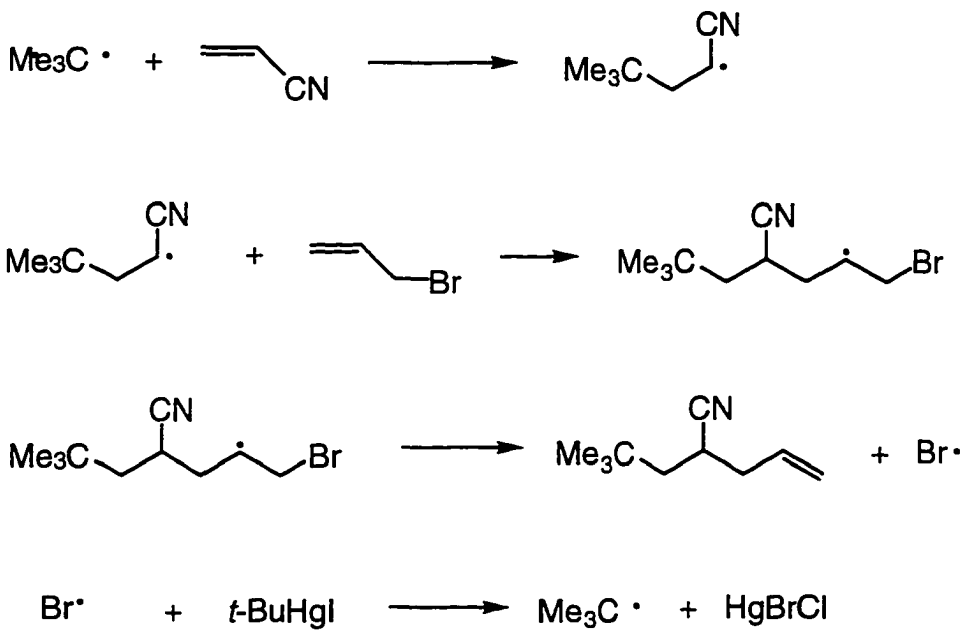
Trapping with allyl bromide

Photolysis of a mixture of acrylonitrile, *t*-BuHgCl , and CH_2=CHCHBr in DMSO or in benzene gives the three-component condensation product in fairly good yields (Eq 9). A chain process is proposed in Scheme 15 in which the adduct radical, an electrophilic radical, reacts readily with allyl bromide to generate the new adduct radical. This radical undergoes β–elinination to give the condensation product and Br•. The Br• serves as a chain carrier and reacts with *t*-BuHgCl to regenerate *t*-Bu• and thus create a chain process.

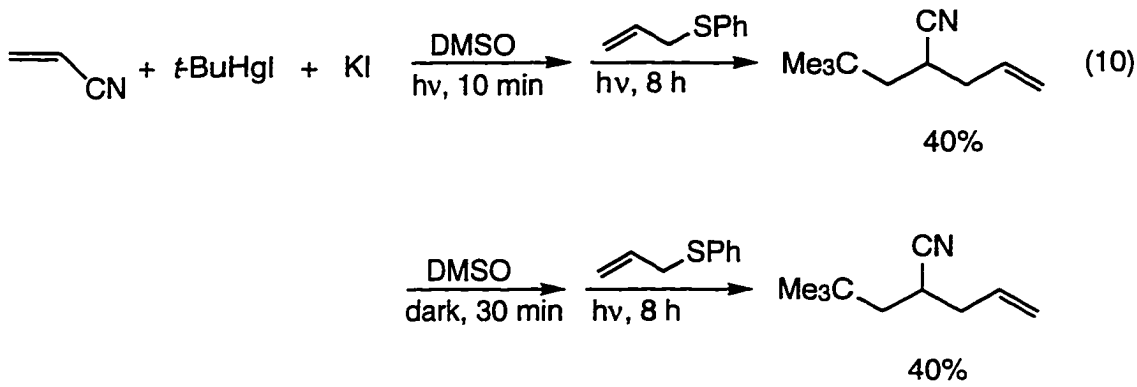


(9)

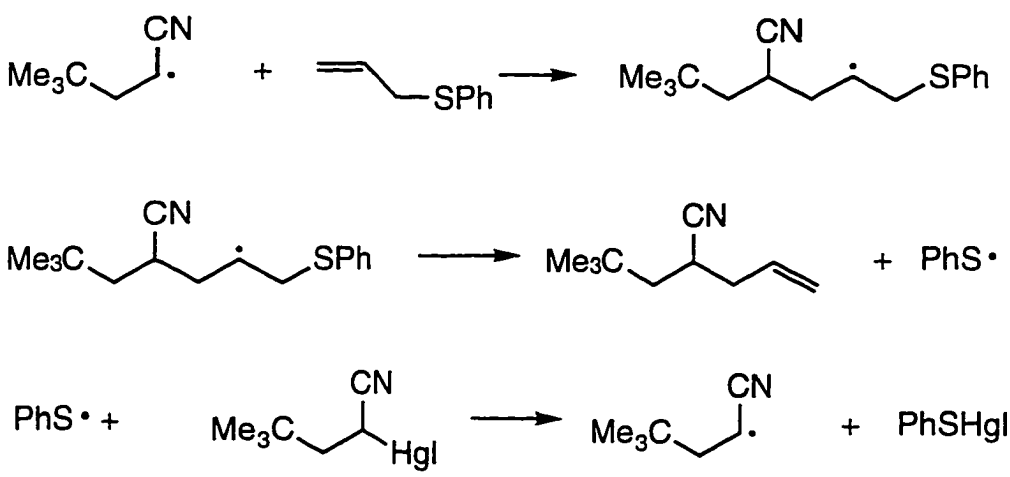
Scheme 15



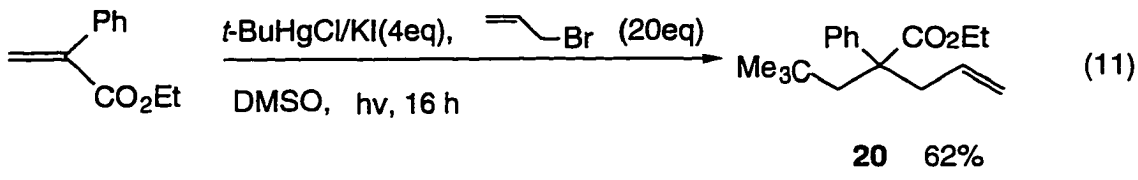
The same type of three-component condensation was also investigated using allyl phenyl sulfide and **2**. In this case, the new adduct radical undergoes a similar β-elimination to generate PhS• radical. The PhS• reacts with the mercurial intermediate to form PhSHgI and *t*-$BuCH_2CH(CN)$•(Scheme 16). In a similar manner, the mercurial intermediate, obtained by the reaction of acrylonitrile and *t*-BuHgI (1.5eq)/KI(4eq) in the dark or with sunlamp, when photolyzed with PhSSPh (4 equiv.) for 8 h gives a 40% yield of *t*-$BuCH_2CH(CN)SPh$.



Scheme 16

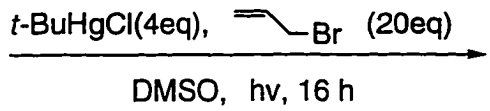


Similar three-component condensation was also achieved for ethyl α-phenylacrylate with allyl bromide in DMSO (Eq 11). The chain process involved is the same as shown in Scheme 15. For this substrate, the presence of KI increases the yield of the three-component condensation product from 42% to 64%. It is believed that KI may not be involved in the chain

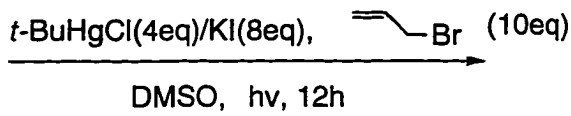


(11)

20 62%



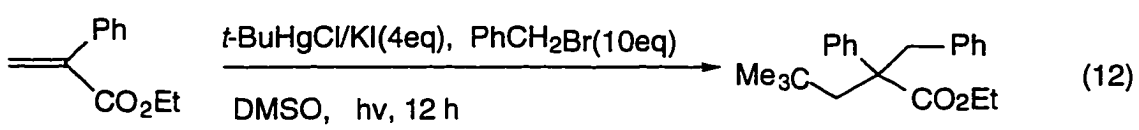
42%



64%

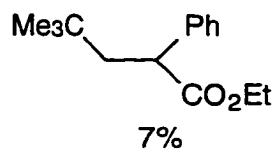
process but converts allyl bromide to allyl iodide. The iodide leads to a more reactive radical adduct which undergoes a faster β-elimination than the corresponding bromide.

Trapping of the adduct radical with $PhCH_2Br$ was also carried out. Low yield of the three-component product **21** was obtained (Eq 12) which is formed possibly via coupling between the adduct radical and $PhCH_2$• since $PhCH_2CH_2Ph$ was also detected.



(12)

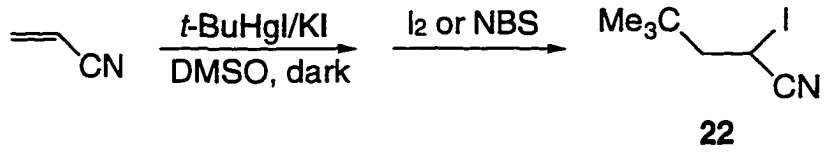
21 26%



7%

Condensation with I_2 and NBS

The intermediates 2 and 3 react quickly with I_2 or NBS to form the corresponding iodides in high yield. Thus, when the reaction product from acrylonitrile, *t*-BuHgX/KI obtained in the dark, is treated with I_2 or NBS, the condensation product is produced (Table 7). When $BrCCl_3$ is used in place of the I_2 or NBS, a fairly good yield of the iodide is also obtained with sunlamp irradiation. The mechanism is depicted in Scheme 17. Presumably the intermediate *t*-$BuCH_2CH(Br)CN$ is rapidly converted to the iodide in the presence of I^-.



22 (13)

Table 7. Three-component condensation of CH_2=CHCN, *t*-BuHgI, and the reagents[a]

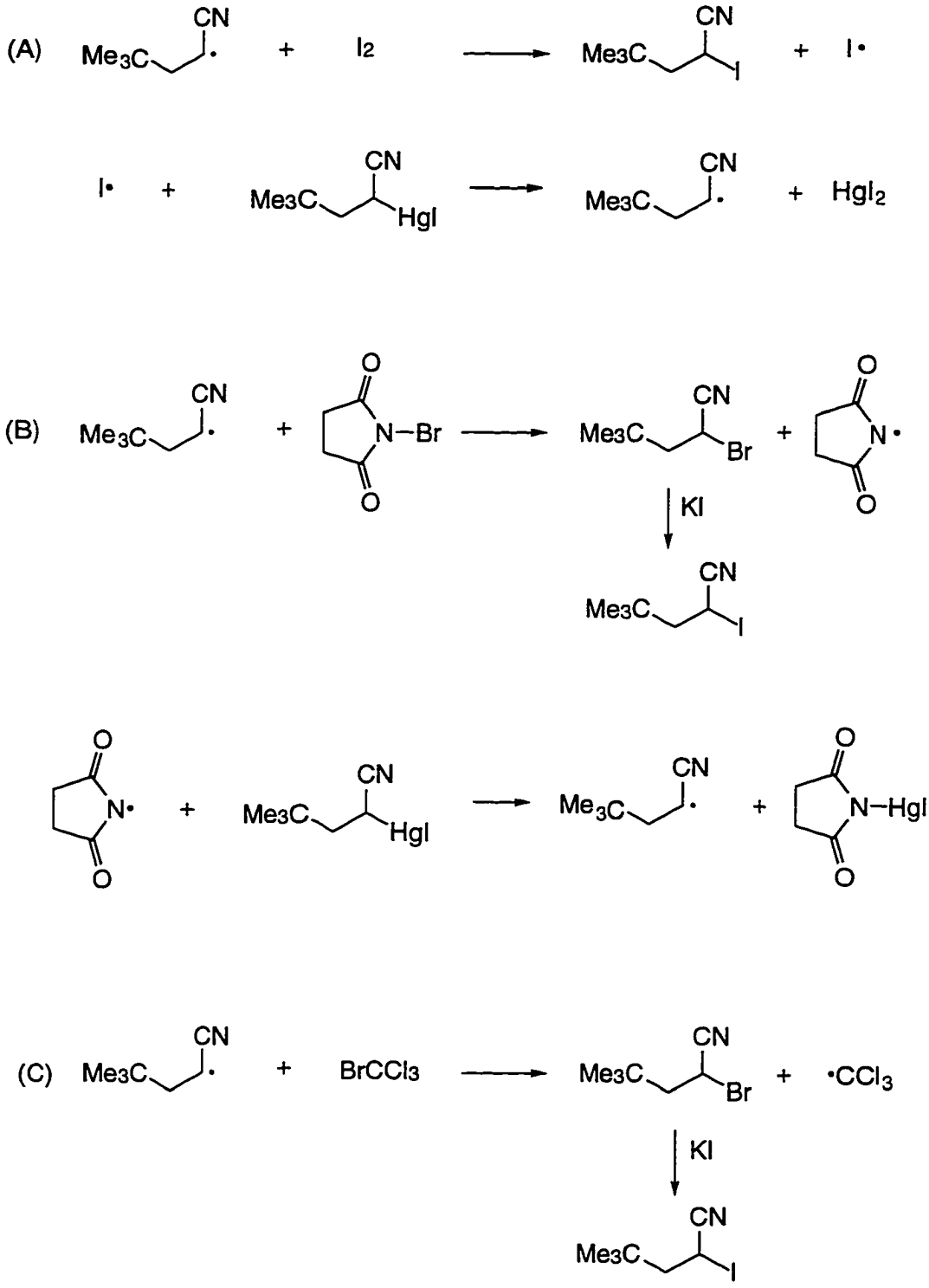
Mol equiv.			
t-BuHgI	KI	Reagent, condition	%Yield of **22**[b]
1.1	4	NBS(2), dark, 12 h	77[c]
1.1	4	NBS(2), hν, 0.5 h	81[c]
1.1	4	I_2(2), dark, 12 h	88
1.1	4	I_2(2), hν, 0.5 h	90
1.1	4	$BrCCl_3$(2), hν, 6 h	58[c]
1.1	4	$BrCCl_3$(2), dark, 18 h	low[c]

a Reagent was added to the mixture made by reaction of acrylonitrile and *t*-BuHgI/KI in 0.6 mL of DMSO-d_6 for 30 min in the dark.

b ^{1}H NMR yield with toluene as an internal standard.

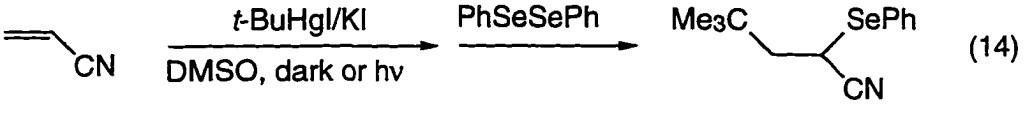
c The initial bromide product was converted to the iodide by the KI.

Scheme 17



Trapping with PhSeSePh

PhSSPh is a good trapping agent for nucleophilic radicals (see Chapter II)[6b]. It does not trap electrophilic radicals efficiently due to a polar effect[18]. The photostimulated reaction between *t*-BuHgX and PhSSPh is quite fast while the intermediate **2** [*t*-$BuCH_2CH(CN)(HgI)$] shows a very low reactivity toward PhSSPh since the product *t*-$BuCH_2CH(CN)(SPh)$ is produced in only trace amounts in the photolytic reaction of **2** with PhSSPh. However, with the more reactive PhSeSePh the adduct radical can be trapped quite successfully by adding PhSeSePh to the mixture of the mercurials **2** and **3** followed by dark or photolytic reaction for several hours (Table 8). Photolysis with sunlamp with 2 equivalent of



(14)

23

Table 8. Trapping of the adduct radical with PhSeSePh[a]

mol equiv			
t-BuHgI	KI	Condition	Yield of **23**[b]
1.1	4	PhSeSePh(1), dark, 12 h	40[c]
1.1	4	PhSeSePh(1), hv, 6 h	60[c]
1.1	4	PhSeSePh(2), hv, 4 h	93[d]

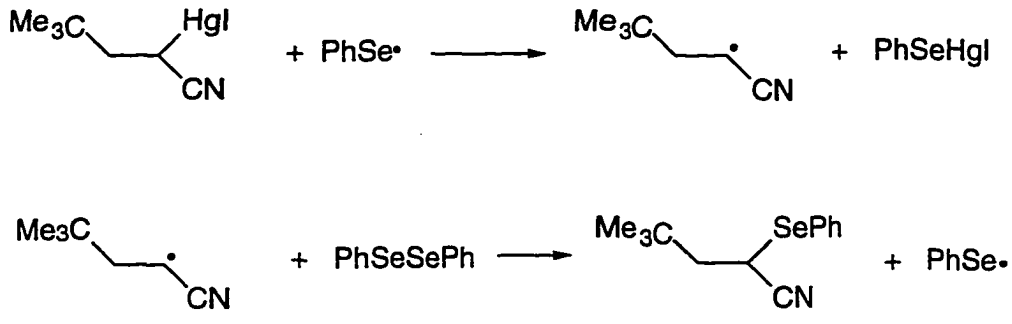
a Reaction of PhSeSePh with the mercurials **2** and **3** obtained from acrylonitrile (0.1 mmol), *t*-BuHgI and KI in 0.6 mL of DMSO-d_6.

b ^1H NMR yield with toluene as an internal standard.

c Dark reaction of acrylonitrile with *t*-BuHgI/KI for 30-60 min followed by addition of PhSeSePh.

d Photolytic reaction of acrylonitrile with *t*-BuHgI/KI for 20 min followed by addition of PhSeSePh. Workup with aqueous $Na_2S_2O_3$

Scheme 18



PhSeSePh gives a higher yield (93%) than the dark reaction with only 1 equivalent of PhSeSePh (40%). A mechanism is outlined in Scheme 18.

Condensation with N-methylenepiperidinium chloride

Generally, electrophilic adduct radicals are unreactive toward electron-deficient species. However, *t*-$BuCH_2CH(CN)HgI$ reacted with *N*-methylenepiperidinium chloride (MPC). The three-component product was observed in low to moderate yield in the dark or with sunlamp (Table 9). Since sunlamp irradiation had essentially no effect on the reaction, it appears that electrophilic substitution is now the most important process, Scheme 19.

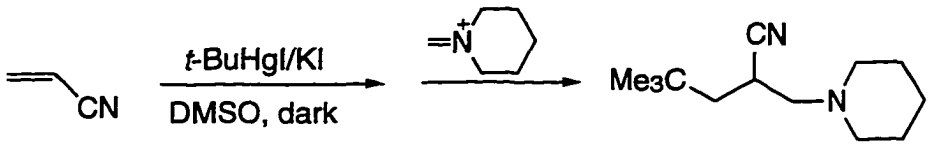
Condensation with (E)-β-iodostyrene

(*E*)-PhCH=CHI undergoes radical substitution processes in which I is replaced by a number of substituents via radical addition followed by elimination (Eq16).[6b,8b,8f] The R group comes from different RHgX so that different products are generated. R can be either a nucleophilic or electrophilic radical.

$$(E)\text{-PhCH=CHI} + \text{RHgX} \longrightarrow (E)\text{- and } (Z)\text{-PhCH=CHR} \qquad (16)$$

R = *i*-Pr, *t*-Bu, *n*-Bu, $(EtO)_2P(O)$, $PhCOCH_2$

Table 9. Condensation reaction of the adduct radical with *N*-methylenepiperidinium chloride[a]



(15)

24

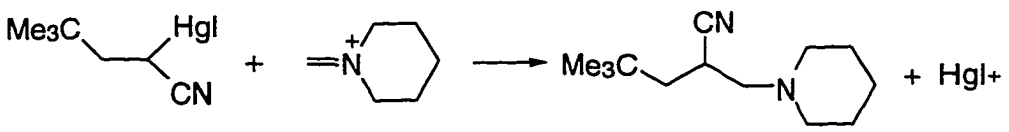
Mol equiv.			
t-BuHgI	KI	Condition	Yield of **24**[b]
1.1	4	MPC (2), 5 h hv	34[c]
1.1	4	MPC (2), 5 h dark	50
1.1	4	MPC (2), 4 h dark	34[c]
2	8	MPC (2), 6 h dark	60

a Reaction of MPC with the mercurial **2** and **3** obtained from acrylonitrile (0.1 mol) and *t*-BuHgI/KI in the dark for 10 min in 4 mL of DMSO. Workup with aqueous $Na_2S_2O_3$.

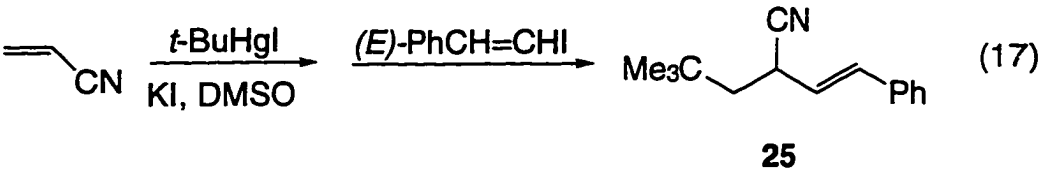
b ^1H NMR yield with toluene as an internal standard.

c All reagents were mixed at the same time.

Scheme 19



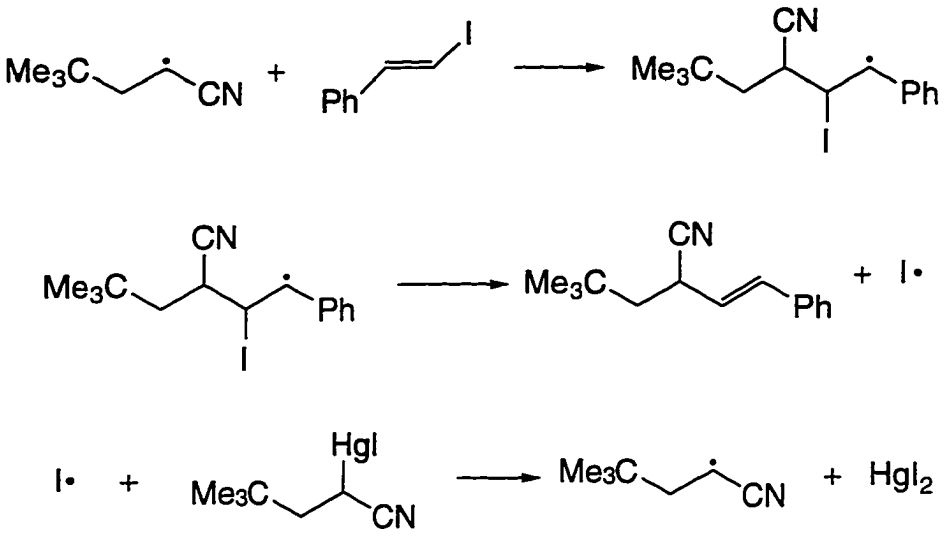
This study shows that the same type of substitution occurs between the adduct mercurial and *(E)*-PhCH=CHI to afford the three-component condensation product (Eq17). The two-stage reaction involves the formation of intermediate **2** and **3**, obtained from acrylonitrile (0.1



(17)

25

Scheme 20



mmol) and *t*-BuHgI (1.5 equiv)/KI (4 equiv.) in DMSO in the dark for 30 min or with sunlamp for 10 min, and follow-up phtolysis with *(E)*-PhCH=CHI (4 equiv) for 20 h, giving **25** in the yield of 30%, see Scheme 20.

Conclusion

The free radical chain process using *t*-BuHgX/KI and *t*-BuHgX/NH_4I provides an efficient method for alkylation of unsaturated nitriles such as acrylonitrile, crotononitrile, and fumaronitrile. High yields of the adduct mercurials and reductive alkylation products are obtained under mild condition without an additional initiator. Reactions proceed smoothly in the dark in DMSO at room temperature while photolysis with sunlamp often accelerates them.

NH_4I, compared with other proton donors such as PTSA, shows some advantages and can be employed as an alternative proton donor for promotion of the reactions. This method encounters difficulties in the reactions of methacrylonitrile and 2-chloroacrylonitrile owing to the slow propagation step in the attack of a 3°-radical upon *t*-BuHgX. The three-component condensation reactions are readily realized by adding a variety of reagents such as allyl bromide, I_2, PhSeSePh, etc. to the adduct mercurials formed from CH_2=CHCN. Thus, new carbon-carbon or carbon-heteroatom bonds are formed in a highly regioselective manner.

Experimental Section

General Consideration

^1H and ^{13}C NMR spectra were recorded on a Nicolet NT300 or Varian VXR 300 spectrometer. Chemical shifts are reported in ppm from internal tetramethylsilane (300 MHz for ^1H NMR) or for ^{13}C NMR measured relative to the central line of internal $CDCl_3$ at 77.000 ppm (75.4 MHz for ^{13}C NMR). GCMS were recorded on a Finnegan 4000 spectrometer with Incos data system or a Varian Magnum spectrometer. High resolution mass spectra were recorded on a Kratos MS-50 spectrometer. Infrared spectra (IR) were recorded on an IBM IR-98 FT spectrometer or Digital FTS-7 FT spectrometer. Analysis data were obtained from a Perkin Elmer SeriesII CHNS/O Analyzer 2400 or from Galbraith Laboratories, Inc. Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected.

Most products were isolated either by flash column chromatography on silica gel (Merck, 230-400 mesh, purchased from Aldrich Chem. Co) with mixed solvents (hexane-ethyl acetate) as eluents or by TLC on silica gel. ^1H NMR spectroscopy yields were determined by integration with a known amount of an internal standard (toluene).

Solvents and Reagents

Solvents were purchased from Fisher and Baker. Dimethyl sulfoxide (DMSO) was distilled from calcium hydride and stored over 4Å Molecular sieves under a nitrogen atmosphere. Diethyl ether and tetrahydrofuran (THF) were distilled from sodium metal and benzene was distilled from calcium hydride. Other solvents were purchased and used without further purification.

Most chemical reagents were purchased from Aldrich Chem. Co. In most cases, the reagents were used without further purification.

Materials

1. *tert*-Butylmercury Chloride

tert-Butylmercury chloride was prepared from mercuric chloride and *tert*-butyllithium by a modified literature method[22]. A solution containing mercuric chloride (0.18 mol) in dry ether (500 mL) was stirred in an ice bath under nitrogen and *tert*-butyllithium (0.17 mol, 1.7 M solution in pentane) was added dropwise. After the addition, the mixture was stirred for at least 4 hours at room temperature. The mixture was then poured into water and extracted 3 times with ether (500 mL each). The combined ether layer was washed with brine solution three times and dried over anhydrous magnesium sulfate. The solution was filtered through a celite-filled sintered glass funnel and the solvent was evaporated. The white precipitate was recrystallized from hexane-ether solution. The white needles melted at 110-113 °C; ^{1}H NMR ($CDCl_3$) δ 1.51 (s, 9H).

In an alternative method of preparation, a solution containing mercuric chloride (0.18 mol) in dry THF (200 mL) was stirred in an ice bath under nitrogen and *tert*-butyllithium (0.17 mol, 1.7 M solution in pentane) was added dropwise. After the addition, the mixture was stirred for

2 hours at room temperature. The solution was filtered through a celite-filled sintered glass funnel and the solvent was evaporated. The white precipitate was dissolved in 1500 mL of ether and washed three times with brine solution. Drying with anhydrous $MgSO_4$, evaporation, and recrystallization gave white needles of *tert*-butylmercury chloride.

2. *tert*-Butylmercury Iodide

tert-Butylmercury iodide was prepared by a modified anion exchange method.[23] *tert*-Butylmercury chloride (0.03 mol) was added in portions to a solution of potassium iodide (0.06 mol) in 40 mL of dimethyl sulfoxide. The solution was stirred for 2 hours at room temperature. The reaction was quenched by adding 100 mL of water and the mixture extracted twice with ether (70 mL) and the combined organic extract filtered through a celite-filled sintered glass funnel and washed three times with water (100 mL). The solution was dried over anhydrous magnesium sulfate and the solvent was evaporated until white crystals precipitated. The solution was filtered immediately. The white crystals turned pale yellow when exposed to the air; ^1H NMR ($CDCl_3$) δ 1.53 (s, 9H). The material decomposed before a clear melting point could be determined. It was stored in the freezer in the dark.

3. Preparation of *(E)*-β-Iodostyrene [24]

Phenylacetylene (50 mmol) and catecholborane (50 mmol) were stirred in a 100 mL flask for 2 hours under nitrogen at 70 °C to form the catechol ester of phenylethenylboric acid. The mixture was cooled to room temperature and stirred with 50 mL of water for 2 hours at room temperature, to effect the hydrolysis of the ester. The resulting mixture was cooled to 0 °C and the white solid, *trans*-phenylethenylboric acid, was collected by filtration and washed free of the catechol using ice-cold water. The boronic acid was then dissolved in 50 mL of ether in a 500 mL flask and cooled to 0 °C. Aqueous NaOH (50 mL, 3 N) was then added followed by 60 mmol of elemental iodine (20% excess) in 150 mL of ether, while stirring at 0 °C. The

mixture was stirred for an additional 30 min at 0 °C. The excess iodine was distroyed with aqueous sodium thiosulfate solution. The ether solution was separated, washed with water, and dried over anhydrous $MgSO_4$. After removing the solvent, the pure β-iodostyrene was obtained in 51% yield by distillation. The identity of the product was confirmed by comparison of its ^1H NMR spectrum with literature[24]. ^1H NMR($CDCl_3$) δ 7.42 (d, 1H, *J*=15.0 Hz), 7.34-7.24 (m, 5H), 6.82 (d, 1H, *J*=15.0 Hz).

4. Preparation of Ethyl 2-Phenylacrylate

Ethyl phenylacetate (25 mmol) and paraformaldehyde (50 mmol) were dissolved in 50 mL of absolute ethanol. A catalytic amount of NaOH (0.5 g) was added to the reaction solution. The reaction mixture was heated to reflux for 4 hours and cooled to room temperature, and then poured to 50 mL of water. The aqueous solution was extracted three times with ether (30 mL). The ether extract was then washed with water (50 mL), 10% HCl solution (50 mL), 5% $NaHCO_3$ solution (50 mL), and then dried over anhydrous $MgSO_4$. The ether was evaporated under vacuum. Ethyl 2-phenylacrylate was purified by flash column chromatography (5% of ethyl acetate in hexane). ^1H NMR ($CDCl_3$) δ 1.330 (t, 3H, *J*=7.2 Hz), 4.29 (q, 2H, *J*=7.2 Hz), 5.882 (d, 1H, *J*= 1.2 Hz), 6.343 (d, 1H, *J*=1.2 Hz), 7.30-7.44 (m, 5H).

Isolation of Bis(1-cyano-3,3-dimethylbutyl)mercury (**3**)

(1-Cyano-3,3-dimethylbutyl)mercury iodide (**2**) in DMSO slowly underwent comproportionation to form the dialkylmercury (**3**). The reaction proceeds more rapidly upon sunlamp photolysis and is essentially complete after 30 min of photolysis. Thus, a mixture of acrylonitrile (0.5 mmol), *t*-butylmercury chloride (0.5 mmol) and KI (1.0 mmol) was irradiated for 30 min in 4 mL of DMSO. The mixture was poured into 50 ml of water, extracted with

CH_2Cl_2, washed with water, and dried with $MgSO_4$. After evaporation of the solvent, the solid was washed carefully with a small amount of ether to give pure **3**.

Procedures for ^{1}H NMR Reaction Monitoring in DMSO-*d*6

Substrates (0.1 mmol)and reagents were put into a NMR tube and 0.5-0.6 mL of DMSO-d_6 was added. Toluene (0.1mmol)was also added to serve as an internal standard for determination of yield. For reactions in the dark, a piece of aluminium foil was wrapped around the NMR tube to prevent any light from coming in. For photolytic reactions, the tubes were irradiated with a 275W Sylvania fluorescent sunlamp at a distance of ca. 25 cm. In this case, the temperature was typically 35-40 °C.

Yields were determined based on integrals of *t*-butyl or other peaks of interest in the products and of the methyl group of toluene. When it was necessary, reaction mixtures were worked up with aqueous $Na_2S_2O_3$ or $NaBH_4$, extracted with methylene chloride, washed with brine, and dried with $MgSO_4$. After evaporation, a $CDCl_3$ solution was prepared and ^{1}H NMR was taken to determine yields and in some cases the mixture was analyzed by GCMS .

(*t*-Bu)$_2$NO• (10 mol%)was added by a syringe together with other reagents in a NMR tube for inhibition. In this case, reactions were inhibited for a period of time in which the starting materials were not consumed and no product was observed.

Procedures for *tret*-Butylation of Unsaturated Nitriles

Unsaturated nitriles or ethyl α-phenylacrylate(0.1 mmol for determination of yields, 0.5-1.0 mmol for isolation of the products), *tert*-butylmercury halide with KI or without KI, and other reagents (NH_4I or DABCO) were placed in flame-dried Pyrex test tube and 4 mL of distilled and predeoxygenated dimethyl sulfoxide (DMSO) was added under nitrogen. With

stirring the solution was irradiated with a 275 W sunlamp *ca.* 25 cm from the reaction tube. For dark reactions, tubes were wrapped with aluminum foil. The reaction mixture was then poured into 15 mL of saturated sodium thiosulfate solution and usually 10-20 min later was extracted three times with methylene chloride (15 mL). The combined organic extract was washed three times with brine, dried over anhydrous $MgSO_4$, and concentrated under vacuum. The mixture was analyzed by GC-MS and by ^1H NMR spectroscopy. The products were isolated by flash column chromatography or by TLC. Yields were determined by proton NMR integration with toluene (0.1 mmol) as an internal standard.

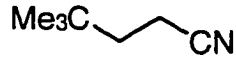
Procedures for Three-Component Condensation Reactions

In most cases, two-stage reactions were monitored in NMR tubes while product isolation used large Pyrex tubes. Basically the procedures were similar to those mentioned above. Acrylonitrile was first allowed to react with *t*-BuHgI/KI in DMSO. As the first period reactions finished, the different reagents, such as I_2, NBS, PhSeSePh, *N*-methylenepyrrolidinium chloride, or *(E)*-β-iodostyrene, were added. The reaction mixture was worked up in the same way as above. The products were isolated by TLC or by flash column chromatography.

For the condensation reaction with allyl bromide, all reagents were mixed at the same time.

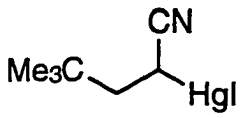
Characterization of Products

4,4-Dimethylpentanenitrile (1)[19]



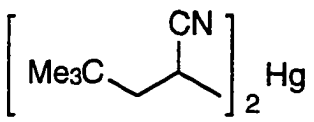
The product was isolated as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300MHz) δ 2.30-2.25 (m, 2H), 1.64-1.58 (m, 2H), 0.93 (s, 9H). The structure was confirmed by comparison of this spectrum with the literature.[19]

2-Iodomercury-4,4-dimethylpentanenitrile (2)



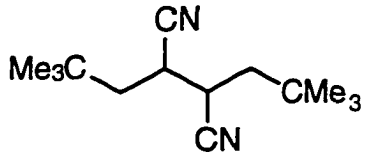
This compound was not isolated. It was detected by ^{1}H NMR (300MHz) in DMSO-d_6. δ 2.28 (dd, *J*=10.5, 4.0 Hz, 1H), 1.80 (dd, *J*=14.2, 4.0 Hz, 1H), 1.70 (dd, *J*=14.2, 10.5 Hz, 1H), 0.92 (s, 9H).

Bis(1-cyano-3,3-dimethylbutyl)mercury (3)



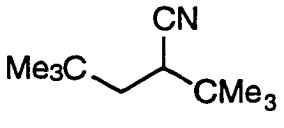
A 1:1 mixture of racemic and meso forms was isolated as a white solid, mp 168-170 °C. ^{1}H NMR ($CDCl_3$, 300MHz) δ 2.259 (dd, *J*=9.0, 5.7 Hz, 0.5H), 2.267 (dd, *J*=9.0, 5.7 Hz, 0.5H), 2.02 (dd, *J*=14.1, 9.0 Hz, 1H),1.80 (dd, *J*=14.1, 5.7 Hz, 1H), 1.02 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 125.97, 43.32, 32.38, 29.29, 28.93; EIMS *m/z* (rel intensity) 110 (12), 96 (6), 69 (6), 57 (100); CIMS(NH_3, solid probe) calcd for M+NH_4^+ *m/z* 442-436, found *m/z* 442 (13), 441 (28), 440 (87), 439 (88), 438 (100), 437 (70), 436 (34), 331 (2), 330 (0.2), 329 (9), 328 (4), 327 (7), 326 (5), 325 (2), 129 (78)110 (83); Anal. calcd for $C_{14}H_{24}N_2Hg$ C, 39.95; H, 5.75; N, 6.65. Found C, 39.74, H, 5.74; N, 6.73.

2,3-Bis(2,2-dimethylpropyl)butanedinitrile (4)



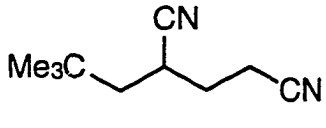
A 1:1 mixture of racemic and meso forms was isolated as a white solid, mp 130-139 °C. ^{1}H NMR ($CDCl_3$, 300MHz) δ 2.84-2.60 (m, 2H), 1.96-1.80 (m, 2H), 1.64-1.52 (two dd, 2H), 1.04 (s, 18H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 120.10/119.65, 43.98/43.77, 31.72/31.54, 30.73/30.67, 29.18 (broad); EIMS *m/z* (rel intensity) 205 (M-15$^+$, 100), 149 (8), 110 (39), 95 (28), 57 (65), 167 (13); CIMS *m/z* (rel intensity) 254 (M$^+$ + 2NH_3, 30), 238 (M+ NH_4^+, 100); HRMS calcd for $C_{13}H_{22}N_2$ (M-15$^+$) 205.1705, found 205.1701.

2-(1.1-Dimethylethyl)-4,4-dimethylpentanenitrile (5)



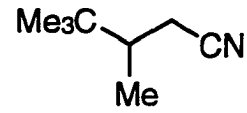
GCMS *m/z* (rel intensity) 168(M + 1$^+$, 2), 152 (3), 110 (8), 96 (24), 57 (100).

2-(2,2-Dimethylpropyl)pentanedinitrile (6)



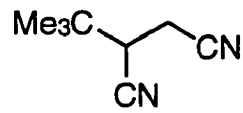
GCMS *m/z* (rel intensity) 165 (M + 1$^+$, 19), 149 (26), 108 (19), 96 (26), 81 (28), 57 (100).

3,4,4-Trimethylpentanenitrile (7)[19]



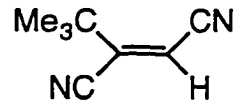
This product was not isolated but obtained in essentially pure form. ^{1}H NMR (DMSO-d_6, 300MHz) δ 2.58 (dd, *J*=16,8, 3.9 Hz, 1H), 2.23 (dd, *J*=16.8, 9.6 Hz, 1H), 1.65-1.53 (m, 1H), 0.978 (d, *J*=7.2 Hz, 3H), 0.855 (s, 9H). The structure was confirmed by comparison of this spectrum with the literature.[19]

2-(1,1-Dimethylethyl)butanedinitrile (8)[19]



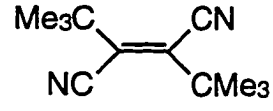
This product was not isolated but obtained in essentially pure form.^{1}H NMR ($CDCl_3$, 300MHz) δ 2.74 (dd, *J*=9.3, 5.1 Hz, 1H), 2.71-2.56 (m, 2H), 1.11 (s, 9H). The structure was confirmed by comparison of this spectrum with the literature.[19]

***(E)*-2-(1,1-dimethylethyl)butenedinitrile (9)**[19]



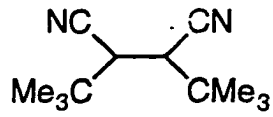
This product was not isolated.^{1}H NMR ($CDCl_3$, 300MHz) δ 5.85 (s, 1H), 1.26 (s, 9H). The structure was confirmed by comparison of this spectrum with the literature.[19]

***(E)*-2,3-Bis(1,1-dimethylethyl)butenedinitrile (10)**[19]



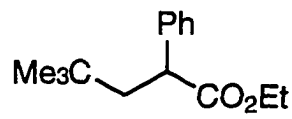
This product was not isolated.^{1}H NMR ($CDCl_3$, 300MHz) δ 1.44 (s, 9H). The structure was confirmed by comparison of this spectrum with the literature.[19]

2,3-Bis(1,1-dimethylethyl)butanedinitrile (11)[19]



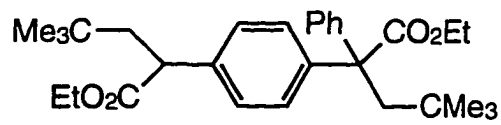
Two isomers were not isolated. One is the meso form and the other one is the racemic form. Their ^{1}H NMR ($CDCl_3$, 300MHz) are as follows: δ 2.64 (s, 2H), 1.25 (s, 18H); 2.56 (s, 2H), 1.15 (s, 18H). The structures of both compound were confirmed by comparison of their spectra with the literature.[19]

Ethyl 4,4-dimethyl-2-phenylpentanoate (12)[25]



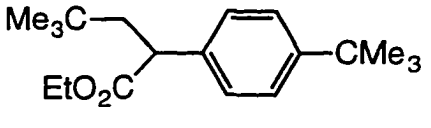
The product was isolated as a colorless liquid.^{1}H NMR ($CDCl_3$, 300MHz) δ 7.20-7.53 (m, 5H), 4.13-4.03 (m, 2 H), 3.63 (dd, *J*=9.4, 3.7 Hz, 1H), 2.30 (dd, *J*= 13.9, 9.3 Hz, 1H), 1.54 (dd, *J*= 13.9, 3.7 Hz, 1H), 1.20 (t, *J*=7.2 Hz, 3H), 0.90 (s, 9H). Its structure was confirmed by comparison of this spectrum with literature data.[25]

1-(1-Phenyl-1-(ethoxycarbonyl)-3,3-dimethyl)butyl-4-(1-(ethoxycarbonyl)-3,3-dimethyl)butylbenzene (13)



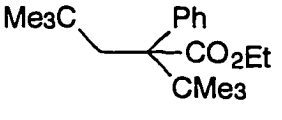
A mixture of two diastereomers was isolated as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.45-7.36 (m, 4H), 7.25-7.17 (m, 2H), 4.13-4.01 (m, 4H), 3.59 (dd, *J*=9.2, 3.7 Hz, 1H), 2.56 (m, 2H), 2.26 (dd, *J*=14.0, 9.2 Hz, 1H), 1.59-1.52 (m, 1H), 1.16 (t, *J*=7.2 Hz, 3H), 1.09 (t, *J*=7.2 Hz, 3H), 0.88 (s, 9H), 0.63 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 174.675(s) and 174.625(s), 173.827(s), 144.878(s), 143.582(s), 139.108(s) and 139.094(s), 129.299(d), 129.093(d), 127.540(d), 126.956(d), 126.322(s), 60.545(t), 60.517(t), 57.254(s), 49.953(t), 47.759(d) and 47.737(d), 47.082(t), 31.340(s), 30.948(s), 30.520(q), 29.381(q), 13.916(q), 13.610(q); EIMS *m/z* (rel intensity) 466 (M^+, 13), 393 (96), 337 (100), 263 (38), 207 (32), 193 (20), 57 (41); HRMS calcd for $C_{30}H_{42}O_4$ 466.3083, found 466.3075.

1-[1-(Ethoxycarbonyl)-3,3-dimethyl)butyl]-4-(1,1-dimethylethyl)benzene (14)



This compound was isolated as a mixture with compound **15** which can not be separated. Colorless liquid. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.31 (d, *J*=8.4 Hz, 2H), 7.24 (dd, *J*=8.4 Hz, 2H), 4.16-4.01(m, 2H), 3.61 (dd, *J*=9.9, 3.0 Hz, 1H), 2.32 (dd, *J*=14.0, 9.9 Hz, 1H), 1.53 (dd, *J*=14.0, 3.0 Hz, 1H),1.30 (s, 9H), 1.20 (t, *J*=7.2 Hz, 3H), 0.90 (s, 9H); GCMS *m/z* (rel intensity) 290 (M^+, 34), 275 (55.63), 217 (50), 161 (29), 147 (24), 57 (100).

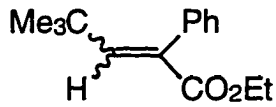
2,2,5,5-Tetramethyl-3-phenyl-3-(ethoxycarbonyl)hexane (15)



This compound was isolated as a mixture with compound **14** which can not be separated. Colorless liquid.^{1}H NMR ($CDCl_3$, 300MHz) δ 2.35 (d, *J*=12 Hz, 1H), 2.30 (d, *J*=12 Hz,

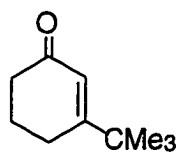
1H), 1.49 (s, 9H), 0.97 (s, 9H); GCMS *m/z* (rel intensity) 290 (M^+, 34), 275 (55.63), 217 (50), 161 (29), 147 (24), 57 (100).

Ethyl 2-phenyl-4,4-dimethyl-2-pentenoate (16)



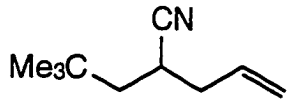
The compounds were not isolated.The *(E)* and *(Z)* forms gave the same GCMS *m/z* (rel intensity) 232 (M^+, 100), 217 (31), 186 (50), 157 (24), 143 (79), 128 (31), 117 (26), 77 (12), 87 (17).

3-(1,1-Dimethylethyl)-2-cyclohexenone (18)



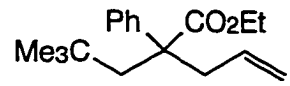
The compound was isolated as a colorless liquid. ^1H NMR ($CDCl_3$, 300MHz) δ 5.96 (s, 1H), 2.38-2.34 (m, 4H), 2.01-1.93 (m, 2H), 1.13 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 200.85, 173.89, 122.99, 37.45, 36.76, 28.23, 25.90, 23.28; EIMS *m/z* (rel intensity) 305 ($2M+1^+$, 39), 249 (42), 191 (25), 153 ($M+1^+$, 98), 97 (69), 57 (100); HRMS calcd for $C_{10}H_{16}O$ 152.1201, found 152.1198

4-Cyano-6,6-dimethyl-1-heptene (19)



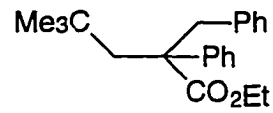
The compound was isolated as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300MHz) δ 5.89-5.75 (m, 1H), 5.23-5.16 (m, 2H), 2.61-2.52 (m, 1H), 2.40-2.31 (m, 2H), 1.68 (dd, *J*=14.1, 10.8 Hz, 1H), 1.38 (dd, *J*=14.1, 2.7 Hz, 1H), 1.00 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 133.13, 122.99, 118.91, 45.59, 38.33, 30.69, 29.29, 26.86; EIMS *m/z* (rel intensity) 151 (M^+, 5), 136 (31), 109 (45), 94 (100), 80 (15); HRMS calcd for $C_{10}H_{17}N$ 151.1361, found 151.1360.

Ethyl 2-phenyl-(2,2-dimethylpropyl)-4-pentenoate (20)



The compound was isolated as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.38-7.29 (m, 5H), 5.57-5.48 (m, 1H), 4.98-4.93 (m, 2H), 4.18-4.06 (m, 2H), 2.93 (d, *J*=6.9 Hz, 2H), 2.13 (s, 2H), 1.17 (t, *J*=7.2 Hz, 3H), 0.86 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 175.92, 143.31, 134.18, 127.96, 126.78, 126.39, 118.03, 60.51, 53.68, 46.88, 41.17, 31.78, 31.33, 13.89; EIMS *m/z* (rel intensity) 274 (M^+, 3), 233 (5), 217 (5), 201 (9), 177 (100), 131 (28), 103 (18); HRMS calcd for $C_{18}H_{26}O_2$ 274.1933, found 274.1941.

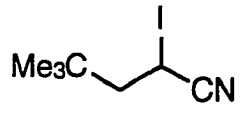
Ethyl 2-phenyl-2-(phenylmethyl)-4,4-dimethylpentanoate (21)



The compound was isolated as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.31-6.73 (m,10H), 4.19-4.04 (m, 2H), 3.47 (d, *J*=13.5 Hz, 1H), 3.23 (d, *J*=13.5 Hz, 1H), 2.14 (d, *J*=14.5 Hz, 1H), 2.25 (d, *J*=14.7 Hz, 1H), 1.21 (t, *J*=7.2 Hz, 3H), 0.85 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 175.39, 142.55, 137.43, 130.49, 127.89, 127.53, 127.41, 126.27,

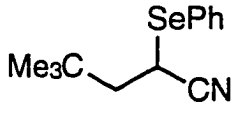
126.11, 60.39, 55.08, 48.84, 46.25, 31.82, 31.36, 13.86; GCMS *m/z* (rel intensity) 324 (M^+, 2), 267 (8), 177 (100), 131 (47), 103, (28), 91 (28), 57 (92).

2-Iodo-4,4-dimethylpentanenitrile (22)



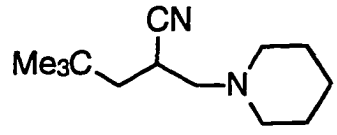
The compound was isolated as a colorless liquid. ^1H NMR ($CDCl_3$, 300MHz) δ 4.26 (dd, *J*=11.4, 3.8 Hz, 1H), 2.31 (dd, *J*=14.4, 11.4 Hz, 1H), 2.12 (dd, *J*=14.4, 3.8 Hz, 1H), 1.03 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 120.61, 52.69, 33.82, 29.15, 28.92; EIMS *m/z* (rel intensity) 237 (M^+, 4), 222 (2), 110 (7), 95 (19), 57 (100); HRMS calcd for $C_7H_{12}IN$ 237.0015, found 237.0016.

2-Phenylseleno-4,4-dimethylpentanenitrile (23)



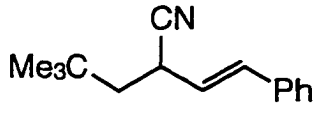
The compound was isolated as a colorless liquid. ^1H NMR ($CDCl_3$, 300MHz) δ 7.75-7.35 (m, 5H), 3.63 (dd, *J*=10.8, 3.6 Hz, 1H), 1.89 (dd, *J*=14.1, 10.8 Hz, 1H), 1.77 (dd, *J*= 14.1, 3.6 Hz, 1H), 0.99 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 136.32, 129.62, 129.46, 126.45, 121.17, 46.87, 32.03, 29.09, 21.51; EIMS *m/z* (rel intensity) 269 (M^+, 6), 267 (M^+, 21), 268 (M^+, 5), 266 (M^+, 2),269 (M^+, 6), 265 (M^+, 16), 264 (M^+, 4), 263 (M^+, 6), 157 (34), 77 (16), 57 (100); HRMS calcd for $C_{13}H_{17}NSe$ 267.0526, found 267.0523.

2-(1-Pyrrolidinylmethyl)-4,4-dimethylpentanenitrile (24)



The compound was isolated as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300MHz) δ 2.67-2.54 (m, 2H), 2.41 (br, 4H), 2.37-2.31 (m, 1H), 1.64-1.53 (m, 6H), 1.49-1.38 (m, 2H), 0.99 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 133.91, 61.92, 54.65, 43.91, 30.70, 29.34, 25.91, 25.70, 24.18; EIMS *m/z* (rel intensity) 208 (M^+, 1), 207 (1), 193 (15), 98 (100); CIMS 417 ($2M+1^+$, 30), 209 ($M+1^+$, 100); HRMS calcd for $C_{13}H_{24}N_2$ 208.1939, found 208.1940.

***(E)*-1-Phenyl-3-cyano-5,5-dimethyl-1-hexene (25)**



The compound was isolated as a white solid, mp 56-58 °C. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.39-7.25 (m, 5H), 6.72 (dd, *J*=15.9, 1.5 Hz, 1H), 6.03 (dd, *J*=15.9, 6.6 Hz, 1H), 3.40 (dddd, *J*=9.6, 6.3, 3.9, 1.5 Hz, 1H), 1.85 (dd, *J*=14.1, 9.3 Hz, 1H), 1.59 (dd, *J*=14.1, 4.2 Hz, 1H), 1.05 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 135.79, 132.38, 128.67, 128.14, 126.47, 124.73, 121.24, 47.24, 30.98, 30.26, 29.41; EIMS *m/z* (rel intensity) 213 (M^+, 35), 198 (4), 157 (16), 143 (100), 142 (41), 115 (30), 91 (13), 71 (27), 57 (86); HRMS calcd for $C_{15}H_{19}N$ 213.1518, found 213.1519.

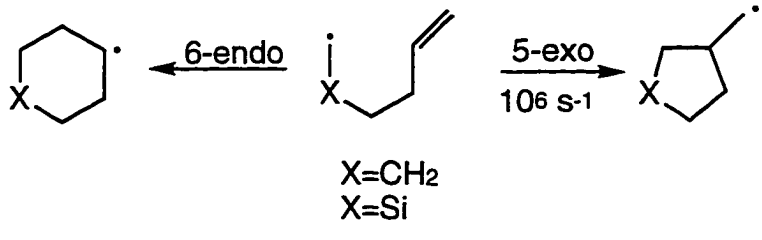
CHAPTER II RADICAL CYCLIZATIONS OF 1,6-DIENES AND OLEFINIC NITRILES

Introduction

The intramolecular radical cyclization reaction is a very important means for formation of carbocyclic and heterocyclic compounds. One of the early examples was the use of 1,6-heptadiene as a substrate in cyclization with 1-iodoperfluoropropane to form the then unexpected five-membered rings.[26] Recent advances in the area have demonstrated that radical cyclization is powerful in organic synthesis and this methodology is widely applied in synthesis of natural products.[27-37] Now the radical cyclization reaction has an established role in synthetic organic chemistry as a highly versatile and often indispensible method of skeleton construction. These cyclization reactions exhibit interesting regioselectivities and stereoselectivities and can be carried out with a variety of functional groups.

Among numerous ring closure modes, 5-exo cyclization during closure of 5-hexen-1-yl radical is one of the most well-known documented processes in free radical chemistry.[38] 5-Exo mode cyclization mainly to the cyclopentylmethyl radical indicates that the cyclization is largely kinetically controlled (Baldwin-Beckwith rule). In many cases 6-endo closure is not observed although it is favored thermodynamically. The 5-Exo ring closure is often a propagation step in a typical radical chain reaction. One example is the Bu_3SnH method in which radical **27** is

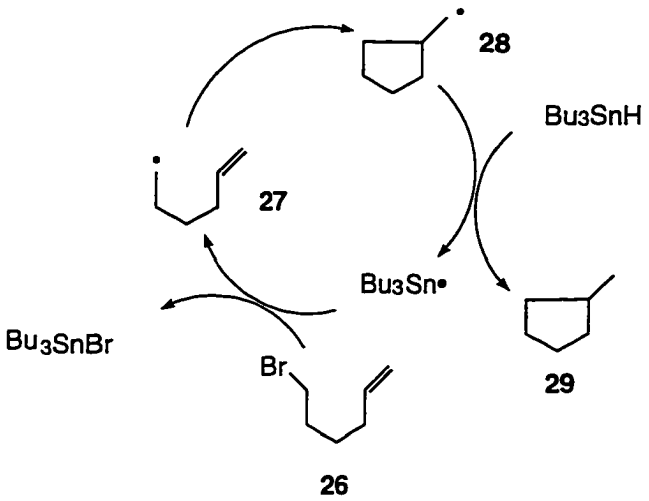
Scheme 21



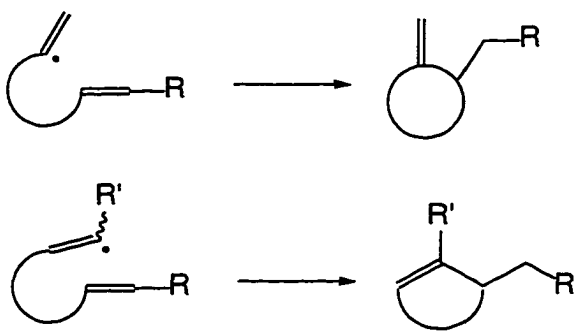
X=CH_2
X=Si

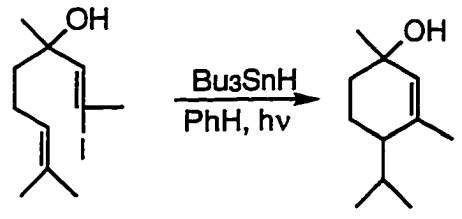
not trapped readily by Bu_3SnH since the intramolecular cyclization is faster whereas hydrogen abstraction by the cyclized radical **28** occurs as the chain propagation step to form the non-radical product **29**and to regenerate $Bu_3Sn\bullet$ which in turn converts the bromide to the radical **27**. Since both the reactivity and the selectivity requirements for chain reaction are met, this type of cyclization reaction is synthetically useful.

Scheme 22

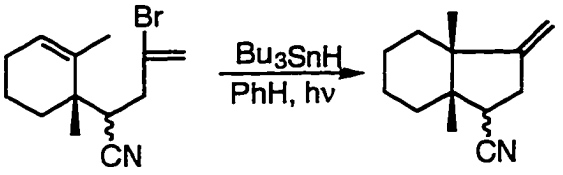


Cyclization of vinyl radicals has been investigated in the same way. The following examples shows both 5-exo and 6-exo mode cyclization were obtained with the tin hydride method (Eq17, 18).[39] However, the utility of 5-exo cyclization sometimes is offset by the





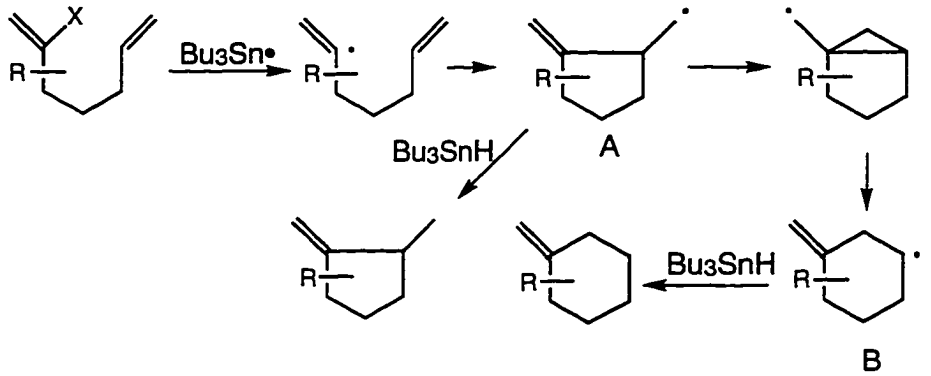
(18)



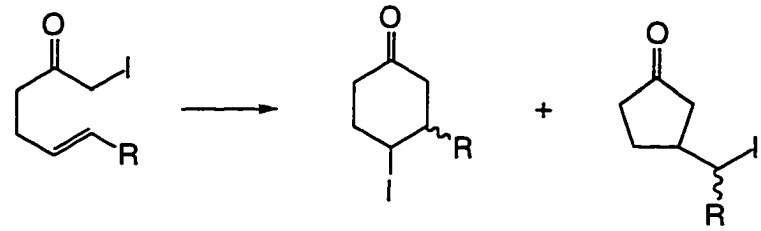
(19)

rearrangement of the cyclized radical A to the more stable B which is the formal product of 6-endo cyclization (Scheme 23).[40]

Scheme 23



A few exceptions to the general rule concerning the cyclization of 5-hexen-1-yl type radicals have been found.[41] 6-Endo cyclization is prefered when X=Si in Scheme 21 and the unusual property is rationalized on stereoelectronic grounds.[38d,e] Exceptions are also found for α-keto radicals in 5-exo/6-endo competition. 6-Endo cyclization products predominate in some cases when there is a carbonyl group inside the rings being formed(Eq 20).[42] The regioselectivity always depends on the structures of the uncyclized radicals. But the more general rule suggests that radical cyclizations proceed kinetically in an exo mode to provide the smaller of the two possible rings. This is also applicable for 6-exo/7endo ring closure. With larger ring formation, endo closure becomes a highly preferred process.

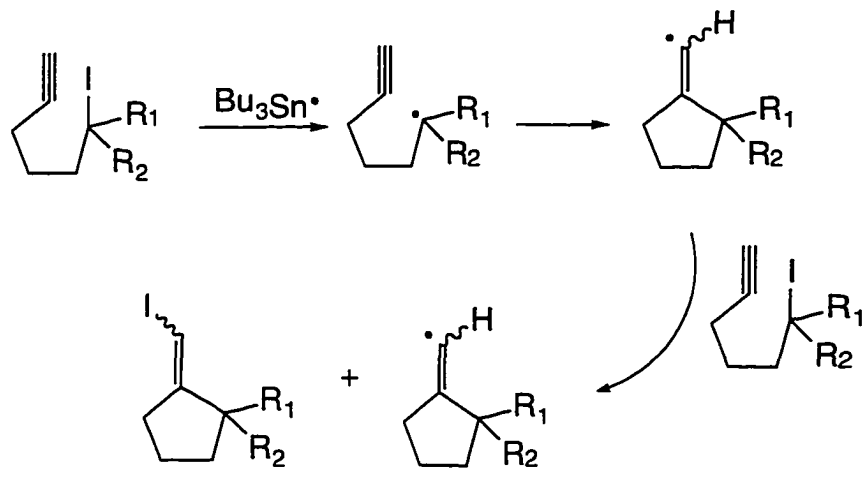


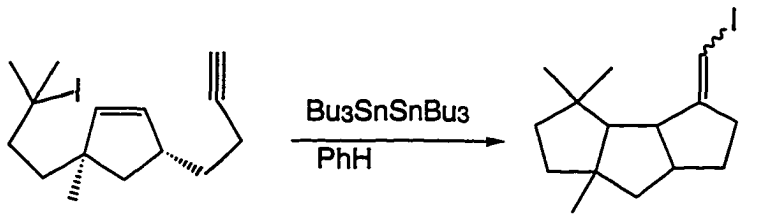
R = H	97	3
R = CH_3	75	25

(20)

A similar five-membered ring closure is also achieved using carbon-carbon triple bonds in place of double bonds.[43,44] In this case another approach is employed to establish the radical chain process. An atom transfer process is described in Scheme 24 in which iodine atom transfers from the substrate to the cyclized radical. A good example is the tandem cyclization of reaction 22 which affords a tricylic compound.

Scheme 24

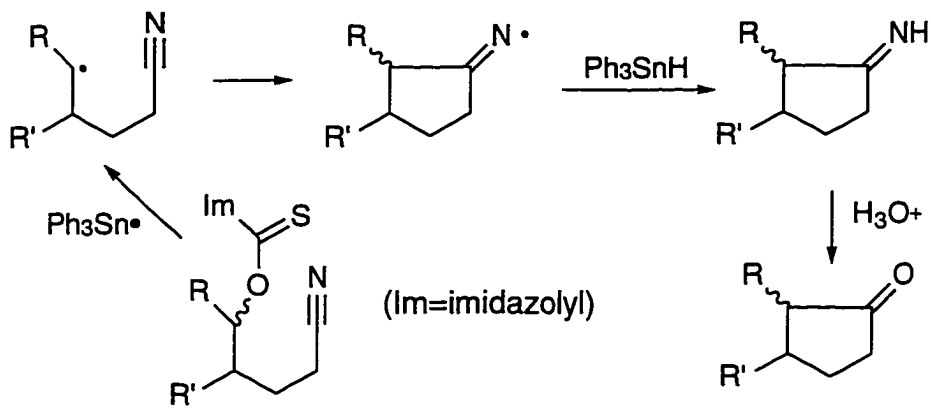




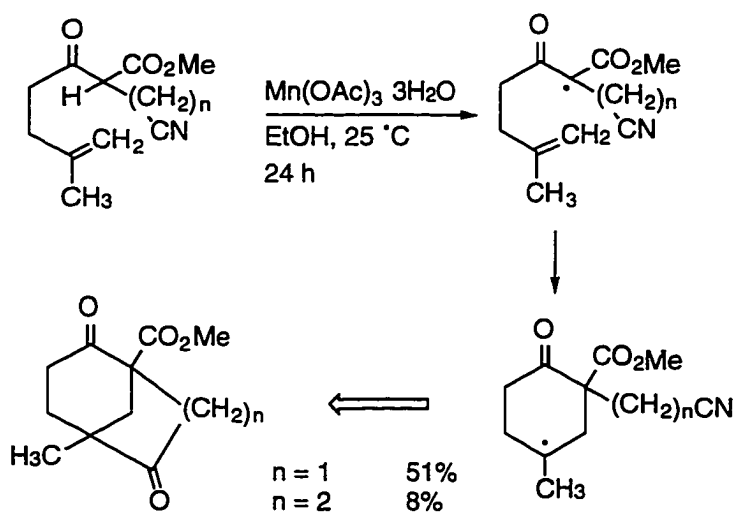
(21)

Cyclization of 4-cyano radicals is another method for forming carbocycles, although this type of cyclization is not as common as for olefinic radicals. Such process involves an addition of radicals to the carbon-nitrogen triple bonds to form the iminyl radicals which are reduced by a tin hydride to afford the imines (Scheme 25).[45] Hydrolysis of the formed imines affords the cyclopentanones.

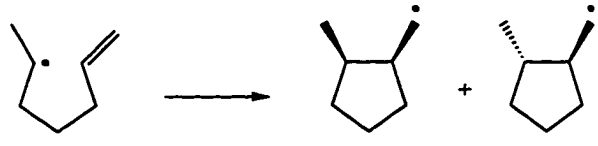
Scheme 25



Mn(III)-based oxidative radical tandem cyclization can be terminated by addition to nitriles to give bicylic ketons as shown below. [46]



One of the important features of radical cyclization is its stereoselectivity. For 1-substituted 5-hexenyl radicals, *cis*-isomers are preferred in most case as shown below.[47] However, the *cis/trans* ratio may vary over a wide rang. The chair-equatorial transition state is believed to be responsible for the *cis* product while the trans product arises from the chair-axial and boat-equatorial transition state. Substituents influence the balance between those transition states and thus change the *cis/trans* ratio.



73 : 27

Results and Discussion

Radical Cyclization of 1,6-Dienes Leading to Cyclopentanes

Photolysis of *t*-BuHgX with 1,6-dienes leads to cyclized products in high yield. The reactions are carried out in DMSO with sunlamp at 35-40 °C for several hours. The products are cyclized five-membered ring mercury compounds. There are two isomers observed and in all cases, except the vinylphosphonates, *cis* isomers are the major products. The *cis/trans* ratio changes slightly from 3.5/1 to 6/1.

Six different 1,6-dienes are investigated and their reactions with *t*-BuHgX were monitored by ^{1}H NMR in DMSO-d_6.

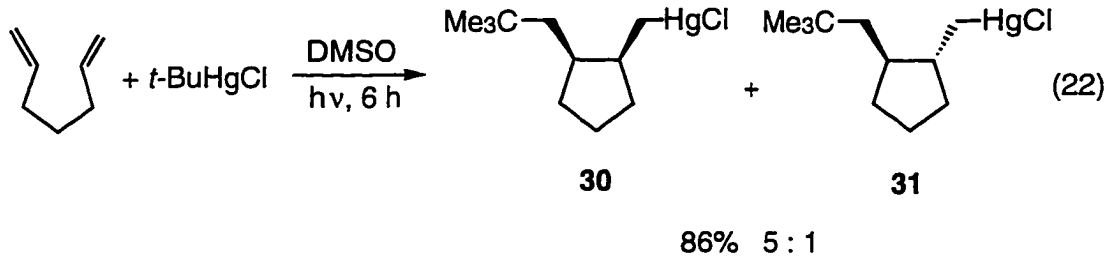
1,6-heptadiene

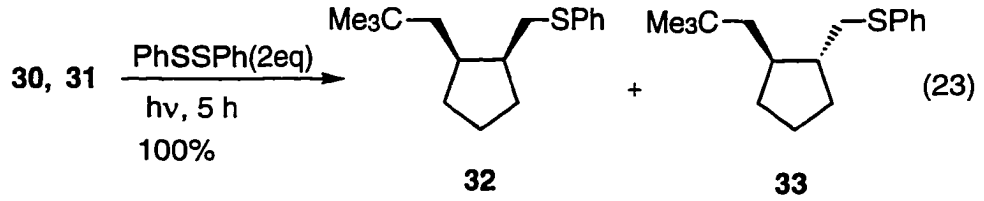
The reaction of 1,6-heptadiene with 2 equivalent of *t*-BuHgCl gives 1,2-disubstituted five-membered ring products in a yield of 86%. Only two isomers **30** *(cis)* and **31** (*trans*) are obtained . The *cis/tran* ratio is 5:1. No 6-endo cyclization product is observed. Compound

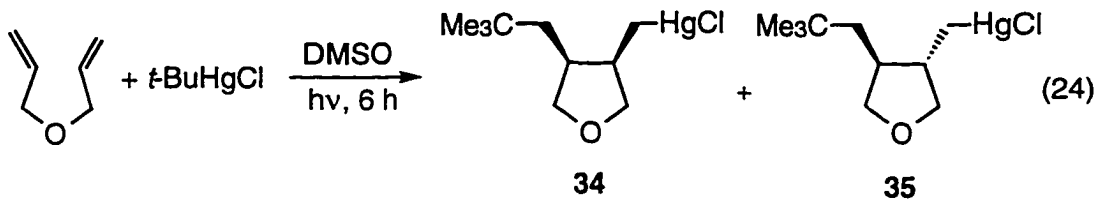
30 and **31** can be easily converted to the sulfides **32** and **33** in high yield with PhSSPh under photolytic condition in the same reaction pot. The *cis* configuration was assigned from the NOESY spectrum of the major isomer of the sulfides.

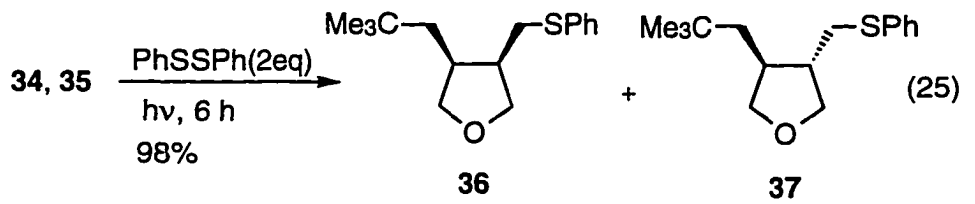
Allyl ether

Similar result is obained for allyl ether. A very high yield (98%) of the cyclized products are formed with a *cis/trans* ratio as 3.5:1 after 6 h photostimulated reaction of allyl ether with 2 equivalent of *t*-BuHgCl in DMSO. The sulfides **36** and **37** are produced in 98% upon





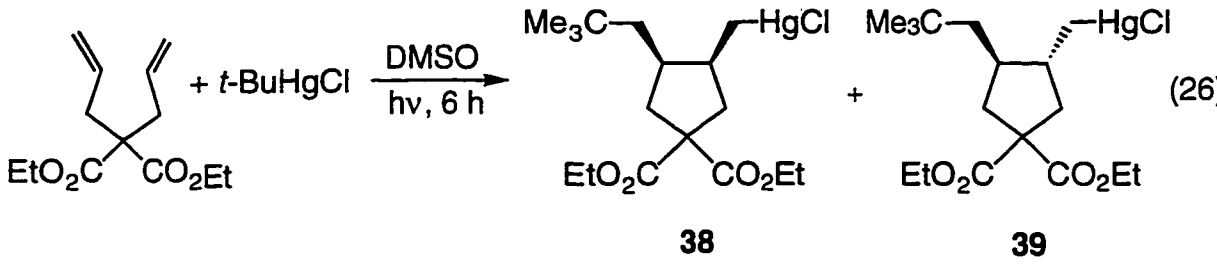


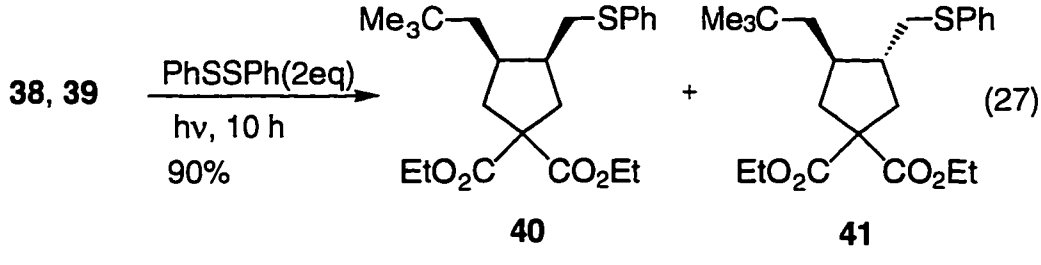


treatment of the reaction mixture with 2 equivalent of PhSSPh. The *cis* configuration was assigned from the NOESY spectrum of the major isomer of the phenyl sulfides.

Diethyl diallylmalonate

The outcome of the reaction of diethyl diallymalonate with *t*-BuHgCl is given below in reaction 26 and 27. The *cis* configuration was determined from the NOESY spectrum of the major isomer of the sulfides.This substrate was tested for a dark reaction also. A moderate yield (54%) was obtained for the reaction with 1.2 equivalent of *t*-BuHgI and 4 equivalent of





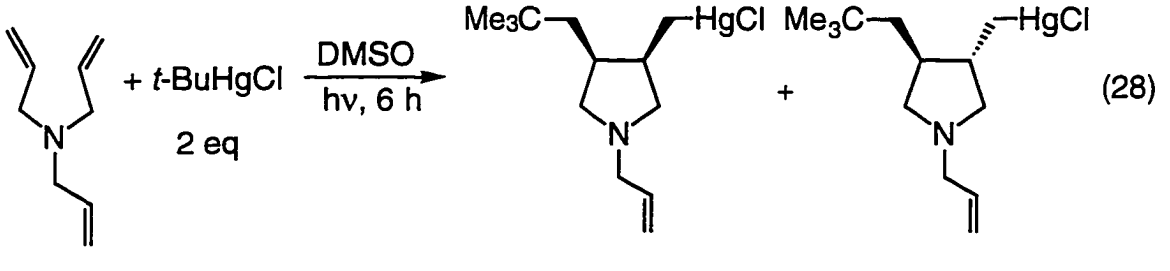
KI for 12 h in the dark. KI shows a small promotion effect in photostimulated reactions where a 44% yield of **38** and **39** is obtained in 70 min with 2 equivalent of *t*-BuHgI with sunlamp irradiation. In the presence of 4 equivalent of KI the yield increases to only 63% in the same condition. In the absence of irradiation, I^- does have a large effect in enhancing the rate of the initiation reaction.

Triallylamine

Under the same reaction conditons used above, triallylamine gives a somewhat lower yield of the cyclized products and the reaction is not as clean as with the above 1,6-dienes (Eq 28, 29). The *cis/trans* ratio as determined by GC of the sulfides was 6:1. The *cis* configuration was determined by the NOESY spectrum of pure **42**. Strong NOE was observed for He^Hf, Ha^Hc, Hb^Hg, Hd^Hi, He^Hh and Hf^Hj. NOE was not observed for He^Hc, He^Hd and Hf^Hb (see the structure on the next page).

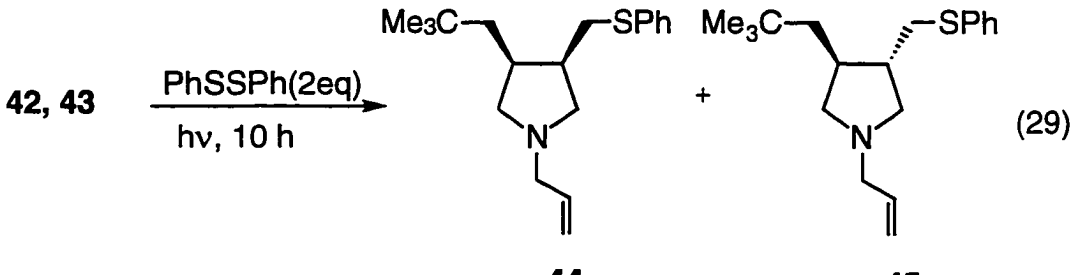
Diallyl vinylphosphonate

This substrate was found to be more reactive than the above 1,6-dienes. Photolysis of with 1.1 equivalent of *t*-BuHgI in DMSO consumes all of the substrate in 1 h. The reactions in the dark are promoted by KI and no starting material is left with 1.1 equivalent of *t*-BuHgI and 4 equivalent of KI in 1.5 h. There are at least three or four cyclized products observed by ^{1}H NMR and three of the cyclized products were isolated after workup. The direct reduction of an

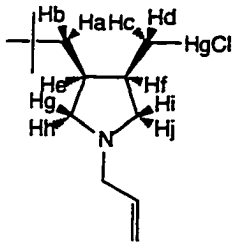


42 **43**

58% 6 : 1

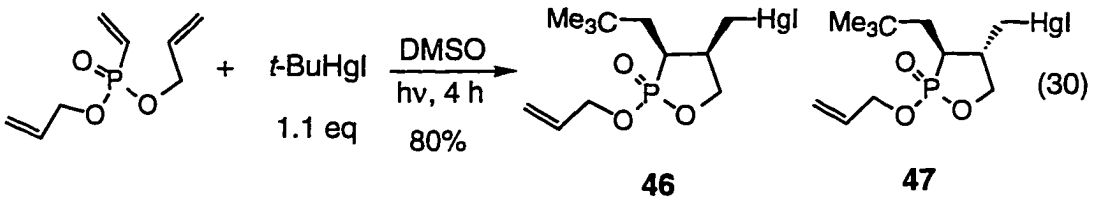


44 **45**

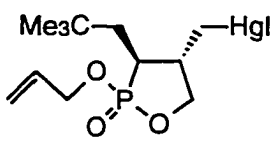


The structure of **42**

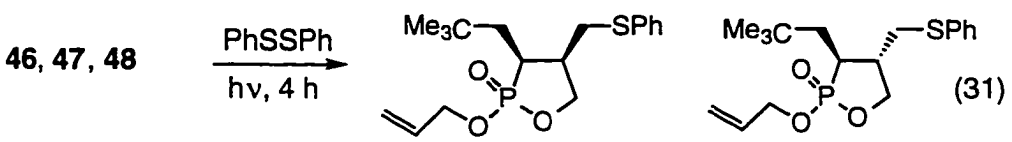
intermediate uncyclized organomercurial may occur with the use of NH_4I in the dark, but the cyclized products still predominate. In the presence of Et_3SiH the direct reduction can compete with cyclization. Dark reaction of the substrate with 3 equivalent of *t*-BuHgCl and Et_3SiH in DMSO for 6 h gives the uncyclized reductive product in 30% and the cyclized products in more than 55%.



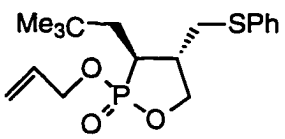
46 **47**



48



49 **50**

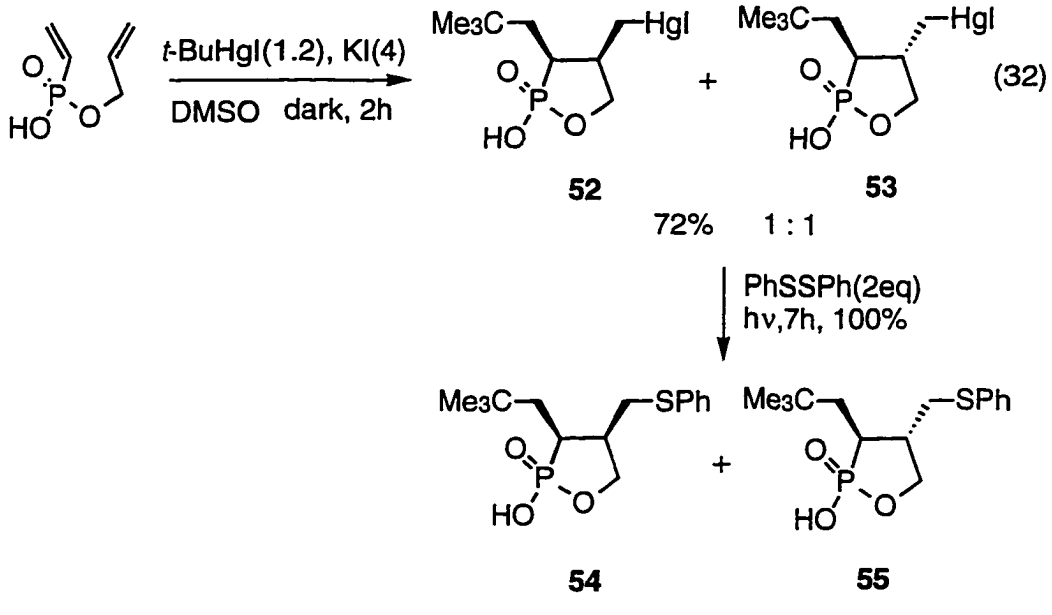


51

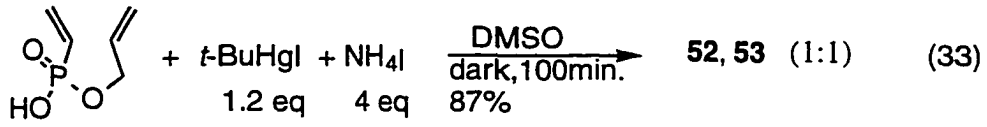
From ^1H NMR monitoring and the isolation of the cyclized products, the isomers **46**, **47** and **48** are formed roughly in the same amount with a total yield of over 80%. This is a quite different result than for simple 1,6-dienes. The cis isomer is not favored for the α,β-unsaturated phosphonate. The configurations of the isolated sulfides were determined from the NOESY spectra.

Allyl vinylphosphonate

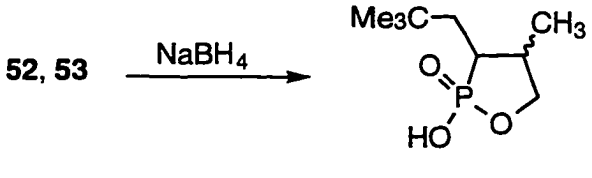
To simplfy stereochemistry in the above cyclization process, allyl vinylphosphonate was investigated. The *cis* and *trans* cyclized products **52** and **53** are observed and the ratio is 1 : 1. Photolysis of the reaction mixture with 2 equivalent of PhSSPh leads to the sulfide **54**



(32)



(33)

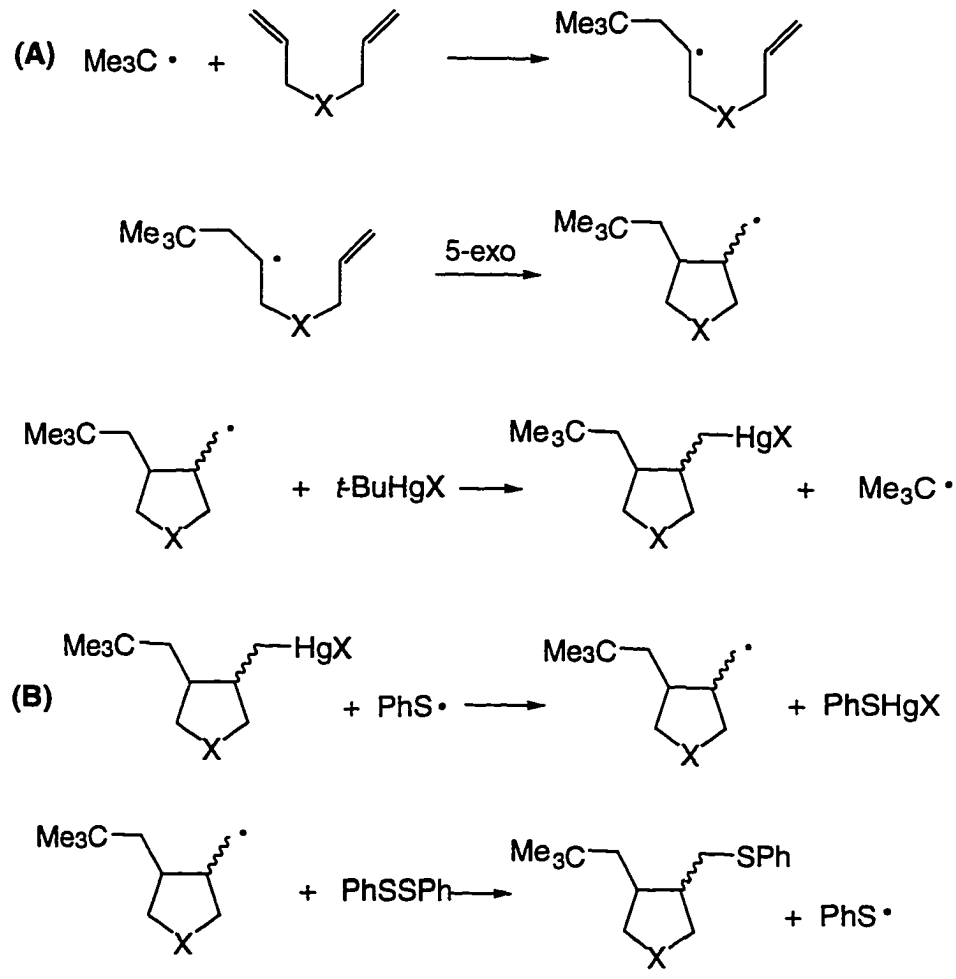


(34)

56 (*cis* : *trans* = 1 : 1)

and **55** in essentially quantitative yield. The reaction of the substrate with 3 equivalent of *t*-BuHgCl and Et_3SiH gives cyclized compounds as the major products with about 15% of the direct reduction product. With NH_4I, **52** and **53** are formed in 87% with little uncyclized reduction product. Isolation of the cyclized phosphonic monoacids is very difficult. Thus, the compound **56** was prepared by the reaction with 1.2 equivalent of *t*-BuHgI with sunlamp irradiation for 1 h in benzene followed by treatment with $NaBH_4$ in methylene chloride. The sample was analyzed as a 1:1 mixture of *cis* and *trans* cyclized products.

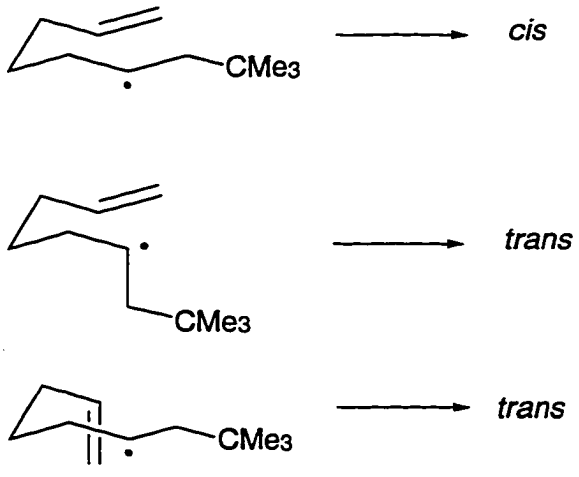
Scheme 26



The above cyclization of 1,6-dienes is a free radical chain process as shown in Scheme 26. The addition of *t*-Bu• to 1,6-dienes forms a secondary alkyl radical which readily cyclizes in the 5-exo mode to give a cyclopentylmethyl radical. This primary radical is relatively reactive and can be trapped by *t*-BuHgX to form the stable cyclized mercury product and a new *t*-Bu•. In (B) the cyclized mercury compound reacts wth PhS• and produces the primary radical which is trapped by PhSSPh to give the sulfide and regenerate PhS•.

No 6-endo product was observed. Other cyclization processes such as 4-exo and 6-exo mode cyclizations were not observed in this system. When 1,5-hexadiene and 1,7-octadiene are allowed to react with *t*-BuHgCl, no cyclized products were obtained except a low yield of uncyclized 1:1 adducts.

The stereochemistry of cyclization is in accord with that observed for simple 1-substituted hexenyl radicals. In all cases, except for the vinylphosphonates, *cis* selectivity was observed.



Three transition states leading to *cis* and *trans* isomers are given here. The first chair conformation perhaps has the lowest energy and thus the *cis* isomer is favored. The seconary and the third conformation giving the *trans* isomer are higher in energy than the first, therefore the *trans* isomer is the minor product.

The reason why there is no *cis/trans* selectivity for the vinylphosphonates is not clear. Further study should continue to rationalize it.

Radical Cyclization of 1,6-Enynes Leading to Methylenecyclopentanes

Photolysis of allyl propargyl ether with *t*-BuHgX in DMSO forms the cyclized mercury compound **57** (*E* and *Z*) and the reductive product **58** (Table 10). The *E* and *Z* isomers were assigned by the ^{1}H NMR coupling of the allylic protons. *t*-BuHgCl and *t*-BuHgI are different in reactivity toward the cyclized vinyl radical (Scheme 27). With *t*-BuHgCl, only **57** is formed

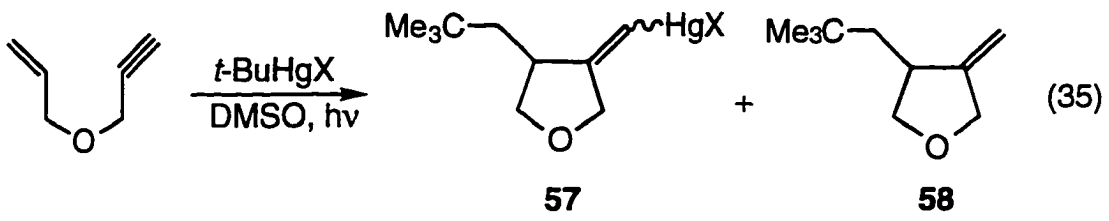
Table 10. Cyclization Reaction of Allyl Propargyl Ether[a]

Mol equiv.			%Yield[b]	
t-BuHgX	KI	Condition	**57** (*Z*:*E* =2.5:1)	**58**
Cl (2)		hυ, 6h	48	
Cl (2)		hυ, 11h	56	
Cl (2)	3	hυ, 4.5h		21
I (2)		hυ, 4.5h		46
I (2)		hυ, 10h		50
I (4)		hυ, 6h		47
Cl (2)		hυ, 10h		44 [c]

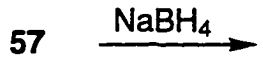
[a] Reaction of allyl propargyl ether (0.1 mmol) with *t*-BuHgX in 0.6 mL of DMSO-*d*6 at 35-40 °C. hυ = sunlamp irradiation.

[b] NMR yield with toluene as an internal standard.

[c] Workup with $NaBH_4$.



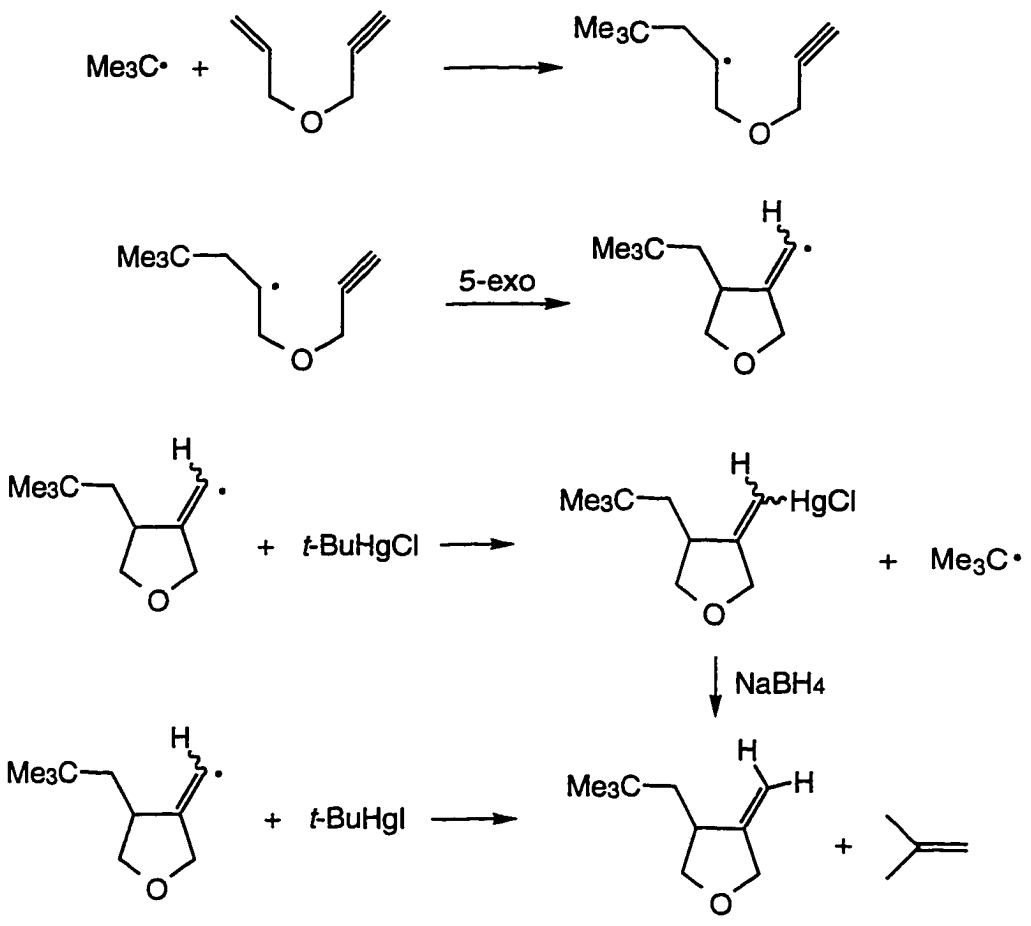
57 **58** (35)



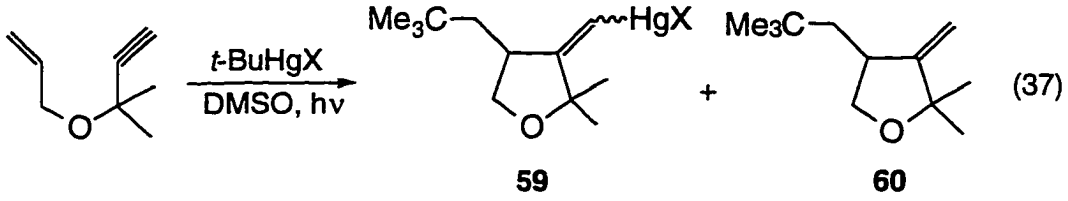
57 **58** (36)

while with *t*-BuHgI only **58** is obained. Treatment of **57** with $NaBH_4$ also gives **58** as shown in Eq 36. The result also indicates that the double bond is more reactive than the triple bond toward $Me_3C\bullet$ radical.

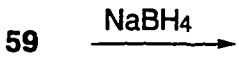
Scheme 27



Similar results are obtained for allyl (1,1-dimethylpropargyl) ether. Higher yield of **59** and **60** are observed under the same condition as above (Table 11). This can be explained by the gem-dimethyl effect. The presence of these two methyl groups leads to the favorable conformation for 5-exo cyclization.



(37)



(38)

Table 11. Cyclization Reaction of Allyl 1,1-Dimethylpropargyl Ether with *t*-BuHgX[a]

		%Yield[b]	
t-BuHgX(mol equiv)	Condition	**59** (*Z*:*E* =1:1.5)	**60**
Cl (2)	hυ, 5 h	75	
I (2)	hυ, 5 h	9	60
Cl (1.2)	hυ, 10 h		40[c]

[a] Reaction of allyl 1,1-dimethylpropargyl ether (0.1 mmol) with *t*-BuHgX in 0.6 mL of DMSO-*d6* at 35-40 °C. hυ = sunlamp irradiation.

[b] NMR yield with toluene as an internal standard.

[c] Workup with $NaBH_4$.

Kinetic Chain Length and Reactivity

Kinetic chain length, as one of the parameters of chemical kinetics, has proven to be valuable approaches to the study of reaction mechanisms and to an understanding of chemical reactivity. A chain reaction is the process in which the low concentrations of reactive

intermediates (chain carriers, such as free radicals) are involved. These intermediates participate in the cycle of a reaction sequence so that the intermediates are regenerated after each cycle. Chain carriers are formed in a chain initiation step, participate in chain propagation steps, and are extinguished by termination steps. In the end, the chain is stopped and the reaction is finished.

Initial kinetic chain length represents the average number of molecules consumed in the reaction for every radical which initiates the chain.[49] Ultimately the initiation reaction must produce stable products via a number of chain propagation steps.[50] Therefore, the magnitude of a kinetic chain length can be used to determine whether the reaction is a chain process or not. The initial kinetic chain length (k.c.l.) of a reaction is defined as the ratio of initial reaction rate to rate of initiation as shown in equation 39. To calculate the kinetic chain length, the rate of the

$$\text{k.c.l.} = \frac{\text{Initial reaction rate}}{\text{Rate of initiation}} \qquad (39)$$

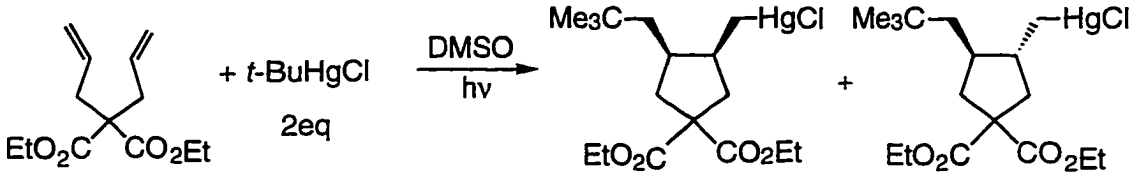
chain initiation must be known. This rate can be conveniently measured from the inhibition period observed with known amounts of free radical scavengers. Free radical chain reactions are very sensitive to inhibition in which a small amount of a radical scavenger can cause a remarkable retardation for the chain reaction. For a given observed rate of reaction, the greater the kinetic chain length, the longer the inhibition time becomes.

The kinetic chain length was measured for the following substrates in photostimulated cyclization reactions using the method described above. The reaction progress was followed by ^{1}H NMR and the initial reaction rate was deduced by extrapolation of the reaction progress curve to time = 0 (Table 12, Figure 2). The rate of initiation is the concentration of the radical inhibitor, di-*tert*-butyl nitroxide (DTBN), divided by the inhibition time during which no reaction is observed. In all cases, 10 mol % of DTBN was used unless otherwise indicated.

Diethyl diallylmalonate

The monitoring result of the reaction of diethyl diallylmalonate with *t*-BuHgCl is given in Table 12. Figure 2 is the plot of the yields against time. From Figure 2, the initial reaction rate is estimated as 0.0128 C/min (C is the initial concentration of the substrate). The rate of initiation is estimated as 0.00192 C/min. The initial kinetic chain length is calculated to be 6.6.

Table 12. Cyclization of Diethyl Diallylmalonate in DMSO[a]



38 **39**

		%Yield of **38** and **39**[b]	
Entry	Time (min)	Without DTBN	With DTBN[c]
1	5	4.3	0
2	10	9	0
3	15	16	0
4	30	30	0
5	45	35	0
6	60	47	6
7	75	53	20
8	95	60	35
9	125	62	53

a Reaction of 0.1 mmol of diethyl diallymalonate with 2 equiv. of *t*-BuHgCl in 0.6 mL of DMSO-d_6 with sunlamp irradiation at 35-40 °C.

b ^{1}H NMR yield with toluene as an internal standard.

c 10 mol% based on the substrate.

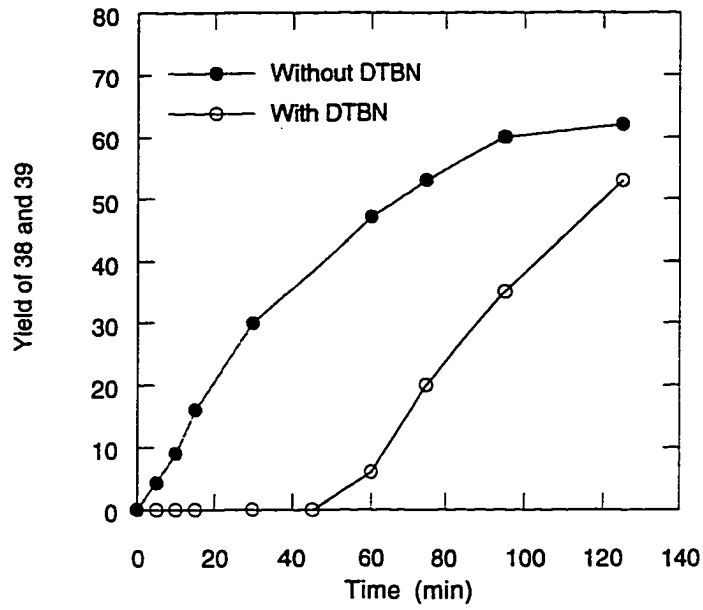
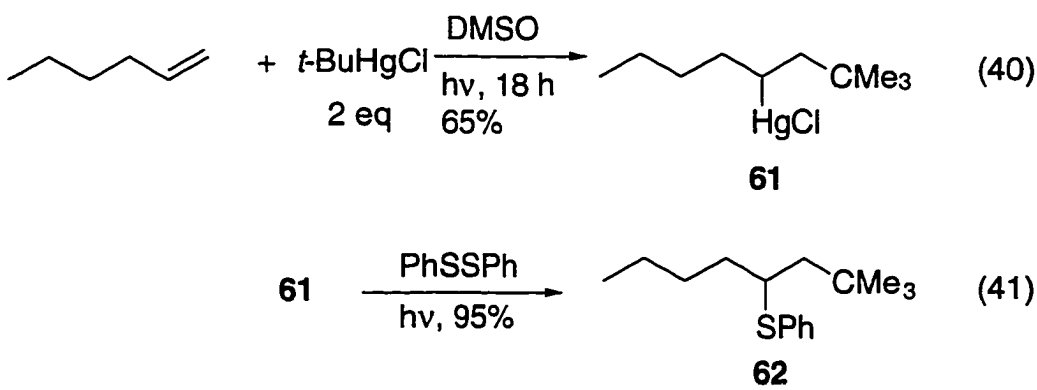


Figure 2. Yield of **38** and **39** with Time.

1-Hexene

Alkylmercury halides can add to an isolated double bond to form a 1:1 adduct. However, unlike the activated alkenes such as acrylates, acrylonitrile and vinylphosphonates, simple double bonds show much lower reactivity. For 1-hexene, photolysis with 2 equivalent of *t*-BuHgCl for 18 h affords **61** in 65% yield (reaction 40 and Scheme 28) which then is converted to **62** with PhSSPh. *t*-BuHgI does not increase the yield of 1:1 adduct (Table 13).



Scheme 28

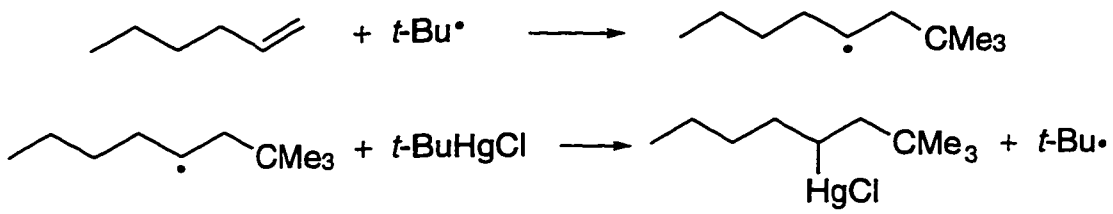


Table 13. Addition of *t*-BuHgCl to 1-Hexene in DMSO[a]

		%Yield of **61**[b]	
Entry	Time (min)	Without DTBN	With DTBN[c]
1	10	0	0
2	25	5.6	0
3	40	10	0
4	60	12.3	5
5	80	-	9
6	110	20	13.6
7	190	31	26
8	280	40	37
t-BuHgI(1.2)	10 h	29[d]	-
t-BuHgI(2)	5 h	43[d]	-
t-BuHgI(2)	10 h	51[d]	-

a Reaction of 0.1 mmol of 1-hexene with 2 equivalent of *t*-BuHgCl in 0.6 mL of DMSO-d_6 with sunlamp irradiation at 35-40 °C.

b ^{1}H NMR yield with toluene as an internal standard.

c 10 mol% based on 1-hexene.

d BuCH(HgI)CH_2Bu-*t* formed.

Compared to the 5-exo cyclization of 1,6-dienes, the less efficient chain process is attributed to the slow trapping of the adduct radical by *t*-BuHgX. In this case, the adduct radical is a secondary radical which is not as reactive as a primary radical toward *t*-BuHgX. The kinetic chain length measurement is then conducted. The data are listed in Table 13 and plotted in Figure 3.

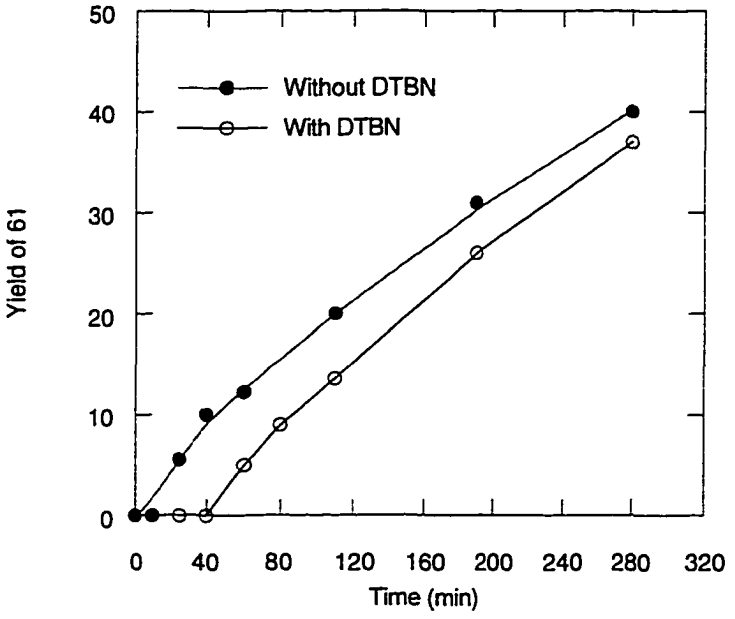


Figure 3. Yield of **61** with Time.

The initial reaction rate is 0.0034 C/min and the rate of initiation is 0.0025 C/min. Thus, the kinetic chain length is calculated to be 1.4.

1,6-Heptadiene

The same measurement was conducted for this substrate (Table 14 and Figure 4). The initial reaction rate is 0.0066 C/min and the rate of initiation is 0.002 C/min. The kinetic chain length is 3.3.

Table 14. Cyclization of 1,6-Heptadiene in DMSO[a]

		%Yield of **30** and **31**[b]	
Entry	Time (min)	Without DTBN	With DTBN[c]
1	5	3.6	0
2	10	6.3	0
3	20	13	0
4	30	18	0
5	45	26	0
6	60	31	4.7
7	75	36	11
8	90	41	20

a Reaction of 0.1 mmol of 1,6-heptadiene with 2 equivalent of *t*-BuHgCl in 0.6 mL of DMSO-d_6 with sunlamp irradiation at 35-40 °C.

b ^{1}H NMR yield with toluene as an internal standard.

c 10 mol% based on 1,6-heptadiene

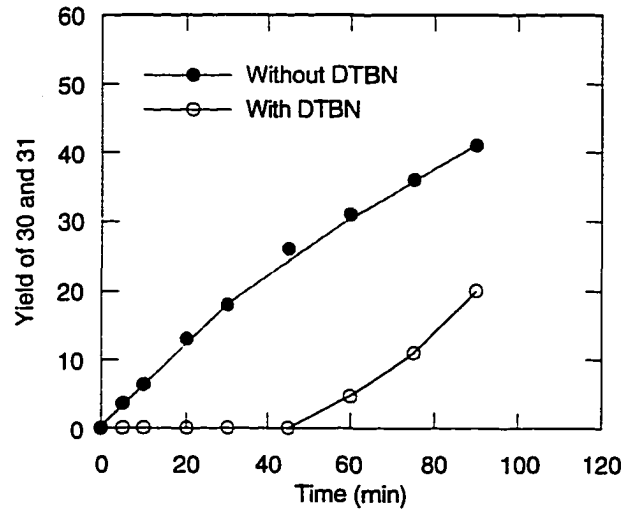


Figure 4. Yield of **30** and **31** with Time.

Allyl ether

Both *t*-BuHgCl and *t*-BuHgI were employed for the data measurement. For *t*-BuHgCl, the initial reaction rate is 0.014 C/min and the rate of initiation is 0.00216 C/min. The kinetic chain length calculated is 6.5. For *t*-BuHgI, the initial reaction rate is 0.0237 C/min and the rate of initiation is 0.00227 C/min, the chain length is 10.4 (Table 15, Figure 5 and 6).

Table 15. Cyclization of Allyl Ether with *t*-BuHgX in DMSO[a]

		%Yield of **34** and **35**[b]	
Entry	Time (min)	Without DTBN	With DTBN[c]
1	5	7 (11)	0 (0)
2	10	12 (19)	0 (0)
3	20	26 (36)	0 (0)
4	30	39 (47)	0 (0)
5	45	52 (59)	0 (1)
6	55	- (61)	- (7)
7	60	64 (-)	0 (-)
8	65	-	- (19)
9	75	78 (-)	1.7 (27)
10	85	-	15 (-)

a Reaction of 0.1 mmol of allyl ether with 2 equivalent of *t*-BuHgCl (I) in 0.6 mL of DMSO-d_6 with sunlamp irradiation at 35-40 °C.

b ^{1}H NMR yield with toluene as an internal standard. The yields of the cyclized mercury iodide are in ( ).

c 10 mol% based on allyl ether. With *t*-BuHgCl, 16 mol% was used.

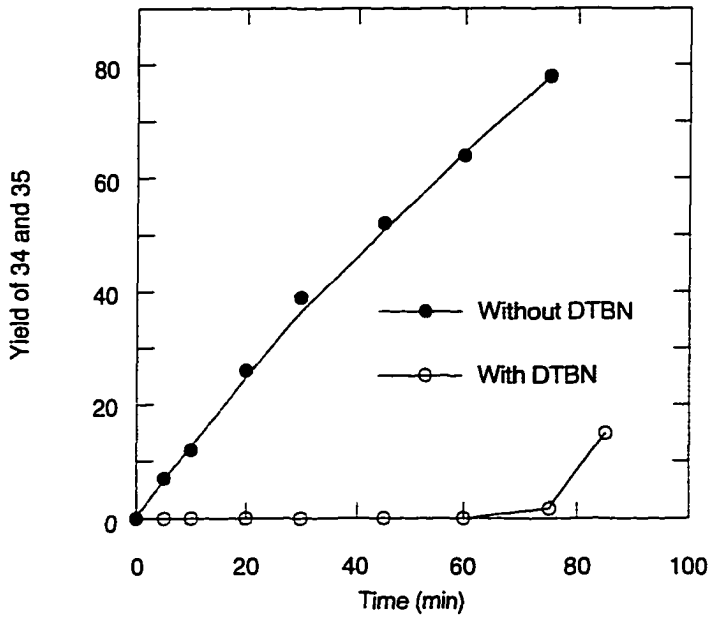


Figure 5. Yield of **34** and **35** with Time with *t*-BuHgCl

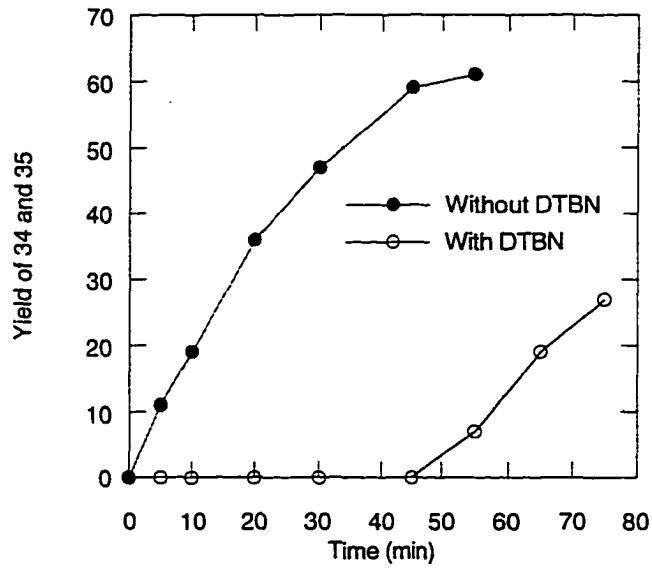


Figure 6. Yield of **34** and **35** with Time with *t*-BuHgI.

Allyl propargyl ether

See Table 16 and Figure 7. The Initial rate is 0.007 C/min and the rate of initiation is 0.00167 C/min. The kinetic chain length is 4.2.

Allyl vinylphosphonate

Measurement is carried out in different reaction conditions for this substrate. Promotion effect by KI is observed in the dark. Inhibition time is more than five days (see Table 17 and Figure 8). The initial rate is 0.051 C/min and the rate of initiation is 0.0000118 C/min. The kinetic chain length is 4300. Table 18 lists the data under photolytic condition without KI. The initial rate is 0.126 C/min and the rate of initiation is 0.00187 C/min (Figure 9). The kinetic chain length calculated is 67.

Table 16. Cyclization of Allyl Propargyl Ether with *t*-BuHgCl in DMSO[a]

		%Yield of **57**[b]	
Entry	Time (min)	Without DTBN	With DTBN[c]
1	15	10	0
2	30	18	0
3	50	26	0
4	70	30	3
5	90	33	9

a Reaction of 0.1 mmol of allyl propargyl ether with 2 equivalent of *t*-BuHgCl in 0.6 mL of DMSO-d_6 with sunlamp irradiation at 35-40 °C.

b ^{1}H NMR yield with toluene as an internal standard.

c 10 mol% based on allyl propargyl ether.

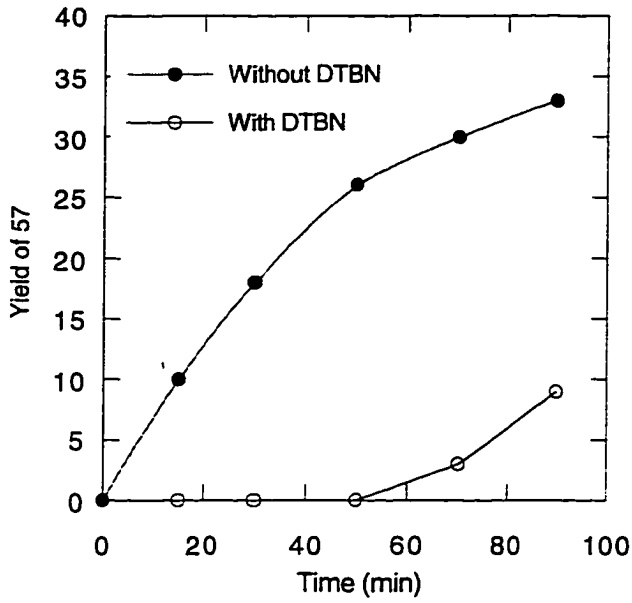


Figure 7. Yield of **57** with Time.

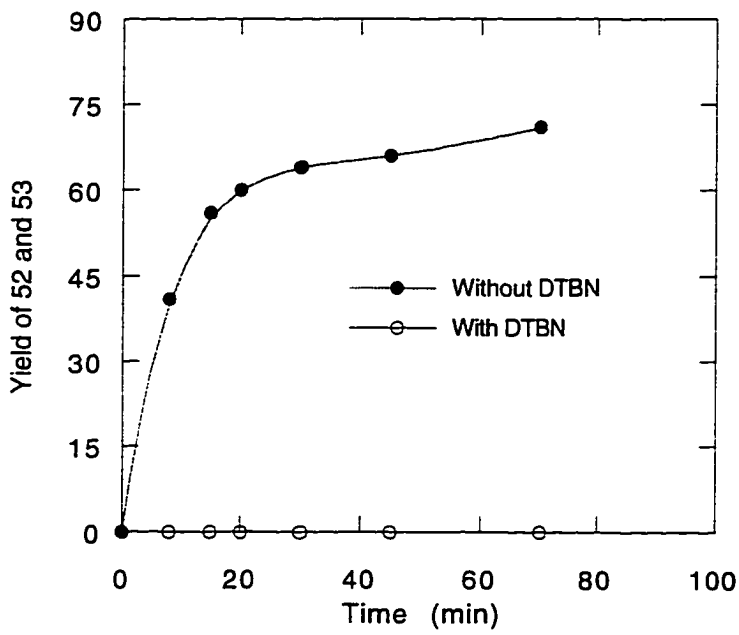


Figure 8. Yield of **52** and **53** with Time with KI in the Dark.

Table 17. Cyclization of Allyl Vinylphosphonate with *t*-BuHgI/KI in DMSO[a]

		%Yield of **52** and **53**[b]	
Entry	Time (min)	Without DTBN	With DTBN[c]
1	8	41	0
2	15	56	0
3	20	60	0
4	30	64	0
5	45	66	0
6	70	71	0
7	five days plus 1360 min	-	18
8	five days plus 1420 min	-	25

a Reaction of 0.1 mmol of allyl vinylphosphonate with 1.2 equivalent of *t*-BuHgI and 4 equivalent of KI in 0.6 mL of DMSO-d_6 in the dark.

b ^{1}H NMR yield with toluene as an internal standard.

c 10 mol% based on allyl vinylphosphonate.

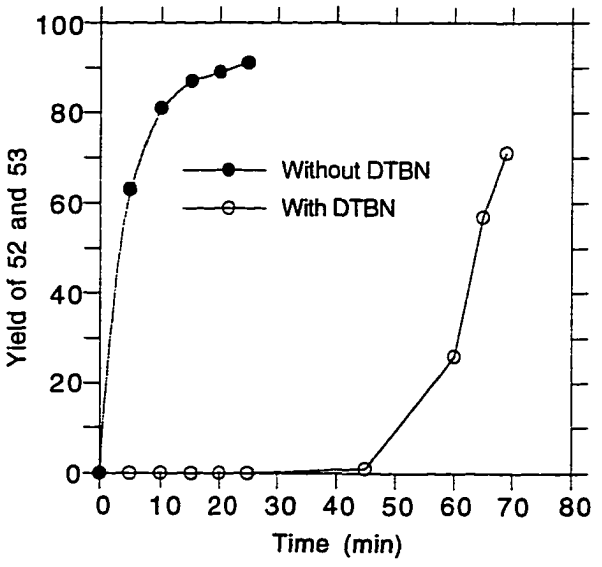


Figure 9. Yield of **52** and **53** with Time with Sunlamp.

Table 18. Cyclization of Allyl Vinylphosphonate with *t*-BuHgI in DMSO[a]

		%Yield of **52** and **53**[b]	
Entry	Time (min)	Without DTBN	With DTBN[c]
1	5	63	0
2	10	81	0
2	15	87	0
3	20	89	0
4	25	91	0
5	45	-	1
6	60	-	26
7	65	-	57
8	69	-	71

a Reaction of 0.1 mmol of allyl vinylphosphonate with 1.2 equivalent of *t*-BuHgI in 0.6 mL of DMSO-d_6 with sunlamp irradiation.

b ^{1}H NMR yield with toluene as an internal standard.

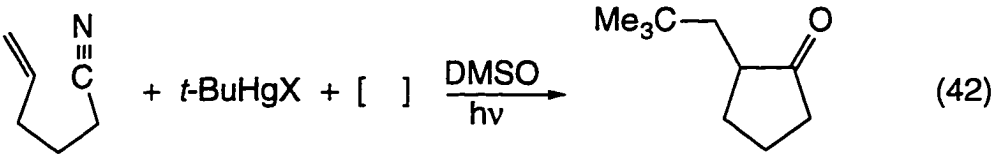
c 10 mol% based on allyl vinylphosphonate.

These results show that the cyclization reactions are chain processes with the kinetic chain length ranging 3.3-6.6 for the1,6-dienes and the 1,6-enyne upon photostimulation. For allyl vinylphosphonate, the value is as high as 67, indicating an unusual reactivity. With KI in the dark, the vinylphosphonate gives a kinetic chain length of 4300 because of the slow rate of initiation.

Radical Cyclization of 5-Enenitriles Leading to Cyclopentanones

Reactions of olefinic nitriles with *t*-BuHgI were investigated. No cyclization is observed when a mixture of 5-hexenenitrile and *tert*-butyl mercury halides in DMSO is irradiated by

sunlamp, and only simple 1:1 adduct products are observed in 37% yield with *t*-BuHgCl (2eq) for 18h and in 35% yield with *t*-BuHgI (2eq) for 5h (see reactions of 1-hexene). Addition of acid has little effect on cyclization (Table 19). However, cyclization is observed when both acid and iodide ion are present. Photolysis of 5-enenitriles with *t*-BuHgI/HI in DMSO gives the cyclopentanones in fair to good yield. In general, the yield of the cyclized products increases with increasing acidity (HI>PTSA>NH_4I).



(42)

63

Table 19. Cyclization of 5-Hexenenitrile[a]

t-BuHgX	Condition	% Yield of **63**[b]
Cl (4)	KI (8), 16 h	4
Cl (4)	NH_4I (8), 12 h	8
Cl (4)	PTSA (4), 12 h	8
I (2)	PTSA (2), KI (4), 3 h	6
I (4)	PTSA (4), 12 h	7
I (4)	PTSA (4), KI (4), 12 h	20
I (2)	Aq. HI (2), 10 h	29
I (4)	Aq. HI (4), 11 h	41
I (4)	Aq. HI (2), 20 h	55

[a] Reaction of 0.1 mmol of 5-hexenenitrile with *t*-BuHgX in 0.6 mL of DMSO-d_6 with sunlamp irradiation at 35-40 °C.

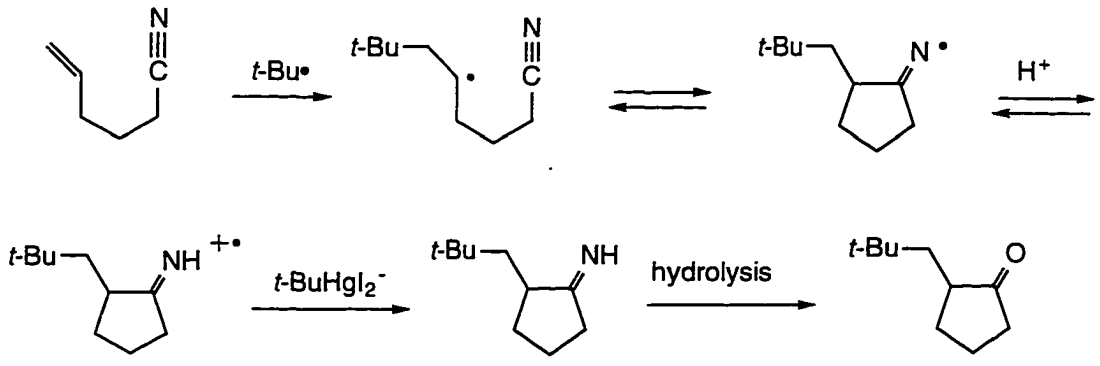
[b] ^1H NMR yield with toluene as an internal standard.

5-Hexenenitrile

Basically, the reactions of 5-hexenenitrile with *t*-BuHgX give very poor yield of the cyclized ketone **63** with NH_4I or PTSA in DMSO but good yields with aqueous HI added. Since *t*-BuHgX decomposes with excess of HI, the appropriate reaction condition involved the use of 4 equivalent of *t*-BuHgI and 2 equivalent of 47% HI which gave **63** in 55%, Table 19 and reaction 42.

The overall reaction process consists of the photostimulated radical addition of *tert*-butyl radical to the double bond. The secondary radical formed undergoes 5-exo mode cyclization onto to -CN triple bond to form the iminyl radical. The iminyl radical is protonated and then reduced via electron transfer process by *t*-$BuHgI_2^-$ to the imine. Hydrolysis of the imine gaves rise to the ketone (Scheme 29).

Scheme 29



Allyl cyanomethyl ether

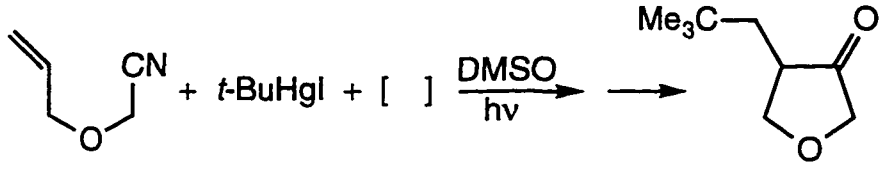
Allyl cyanomethyl ether behaves similarly to 5-hexenenitrile in cyclization reactions (Eq 43, Table 20).

Allyl bis(cyanomethyl)amine

Although two cyano groups are present in the substrate, the reaction still gives low yield of the cyclized product **65** (Eq 44).

2,2-Dimethyl-5-hexenenitrile

The substrate bears gem-dimethyl groups at the α position. Promotion effect was expected based on the two methyl groups, but actually the yields of **66** are even lower than that for 5-hexenenitrile (Eq 45 and Table 21).



(43)

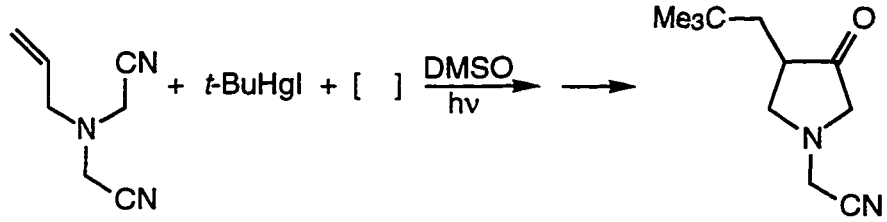
64

Table 20. Cyclization of Allyl Cyanomethyl Ether [a]

t-BuHgI(eq)	Condition	%Yield of **64**[b]
2	KI(4), PTSA(2), 12h	27
4	HI(2), 24h	60
8	HI(8), 12h	58

[a] Reaction of 0.1 mmol of allyl cyanomethyl ether with *t*-BuHgI in 0.6 mL of DMSO-d_6 with sunlamp irradiation under hv at 35-40 °C.

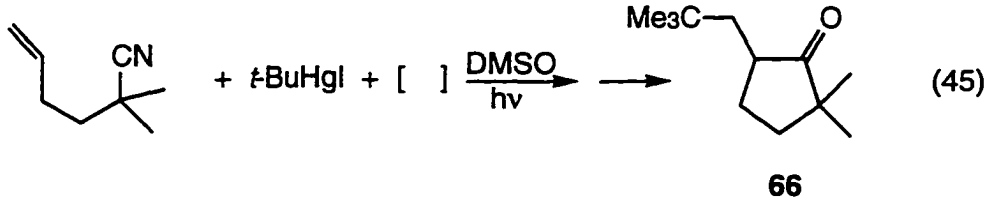
[b] ^{1}H NMR yield with toluene as an internal standard.



(44)

65

4 equiv. *t*-BuHgI	HI(2), 10 h	15%
4 equiv. *t*-BuHgI	HI(4), 22 h	34%



(45)

66

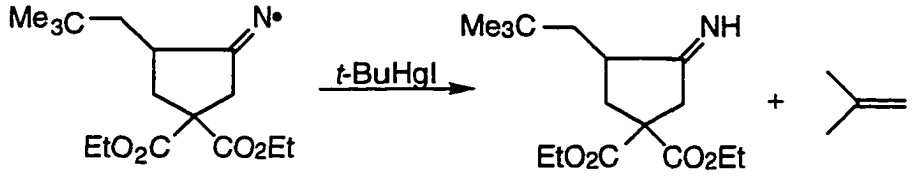
Table 21. Cyclization of 2,2-Dimethyl-5-hexenenitrile in DMSO[a]

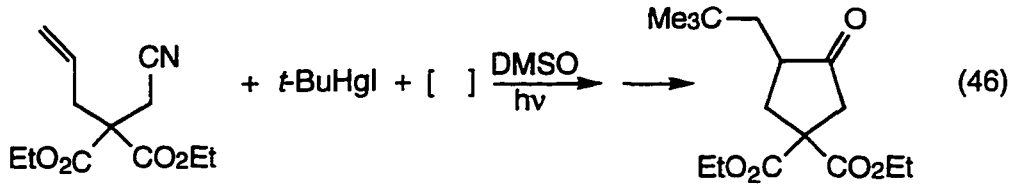
t-BuHgI(eq)	Condition	%Yield of **66**[b]
4	KI(4), PTSA(2), 5 h	8
4	KI(4), PTSA(4), 6 h	9
4	HI(4), 6 h	24
8	HI(8), 12 h	34

a, b see Table 20.

3,3-Bis(ethoxycarbonyl)-5-hexenenitrile

A gem-diester group effect is observed. In this case, the reaction is faster and the yield higher than that without the ester substituents. An 80% yield of **67** was obtained with 4 equivalent of *t*-BuHgI and 2 equivalent of KI for 8 h. In the absence of an acid the reaction still gives a good yield (Table 22). It is assumed that the cyclized iminyl radical is directively trapped by *t*-BuHgI to form the imine. With the mild proton source NH_4I, a 78% yield is obtained even in the dark for 18 h.





(46)

67

Table 22. Cyclization of 3,3-Bis(ethoxycarbonyl)-5-hexenenitrile in DMSO[a]

t-BuHgI(eq)	Condition	%Yield of **67**[b]
4	HI (2), 8 h	80[c]
4	12 h	74
4	KI(2), 12 h	50
1.2	NH_4I (2), 5 h	<10
1.2	PTSA (2), 5 h	34
1.2	5 h	28
4	KI (2), 24 h	10[d]
4	NH_4I (4), 18 h	78[e]

a Reaction of 0.1 mmol 3,3-Bis(ethoxycarbonyl)-5-hexenenitrile with *t*-BuHgI in 0.6 mL of DMSO-d_6 with sunlamp irradiation at 35-40 °C.

b Worup with $Na_2S_2O_3$. ^1H NMR yield with toluene as an internal standard.

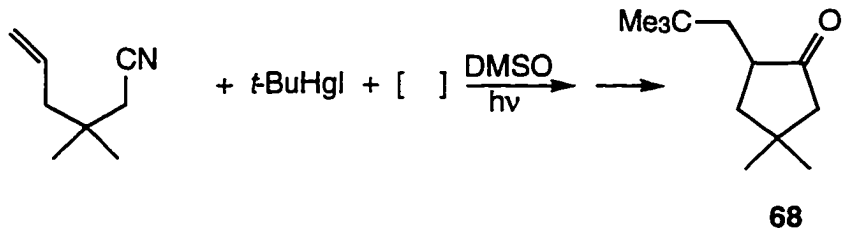
c No workup performed.

d In the dark at room temperature.

e Dark reaction followed by 6*N* HCl workup.

3,3-Dimethyl-5-hexenenitrile

No significant similar effect is observed for the methyl substituents in this substrate. since the yield of **68** is not increased over that for 5-hexenitrile. The methyl groups should have less influence on cyclization than two ester groups.However, the reaction without HI gives a 40% yield of **68** which is somewhat higher than observed for the unsubstituted 5-enenitriles (Table 23).



(47)

68

Table 23. Cyclization of 3,3 Dimethyl-5-hexenenitrile in DMSO[a]

Entry	*t*-BuHgI	Condition	%Yield of **68**[b]
1	4	HI(2), 12 h	55
2	4	12h	40[c]
3	4	NH_4I(4), 12 h	10[c]

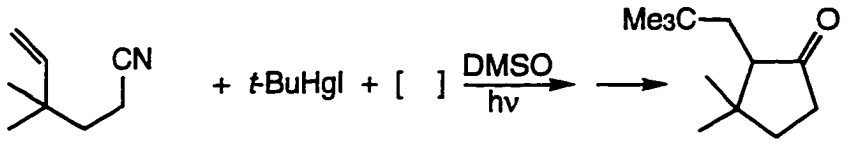
a Reaction of 0.1 mmol 3,3-dimethyl-5-hexenenitrile with *t*-BuHgI in 0.6 mL of DMSO-d_6 with sunlamp irradiation at 35-40 °C.

b ^1H NMR yield with toluene as an internal standard.

c Worup with $Na_2S_2O_3$.

4,4-Dimethyl-5-hexenenitrile

A very slow reaction and poor yield was observed for this substrate. In this case, the addition of *t*-Bu• to the -C=C- bond is slow because of steric hindrance (Eq 48).



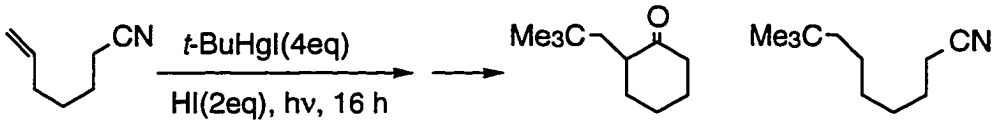
(48)

69

4 eq *t*-BuHgI	12 h	10%
4 eq *t*-BuHgI	HI(2), 12 h	10%

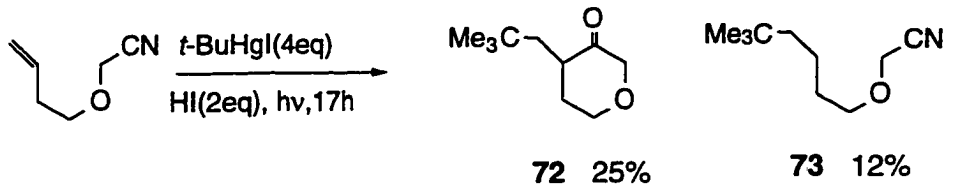
Radical Cyclization of 6-Enenitriles Leading to Cyclohexanones

Four different substrates were studied in the formation of six-membered rings. It is not surprising that some difficulty exists in forming these larger rings. Besides the cyclized cyclohexanones, a lot of direct reduction products are found. For 6-heptenenitrile, only 9% of the cyclized ketone was obtained while 23% of the reduction product was formed. For cyanomethyl homoallyl ether, 25% of **72** was produced and only 12% of the reduction product was formed. Some degree of a gem-diester group effect was observed for the last two substrates. 3,3-Bis(ethoxycarbonyl)-6-heptenenitrile gives the cyclized ketone **74** in 34% yield and 4,4-bis(ethoxycarbonyl)-6-heptenenitrile produces the cylized ketone **76** in 22% yield. From these results it is obvious that 6-exo cyclization is more difficult than 5-exo cyclization.

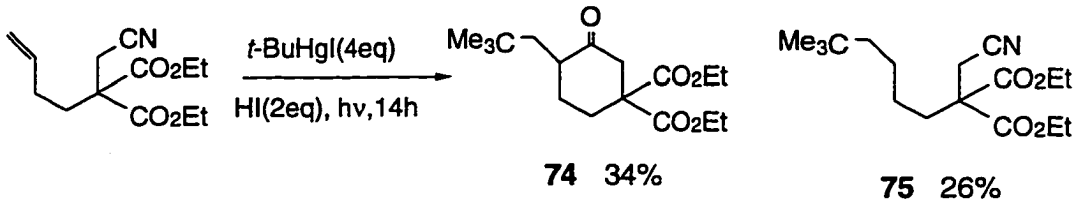


(49)

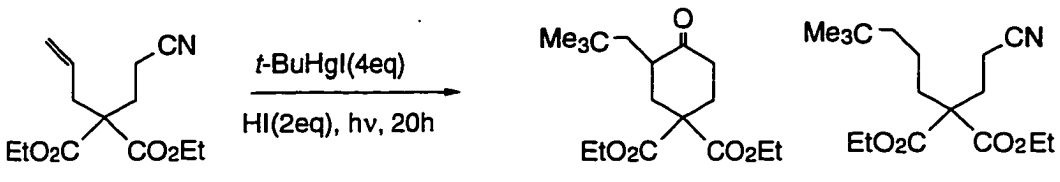
70 9% **71** 23%



72 25% 73 12% (50)



74 34% 75 26% (51)



76 22% 77 33% (52)

Cyclization of Other Substrates

Addition of an alkyl radical to a carbonyl group is reversible. When X• is more stable than R•, a substitution will occur. Such processes are often involved in radical ring expansion.[51] A recent example utilized intramolecular addition of aminyl radicals to carbonyl groups to achieve ring expansion leading to lactams.[52] Intermolecular addition is very difficult [53] unless the adduct radicals are trapped immediately.[54] This study has tested several carboxylic derivatives for intramolecular radical substutution. The results show that in some cases cyclization can be observed with X = SPh which participates in a radical chain reaction. For those substrates with X = Cl, OEt, and OH, no cyclization occurs.

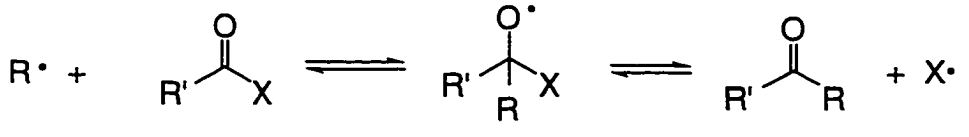


Table 24 lists the reaction results for *S*-phenyl 3,3-bis(ethoxycarbonyl)thiohex-5-enoate. Photolysis with *t*-BuHgX gives a fairly good yield of **67**. A mechanism is proposed in Scheme 30.

(53)

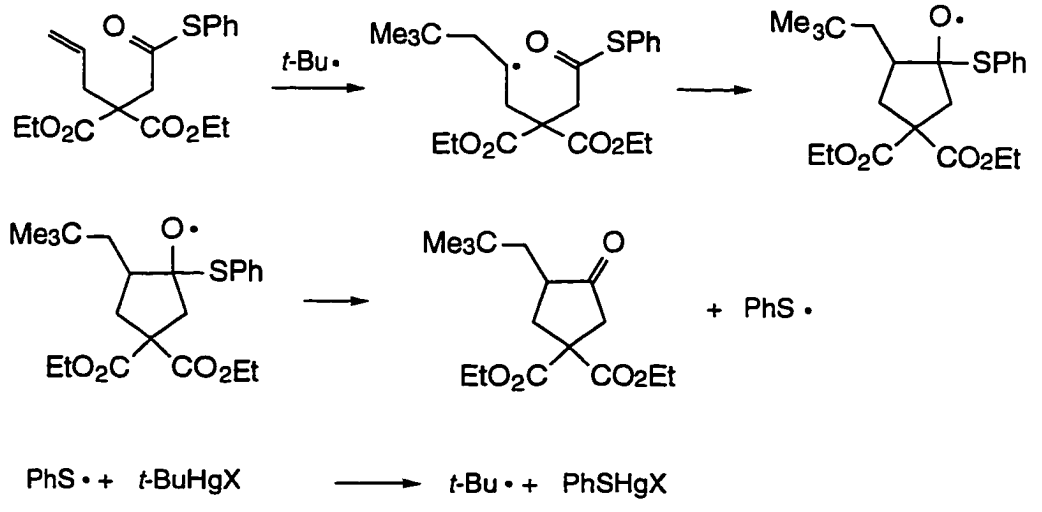
Table 24. Cyclization of *S*-Phenyl 3,3-Bis(ethoxycarbonyl)thiohex-5-enoate[a]

Entry	*t*-BuHgX	Condition	%Yield of **67**[b]
1	I (2.5)	5 h	26
2	I (2.5)	18 h	50
3	Cl (4)	18 h	65

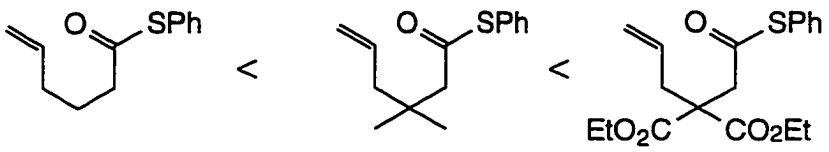
a Reaction of the substrate (0.1 mmol) with *t*-BuHgX in 0.6 mL of DMSO-d_6 with sunlamp irradiation at 35-40 °C.

b ^{1}H NMR yield with toluene as an internal standard.

Scheme 30

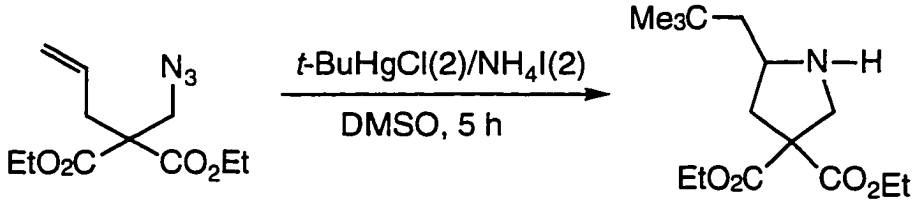


Once again the gem-diester group effect plays a key role in the cyclization. Only a trace of the cyclized ketone is formed for *S*-phenyl thiohex-5-enoate while 65% of the cyclized product is obtained for *S*-phenyl 3,3-bis(ethoxycarbonyl)thiohex-5-enoate. The gem-dimethyl group has much small effect on cyclization rate than the gem-diester group in cyclization since CH_2=$CHCH_2C(Me)_2CH_2C(O)SPh$ gave only 18% of the cyclized ketone.



Cyclization yields trace 18% 65%

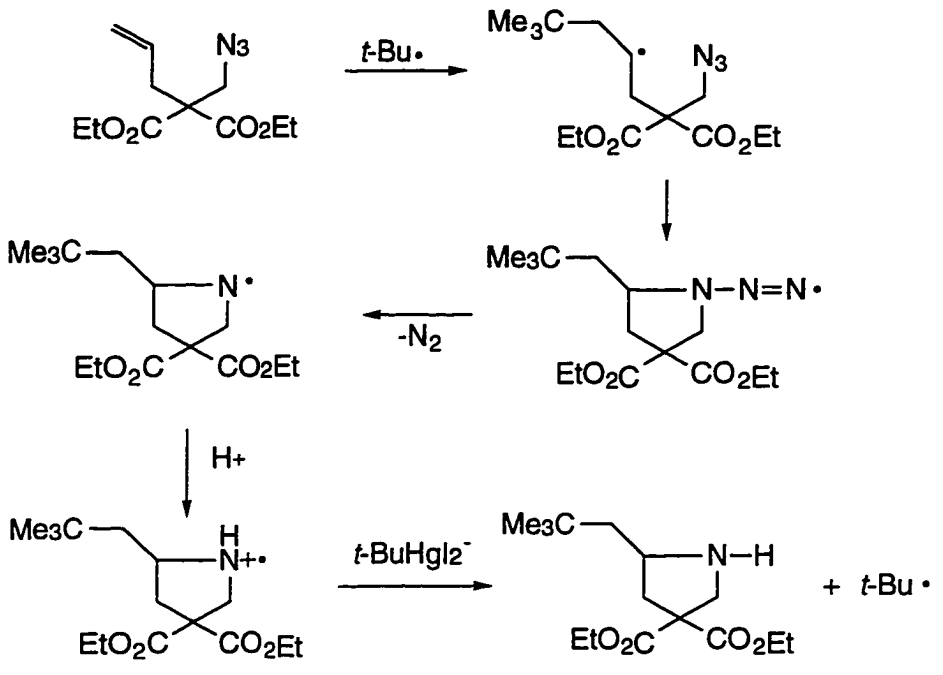
Azides undergo cyclization reactions via a radical pathway.[55] Reaction 54 was tested in *t*-BuHgX system. *t*-BuHgX alone gave little cyclization (only 8% of **78** was formed) but the combination of *t*-BuHgX and NH_4I affords the cyclized amine **78** in 50% yield in DMSO upon photolysis. Based on these observations a mechanism is drawn in Scheme 31. The stronger proton donor HI could not be used because in this case the starting material is not stable toward aqueous HI.



(54)

78 50%

Scheme 31



Conclusion

tert-Butylmercury halides initiate a facile radical cyclization of 1,6-dienes under mild conditions. Photolysis in DMSO affords high yields of cyclopentylmethyl mercury halides which can be converted to the corresponding sulfides with phenyl disulfide or reduced by $NaBH_4$. As a general rule, *cis*-isomers are favored. With *t*-BuHgX/HI 5-enenitriles generate the cyclized ketones via a radical reaction sequence. Less efficient cyclization is also observed for 6-enenitriles. A gem-diester group enhances the cyclization and in some cases cyclized products are only observed with gem-diester substitution.

Experimental Section

General Consideration

2D NMR spectra were recorded on a Bruker DRX 400 spectrometer. Also see the Experimental Section, Chapter I for a description of other instrumentation as well as reaction and isolation techniques.

Solvents and Reagents

See Experimental Section, Chapter I for a description of solvents and reagents.

Materials

1. Diallyl Vinylphosphonate

This compound was prepared by a modified literature method.[56] A mixture of 13.2 g of $AlCl_3$, 4 mL of 1,2-dichloroethane and 8.8 mL of PCl_3 was refluxed for 1 hour. The excess of PCl_3 was removed in vacuo, and the complex was dissolved in 160 mL of CH_2Cl_2. 17 mL of allyl alcohol was added in portions under stirring at room temperature. After 1 h of stirring, water was added until the gelatinous precipitate coagulated. The organic layer was washed with aqeuous $NaHCO_3$ and dried over $MgSO_4$. The solvent was evaporated. 5 mL of THF and 5 mL of Et_3N were added and the mixture was refluxed overnight. Usual workup and vacuo distillation (73-75 ° C/0.5mm) gave the pure product. ^1H NMR ($CDCl_3$, 300MHz) δ 6.40–5.88 (m, 5H).5.40-5.23 (m, 4H), 4.57–4.52 (m, 4H).

2. Allyl Vinylphosphonate

This compound was prepared based on a general method for a phosphonic monoester.[57] To a boiling solution of 3.24 g of vinylphosphonic acid and 2 mL of allyl alcohol in 75 mL of dry THF was added in portions a solution of 6.78 g of dicyclohexylcarbodiimide in 30 mL of THF within 2.5 h. *N*, *N'*-Dicyclohexylurea separated and was filtered off after the mixture had been refluxed for 14 h. The solvent was evaporated in vacuo, 75 mL of 0.5 *N* NaOH was added, the solid precipitate was then filtered and 75 mL of 6 *N* HCl was added. The product was extracted with CH_2Cl_2 for five times and dried over $MgSO_4$. The solvent was evaporated. The product was an oily liquid which was quite pure by NMR pure and was used without further purification (1.82 g) in 40% yield. ^{1}H NMR ($CDCl_3$, 300MHz) δ 6.36–6.02 (m, 3H), 6.00-5.88 (m, 1H), 5.39-5.32 (dt, *J*=17.1, 1.5 Hz, 1H), 5.25-5.21 (dq, *J*=10.5, 1.2 Hz, 1H), 4.53-4.48 (m, 2H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 134.85 (d, J_{ccop} =1.6 Hz), 132.70 (d, J_{ccp} =6.9 Hz), 125.95 (d, J_{cp} =188 Hz), 117.78, 66.04 (d, J_{cop} =5.7 Hz).

3. 5-Hexenenitrile

This compound was prepared according to the litrature method.[58] To a solution of 16 mmol of NaCN in 5 mL of DMSO was added dropwise 13.6 mmol of 5-bromopentene at a temperature at 90-100 °C. Stirring was continued for 10 min after the addition. Usual workup and distillation gave the pure product (88-89 °C/11mm) in 90% yield.^{1}H NMR ($CDCl_3$, 300MHz) δ 5.82–5.68 (m, 1H), 5.14-5.04 (m, 2H), 2.36 (t, *J*=7.2 Hz, 2 H), 2.26-2.18 (m, 2 H), 1.77 (p, *J*=7.2 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 135.93, 119.45, 116.56, 32.24, 24.37, 16.20.

4. Allyl Cyanomethyl Ether

To a solution of 0.075 mol of allyl alcohol and 0.064 mol of KOH in 20 mL of THF which had been stirred for 20 min was added dropwise a solution of 0.025 mol of bromoacetonitrile

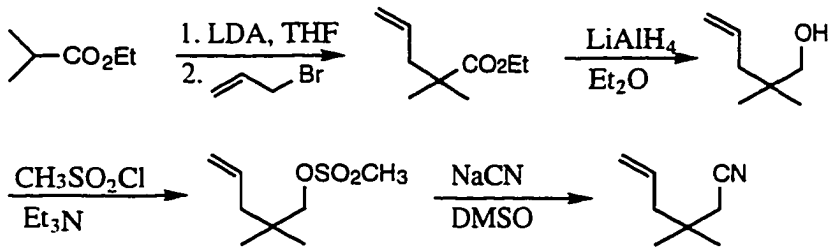
in 5 mL of THF at room temperature. The mixture was stirred for 1 h after the addition and normal workup and distillation under vacuo gave 1.81 g of the product in 74% yield. ^{1}H NMR ($CDCl_3$, 400MHz) δ 5.88 (m, 1H), 5.36 (m, 2H), 4.26 (s, 2H), 4.14 (dt, *J*=6.0, 1.2 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 132.15, 119.68, 115.90, 71.93, 54.77.

5. 2,2 -Dimethyl-5-hexenenitrile

To a solution of 4.9 mL of diisopropylamine in 30 mL of THF was added 12.8 mL of BuLi (2.5M in THF) at -78 °C. After 10 min, a solution of 2 g of isobutyronitrile in 5mL of THF was added dropwise. Then a solution of 3 mL of 4-bromopentene in 5 mL THF was added slowly. The mixture was kept at -78 °C for 1 h before it was allowed to warm up to room temperature. Normal workup and distillation gave the product in the yield of 66%.^{1}H NMR ($CDCl_3$, 300MHz) δ 5.89–5.75 (m, 1H), 5.12-4.99 (m, 2H), 2.29-2.21 (m, 2H), 1.65-1.59 (m, 2 H), 1.36 (s, 6H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 136.91, 124.76, 115.35, 40.08, 32.09, 29.43, 26.55

6. 3,3 -Dimethyl-5-hexenenitrile

This compound was prepared in four steps as shown below.



a. To a solution of LDA freshly-prepared from 15 mL of diisopropylamine and 40 mL of BuLi (2.5M in THF) in 250 mL of THF was added dropwise a solution of 10 g of ethyl 2-methylpropanoate in 20 mL of THF at -78 °C under argon. After 20 min at -78 °C a solution of 9 mL of allyl bromide in 10 mL of THF was added dropwise and stirred for an additional

20 min. The reaction mixture was then allowed to warm to room temperature slowly. The reaction was quenched by the addition of H_2O. Normal workup and distillation afforded the ester (75-77 °C/8mm) in 65% yield.

b. A solution of the ester in a amall amount of ether was added to a suspension of $LiAlH_4$ in ether with stirring at -40 °C. After addition, the reaction mixture was stirred for 30 min and allowed to warm to room temperature. After 30 min, the mixture was treated with aq. HCl. Usual workup and distillation gave the alcohol in 68% yield.

c. The reaction of the alcohol with methanesulfonyl chloride (1.2 equiv.)in the presence of triethylamine (1.5 equiv.) in CH_2Cl_2 at -5-25 °C in 4 h afforded the the methanesulfonate in 90% yield. ^1H NMR ($CDCl_3$, 300MHz) δ 5.86–5.72 (m, 1H), 5.13-5.04 (m, 2H), 3.90 (s, 2H), 3.00 (s, 3H), 2.07 (d, *J*=7.5 Hz, 2H), 0.97 (s, 6H).

d. The treatment of the methanesulfonate with NaCN (2 equiv.) in DMSO for 12 h at 140 °C gave 3,3-dimethyl-5-hexenenitrile in 88% yield. ^1H NMR ($CDCl_3$, 300MHz) δ 5.85–5.71 (m, 1H), 5.15–5.08 (m, 2H), 2.21 (s, 2H), 2.11 (d, *J*=7.5 Hz, 2H), 1.07 (s, 6H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 133.31, 118.93, 118.34, 45.59, 33.26, 29.85, 26.61.

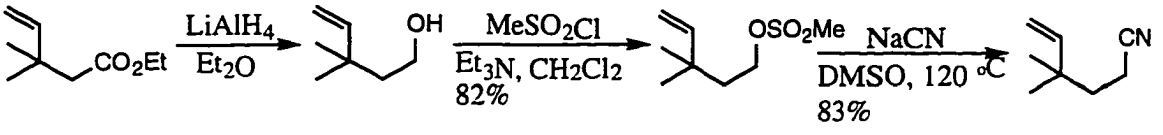
7. 3,3-Bis(ethoxycarbonyl)-5-hexenenitrile

A solution of 2.84 g of diethyl allylmalonate (14.2 mmol) in 5 mL of THF was added dropwise at -78 °C to a solution of LDA freshly-prepared from 3.5 mL of diisopropylamine and 6.8 mL of BuLi (2.5 M in THF). After addition, the reaction mixture was kept for 20 min and a solution of 1.4 mL of bromoacetonitrile in 5 mL of THF was added dropwise. The reaction mixture was allowed to warm to room temperature over 1.5 h. Usual workup and distillation gave 2.8 g of the product (112-114 °C) in 84% yield. ^1H NMR ($CDCl_3$, 300MHz) δ 5.70 -5.56 (m, 1H), 5.32-5.20 (m, 2H), 4.26 (q, *J*=7.2 Hz, 4H), 2.92 (s, 2H), 2.83 (d, *J*=7.5 Hz, 2H), 1.29 (t, *J*=7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 168.08, 130.38, 120.99, 116.05, 62.26, 54.74, 37.00, 21.45, 13.75.

8. Allyl Bis(cyanomethyl)amine

A mixture of iminodiacetonitrile (24.5 mmol, tech. grade) and allyl bromide (24.5 mmol) was stirred overnight at room temperature in DMF. Normal workup and distillation gave the product as a liquid (92 °C/0.3 mm) in 60% yield. ^{1}H NMR ($CDCl_3$, 300MHz) δ 5.84-5.71 (m, 1H), 5.44-5.32 (m, 2H), 3.63 (s, 4H), 3.27 (d, *J*=6.3 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 131.97, 121.18, 114.16, 56.63, 41.40.

9. 4,4-Dimethyl-5-hexenenitrile



The compound was prepared using the same procedures described for 3,3-dimethyl-5-hexenenitrile. It was obtained as a colorless liquid (92-95 °C/8 mm). ^{1}H NMR ($CDCl_3$, 300MHz) δ 5.68 (dd, *J*=17.4, 10.8 Hz, 1H), 5.06-4.94 (m, 2H), 2.25-2.19 (m, 2H), 1.72-1.67 (m, 2H), 1.03 (s, 6H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 145.56, 120.31, 112.64, 37.56, 36.37, 26.07, 12.68.

10. 6-Heptenenitrile

The compound was prepared in the same way as 5-hexenenitrile.^{1}H NMR ($CDCl_3$, 300MHz) δ 5.83-5.69 (m, 1H), 5.05-4.95 (m, 2H), 2.33 (t, *J*=6.9 Hz, 2H), 2.12-2.04 (m, 2H), 1.71-1.48 (m, 4H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 137.48, 119.61, 115.28, 32.68, 27.64, 24.64, 16.91.

11. 3-Butenyl Cyanomethyl Ether

The compound was made by stirring a mixture of glucolonitrile and 4-bromo-1-butene containing KOH in CH_2Cl_2 at room temperature for several hours. Distillation gave a poor

yield of a pure product. ^{1}H NMR ($CDCl_3$, 300MHz) δ 5.87-5.74 (m, 1H), 5.17-5.07 (m, 2H), 4.26 (s, 2H), 3.65 (t, *J*=6.6 Hz, 2H), 2.43-2.35 (m, 2H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 133.99, 117.15, 115.96, 70.87, 56.20, 33.49.

12. 3,3-Bis(ethoxycarbonyl)-6-heptenenitrile

The compound was prepared in two steps in which diethyl cyanomethylmalonate was first made. To a solution of freshly-prepared LDA in THF was added dropwise diethyl malonate at -78 °C. Bromoacetonitrile (1 equiv.) was then added dropwise after the temperature reached -78 °C. The mixture was allowed to warm to room temperature slowly. Normal workup and distillation afforded diethyl cyanomethylmalonate (113-116 °C/0.5 mm) in 70% yield. The title compound was obtained by refluxing a mixture of cyanomethylmalonate (1.5 g), homoallyl bromide (1.2 equiv.) and potassium *tert*-butoxide (1.2 equiv.) in THF for 24 hours. Workup and purification by flash chromatography (5:1 hexane-ethyl acetate) on silica gel gave the product in the yield of 47%.

13. 4,4-Bis(ethoxycarbonyl)-6-heptenenitrile

To a solution of diethyl allylmalonate (7.5 mmol) and acrylonitrile (11 mmol) in 25 mL of THF was added sodium ethoxide (1 mmol in a small amount of ethanol) at room temperature and the reaction mixture was stirred for 1 h. After evaporation of the solvent in vacuo, the residue was dissolved in ether and was washed with 5% $NaHCO_3$ and sat. NaCl, and dried over $MgSO_4$. Removal of the solvent and distillation of the residue gave the product (126-128 °C/0.3 mm) in 80% yield.^{1}H NMR ($CDCl_3$, 300MHz) δ 5.70-5.56 (m, 1H), 5.20-5.13 (m, 2H), 4.26-4.19 (m, 4H), 2.68-2.65 (m, 2H), 2.46-2.41 (m, 2H), 2.24-2.19 (m, 2H), 1.27 (t, *J*=7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 169.80, 131.26, 119.87, 118.89, 61.63, 56.03, 37.60, 28.53, 13.84, 12.66.

14. *S*-Phenyl 3,3-bis(ethoxycarbonyl)thiohex-5-enoate

Three steps were used to make the compound. A solution of diethyl allylmalonate (0.024 mol) in 5 mL of THF was added dropwise to a LDA soution in about 200 mL of THF made from diisopropylamine (0.036 mol) and BuLi (0.028 mol, 2.5 M in THF) at -78 °C. 5g of sodium iodoacetate (0.024 mol) was added in portions and the mixture was refluxed for 2 hours. After the reaction was complete, the solvent was evaporated in vacuo. The residue was treated with 10% HCl(150 mL), and extracted with CH_2Cl_2 for three times. The solution was washed with brine and dried over $MgSO_4$. Evaporation of the solvent gave the pure acid. ^1H NMR ($CDCl_3$, 300MHz) δ 11.10 (br, 1H), 5.74-5.60 (m, 1H), 5.16-5.10 (m, 2 H), 4.21 (q, *J*=7.2 Hz, 4 H), 3.00 (s, 2H), 2.79 (d, *J*=7.5 Hz, 2 H), 1.25 (t, *J*=7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 176.42, 169.65, 131.82, 119.88, 61.68, 54.94, 37.50, 36.82, 13.77.

To a solution of the acid(10 mmol) in CH_2Cl_2 was added dropwise oxalyl chloride(20 mmol) at room temperature. The reaction was completed in 3 h and the excess of oxalyl chloride and the solvent were evaporated in vacuo. The acid chloride was not purified and used for the next step. Triethylamine(15 mmol) was added dropwise to a solution of the acid chloride and thiophenol(12 mmol) in 25 mL of CH_2Cl_2 under stirring and the reaction mixture was stirred for 10 h at room temperature. The mixture was poured into 5% HCl and extracted with CH_2Cl_2 (two times). The combined organic layer was washed with 5% $NaHCO_3$ and NaCl and dried over $MgSO_4$. Removal of the solvent and purification of the residue by column chromatography on silica gel afforded the thiolester. ^1H NMR ($CDCl_3$, 300MHz) δ 7.39 (s, 5H), 5.77-5.63 (m, 1H), 5.20-5.14 (m, 2H), 4.20 (q, *J*=7.2 Hz, 4H), 3.33 (s, 2H), 2.79 (d, *J*=7.5 Hz, 2H), 1.25 (t, *J*=7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 194.16, 169.51, 134.38, 132.05, 129.46, 129.16, 127.19, 120.03, 61.74, 55.74, 45.18, 37.19, 13.92.

15. *S*-Phenyl Thiohex-5-enoate

Hydrolysis of 5-hexenenitrile (60 h refluxing in ethanol-H_2O solution of KOH) yielded the corresponding acid (the mixture was acidified with HCl and extracted with CH_2Cl_2)which was treated with oxalyl chloride (1.2 equiv.) in CH_2Cl_2 for 5 h at 0 °C to give the acid chloride (excess of oxalyl chloride was evaporated together with the solvent under reduced pressure without workup). The reaction of the acid chloride with thiophenol (0.8 equiv.) in the presence of triethylamine(1.5 equiv.) in CH_2Cl_2 for 5 h at 0-25 °C afforded the title product (10% HCl was used to wash away triethylamine and 5% NaOH used to remove the unreacted acid chloride). ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.40 (s, 5H), 5.84-5.71 (m, 1H), 5.09-4.99 (m, 2H), 2.66 (t, *J*=7.2 Hz, 2H), 2.13 (q, *J*=7.2 Hz, 2H), 1.81 (p, *J*=7.5 Hz, 2H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 197.27, 137.36, 134.42, 129.27, 129.11, 127.80, 115.64, 42.81, 32.78, 24.55

16. *S*-Phenyl 3,3-Dimethylthiohex-5-enoate

The compound was prepared from 3,3-dimethyl 5-hexenenitrile following the same method and the procedures as for *S*-phenyl thiohex-5-enoate.^{1}H NMR ($CDCl_3$, 300MHz) δ 7.39 (s, 5H), 5.90-5.76 (m, 1H), 5.11-5.03 (m, 2H), 2.54 (s, 2H), 2.12 (d, *J*=7.5 Hz, 2H), 1.05 (s, 6H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 195.88, 134.51, 134.34, 129.26, 129.10, 127.44, 118.05, 53.91, 46.44, 34.60, 27.14.

17. 4,4-bis(ethoxycarbonyl)-5-azido-1-pentene

A mixture of diethyl allylmalonate (15 mmol), formaldehyde (30 mmol, 37% aqueous solution), and K_2CO_3 (0.2 g) was stirred for 1 h at room temperature. Workup with water and extraction with ether gave 2,2-bis(ethoxycarbonyl)-4-penten-1-ol and its condensation product with formaldehyde in a ratio of about 60 to 40. The latter was transfered to the former easily . Thus the mixture was refluxed in methanol in the presence of PTSA (0.5 g) for 1 h and usual

workup gave 2,2-bis(ethoxycarbonyl)-4-penten-1-ol in the yield of 95%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 5.81-5.67 (m, 1H), 5.20-5.09 (m, 2H), 4.23 (q, *J*=7.2 Hz, 4 H), 3.94 (m, 2H), 2.71-2.68 (m, 2H), 2.63 (m, 1H), 1.28 (t, *J*=7.2 Hz, 6H).

Triflic anhydride (21 mmol) in 15 mL of dichloromethane was added to a solution of pyridine (22 mmol) in 70 mL of dicholromethane maintained at -5-0 °C. To this soluiton was added 3.2 g (14 mmol) of the alcohol obained above in 5 mL of dichloromethane and the mixture was stirred for 2 h at 0-25 °C befor being poured into 100 mL of 5% sodium bicarbonate solution. The organic layer was separated, washed with 5% sulfric acid and 5% sodium bicarbonate solution, and dried over $MgSO_4$. Evaporation of the solvent gave the pure corresponding triflic ester in 90%. ^{1}H NMR ($CDCl_3$, 300MHz) δ 5.70-5.56 (m, 1H), 5.26-5.21 (m, 2H), 4.84 (s, 2H), 4.25 (q, *J*=7.2 Hz, 4H), 2.82 (d, *J*=7.5 Hz, 2H), 1.28 (t, *J*=7.2 Hz, 6H).

0.26 g (4 mmol) of sodium azide and 10 mL of dimethyl sulfoxide were placed in a flask and 0.8 g (2.2 mmol) of the triflic ester was added dropwise under stirring at room temperature. After addition, stirring was continued for 0.5 h. 50 mL of water was added and the mixture was extracted with ether for two times. The organic layer was washed with brine for three times and dried over $MgSO_4$. Evaporation of the solvent gave the title compound in 95% yield. ^{1}H NMR ($CDCl_3$, 300MHz) δ 5.70-5.56 (m, 1H), 5.22-5.14 (m, 2H), 4.22 (q, *J*=7.2 Hz, 4H), 3.78 (s, 2H), 2.74 (d, *J*=7.5 Hz, 2H), 1.27 (t, *J*=7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 168.86, 131.42, 120.09, 61.73, 57.74, 52.45, 36.62, 13.93.

General Procedure for Cyclization of 1,6-Dienes

In most cases, reactions were monitored by ^{1}H NMR. 1,6-Dienes(0.1 mmol), the reagents and 0.6 mL of DMSO-d_6 were put in a 5mm NMR tube. For photolysis the tube was exposed to a 275W sunlamp at a distance of *ca.* 25cm or the tube was wrapped with Al foil at

room temperature for dark reaction. Before taking a NMR speatrum, 0.1 mmol of toluene was added as an internal standard. When necessary, the reaction mixture was worked up with aqueous $Na_2S_2O_3$, extracted with methylene chloride, washed with brine, and dried with $MgSO_4$. After removing the solvent, a $CDCl_3$ solution was prepared for ^1H NMR measurement.

General Procedure for Cyclization of Olefinic Nitriles

The procedures are basically the same as above.

Procedure for Measurement of Kinetic Chain Length

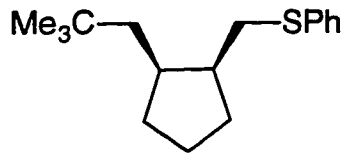
Two parallel reactions were monitored at the same time by NMR to determine a kinetic chain length under the same reaction condition. The substrate and reagents were dissolved with 0.6 mL of DMSO-d_6 in a NMR tube. For inhibition studies DTBN was added to a second tube containing the same materials as the first one. ^1H NMR were taken to determine yields as a function of time. Data were plotted to get the initial rates and the rates of initiation and the chain lengths were thus obtained in the way as described in the discussion.

Isolation of Products

1-2 mmol scale reactions were used to isolate products. A Pyrex test tube was loaded with the substrate and the reagents and 4 mL of DMSO added to dissolve them. The tube was capped with a septum and exposed to a 275W sunlamp at a distance of *ca.* 25cm. Workup procedure was the same as above. Isolation was performed on TLC plates.

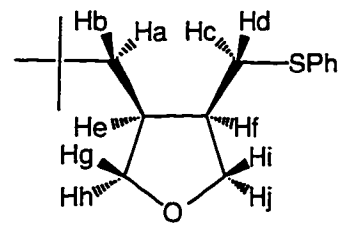
Characterization of Products

cis-1-(Phenylthiomethyl)-2-(2,2-dimethylpropyl)cyclopantane (32)



The product was isolated as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300MHz) δ 0.90 (s, 9 H), 1.09 (dd, J = 13.8, 8.4 Hz, 1 H), 1.82 (dd, J = 13.8, 3.3 Hz, 1 H), 1.18-2.14 (m, 8 H), 2.62 (dd, J = 12.0, 10.8 Hz, 1 H), 3.05 (dd, J = 12.0, 4.5 Hz, 1 H), 7.11-7.34 (m, 5 H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 22.19, 29.96, 30.11, 30.90, 32.16, 34.25, 39.52, 43.33, 43.63, 125.50, 128.73, 128.80, 137.55; EIMS *m/z* (rel.intensity) 262 (M^+, 61), 247 (4), 205 (46), 123 (29), 110 (66), 96 (55), 57 (100); HRMS Calcd for $C_{17}H_{26}S$ 262.1755, found 262.1759.

cis-3-(Phenylthiomethyl)-4-(2,2-dimethylpropyl)tetrahydrofuran (36)



The product was isolated as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300MHz) δ 0.90 (s, 9 H), 1.20 (dd, J = 13.8, 8.7 Hz, 1 H), 1.51 (dd, J = 13.8, 3.3 Hz, 1 H), 2.27-2.40 (m, 2 H), 2.72 (dd, J = 12.6, 10.8 Hz, 1 H), 3.11 (ddd, J = 12.9, 4.2, 1.2 Hz, 1 H), 3.42 (t, J = 8.4 Hz, 1 H), 3.81 (ddd, J = 8.7, 5.4, 1.2 Hz, 1 H), 3.91 (dd, J = 8.7, 3.0 Hz, 1 H), 3.99 (dd, J = 8.1, 8.1 Hz, 1 H), 7.16-7.36 (m, 5 H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 29.82, 30.65, 32.60, 38.84, 41.48, 42.75, 71.74, 73.18, 126.09, 128.87, 129.48, 136.29; EIMS *m/z*

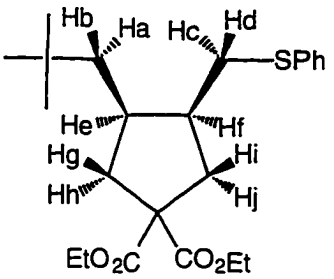
(rel.intensity) 264 (M^+, 82), 249 (10), 207 (27), 154 (26), 139 (26) 123 (41), 110 (43), 83 (31), 70 (58), 57 (100); HRMS Calcd for $C_{16}H_{24}OS$ 264.1548, found 264.1553.

NOESY spectrum and chemical shift assignment

Strong NOE are observed for Ha^Hc, Hc^Hb, Hg^Hb, Hg^Hd, Hh^He and Hj^Hf

proton	chemical shift δ
Ha	1.51 (dd, *J* = 13.8, 3.3 Hz)
Hb	1.20 (dd, *J* = 13.8, 8.7 Hz)
Hc	3.11 (ddd, *J* = 12.9, 4.2, 1.2 Hz)
Hd	2.72 (dd, *J* = 12.6, 10.8 Hz)
He	2.27-2.40 (m)
Hf	2.27-2.40 (m)
Hg	3.42 (t, *J* = 8.4 Hz)
Hh	3.99 (dd, *J* = 8.1, 8.1 Hz)
Hi	3.91 (dd, *J* = 8.7, 3.0 Hz)
Hj	3.81 (ddd, *J* = 8.7, 5.4, 1.2 Hz)

***cis*-1,1-Bis(ethoxycarbonyl)-3-(phenylthiomethyl)-4-(2,2-dimethylpropyl) cyclopentane (40)**



The product was isolated as a colorless liquid.^{1}H NMR ($CDCl_3$, 300MHz) δ 0.90 (s, 9 H), 1.15 (dd, *J* = 13.8, 7.8 Hz, 1 H), 1.23 (t, *J* = 7.2 Hz, 6 H), 1.41 (dd, *J* = 13.8, 3.3 Hz, 1 H), 2.02 (dd, *J* = 12.6,9.9 Hz, 1 H), 2.08-2.26 (m, 2 H), 2.35-2.49 (m, 3 H), 2.64 (dd, *J* = 12.3, 10.8 Hz, 1 H), 3.05 (dd, *J* = 12.3, 4.5 Hz, 1 H), 4.13-4.21 (m, 4 H), 7.14-7.35 (m, 5 H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 13.95, 29.95, 30.77, 34.25, 38.01, 38.98, 40.44, 42.78, 42.89, 58.74, 61.32, 61.38, 125.90, 128.75, 129.54, 136.61, 172.72, 172.74; EIMS *m/z*

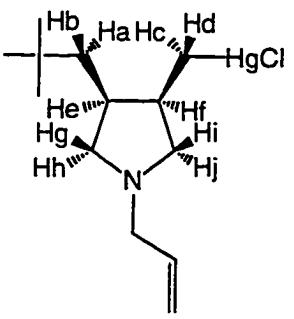
(rel. intensity) 406 (M^+, 55), 349 (25), 297 (38), 223 (42), 173 (86), 166 (100), 165 (85), 93 (43), 69 (68), 57 (83); HRMS Calcd for $C_{23}H_{34}O_4S$ 406.2178, found 406.2178

NOESY spectrum and chemical shift assignment

Strong NOE are observed for Hc^Ha, Hd^Hg, Hb^Hg, Hd^Hi and He^Hh

proton	chemical shift δ
Ha	1.41 (dd, *J* = 13.8, 3.3 Hz)
Hb	1.15 (dd, *J* = 13.8, 7.8 Hz)
Hc	3.05 (dd, *J* = 12.3, 4.5 Hz)
Hd	2.64 (dd, *J* = 12.3, 10.8 Hz)
He	2.08-2.26 (m)
Hf	2.08-2.26 (m)
Hg	2.02 (dd, *J* = 12.6, 9.9 Hz)
Hh	2.35-2.49 (m)
Hi	2.35-2.49 (m)
Hj	2.35-2.49 (m)

***cis*-*N*-Allyl-3-(chloromercurymethyl)-4-(2,2-dimethylpropyl)pyrrolidine (42)**



The product was isolated as a white solid. ^1H NMR ($CDCl_3$, 300Hz) δ 0.87 (s, 9 H), 1.28 (dd, *J* = 13.8, 9.3 Hz, 1 H), 1.46 (dd, *J* = 13.8, 3.3 Hz, 1 H), 1.81 (dd, *J* = 12.3, 4.5 Hz, 1 H), 1.92 (dt, *J* = 12.3, 2.1 Hz, 1 H), 2.16-2.28 (m, 1 H), 2.41-2.54 (m, 3 H), 2.60 (dd, *J* = 10.2, 6.9 Hz, 1 H), 2.67-2.73 (m, 1H), 3.18-3.36 (m, 2 H), 5.07-5.21 (m, 2 H), 5.98-6.12 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75Hz) δ 29.86, 30.29, 30.83, 36.18, 41.59, 45.18, 58.15,

58.37, 60.93, 117.40, 135.18; EIMS *m/z* (rel.intensity) 431 (M^+, 3), 416 (3), 194 (100), 136 (5); HRMS Calcd for $C_{13}H_{24}ClHgN$ 431.1304, found 431.1306

NOESY spectrum

Strong NOE are observed for He^Hf, Ha^Hc, Hb^Hg, Hd^Hi, He^Hh and Hf^Hj.

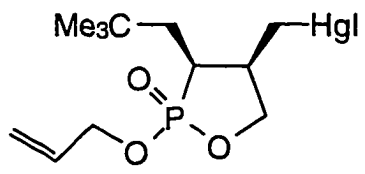
NOE are not observed for He^Hc, He^Hd and Hf^Hb.

COSY spectrum and chemical shift assignment

Strong COSY are observed for Hf^Hc, Hf^Hd, He^Hb, He^Ha, He^Hf

protone	chemical shift δ
Ha	1.46 (dd, *J* = 13.8, 3.3 Hz)
Hb	1.28 (dd, *J* = 13.8, 9.3 Hz)
Hc	1.92 (dt, *J* = 12.3, 2.1 Hz)
Hd	1.81 (dd, *J* = 12.3, 4.5 Hz)
He	2.16-2.28 (m)
Hf	2.67-2.73 (m)
Hg	2.60 (dd, *J* = 10.2, 6.9 Hz)
Hh	2.41-2.54 (m)
Hi	2.41-2.54 (m)
Hj	2.41-2.54 (m)

Allyl (2α,3α,4α)-3-(2,2-dimethylpropyl)-4-(iodomercurymethyl) propylphostonate (46)

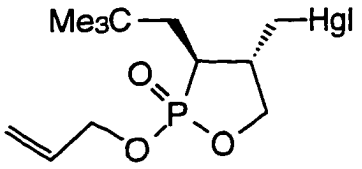


(NOE favored structure)

^{1}H NMR ($CDCl_3$, 300MHz) δ 0.98 (s, 9 H), 1.50 (ddd, J_{HCCP} = 20.4, *J* = 14.4, 5.1 Hz, 1 H), 1.81 (ddd, J_{HCCCP} = 18.3, *J* = 14.4, 6.9 Hz, 1 H), 1.97-2.17 (m, 3 H), 3.21-3.39 (m, 1 H), 3.99 (ddd, J_{HCOP} = 20.1, *J* = 9.3, 1.5 Hz, 1 H), 4.16 (ddd, *J* = 9.3, 4.5, J_{HCOP} = 1.5 Hz, 1 H), 4.57-4.62(m, 2 H), 5.23-5.39 (m, 2 H), 5.87-6.00 (m, 1 H); ^{13}C NMR ($CDCl_3$,

75MHz) δ 29.36, 30.90 (d, J_{CCP} = 7.5 Hz), 33.04 (d, J_{CP} = 119 Hz), 36.91, 37.03, 42.29 (d, J_{CCP} = 6.8 Hz), 66.95 (d, J_{COP} = 6.8 Hz), 73.21 (d, J_{COP} = 9.0 Hz), 118.26, 132.77 (d, J_{CCOP} = 6.0 Hz); EIMS *m/z* (rel. intensity) 574 (M^+, 4), 572 (M, 4), 559 (6), 557 (6), 517 (29), 516 (23), 515 (36), 514 (28), 513 (16), 245 (100), 189 (34), 147 (55), 109 (28), 57 (68); HRMS Calcd for $C_{12}H_{22}HgIO_3P$ 574.0058, found 574.0060.

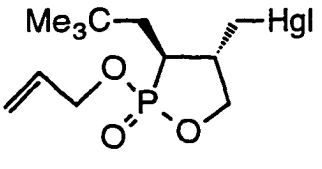
Allyl (2α,3α,4β)-3-(2,2-dimethylpropyl)-4-(iodomercurymethyl) propylphostonate (47)



(NOE favored structure)

^{1}H NMR ($CDCl_3$, 300Hz) δ 0.98 (s, 9 H), 1.39 (ddd, J_{HCCP} = 28.5, J = 14.4, 1.5 Hz, 1 H), 1.45-1.54 (m, 1 H), 1.92 (dd, J = 12, 8.4 Hz, 1 H), 2.05 (ddd, J_{HCCP} = 20.7, J = 14.4, 9.6 Hz, 1 H), 2.22 (dd, J = 12, 5.1 Hz, 1 H), 2.60-2.74 (m, 1 H), 3.55 (ddd, J_{HCOP} = 10.5, J = 9.0, 1.8 Hz, 1 H), 4.30 (ddd, J_{HCOP} = 22.2, J = 9.0,6.4 Hz, 1 H), 4.52-4.68 (m, 2 H), 5.24-5.40(m, 2 H), 5.89-6.02 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 29.29, 30.69 (d, J_{CCCP} = 2.3 Hz), 37.85 (d, J_{CP} = 121 Hz), 40.29 (d, J_{CCP} = 15.3 Hz), 41.11, 44.97 (d, J_{CCP} = 9.0 Hz), 66.94 (d, J_{COP} = 7.4 Hz), 71.50 (d, J_{COP} = 6.6 Hz), 118.44, 132.90 (d, J_{CCOP} = 5.9 Hz); EIMS *m/z* (rel. intensity) 559 (7), 515 (64), 245 (57), 189 (24), 147 (31), 107 (15),57 (39); HRMS Calcd for $C_{12}H_{22}O_3P$ (M-HgI) 245.1307, found 245.1307.

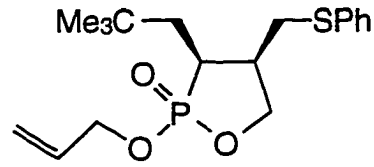
Allyl (2β,3α,4β)-3-(2,2-dimethylpropyl)-4-(iodomercurymethyl) propylphostonate (48)



(NOE favored structure)

^{1}H NMR ($CDCl_3$, 300MHz) δ 1.01 (s, 9 H), 1.46 (ddd, J_{HCCP} = 30.3, J = 13.8, 2.1 Hz, 1 H), 1.56-1.75 (m, 1 H), 1.72 (ddd, J_{HCCP} = 26.7, J = 14.1, 9.3 Hz, 1 H), 1.92 (dd, J = 12, 8.4 Hz, 1 H), 2.25 (dd, J = 12, 4.8 Hz, 1 H), 2.64-2.78 (m, 1 H), 3.72 (ddd, J_{HCOP} = 10.2, J = 9.0, 4.8 Hz, 1 H), 4.30 (ddd,J_{HCOP} = 16.2, J = 9.0, 6.9 Hz, 1 H), 4.54-4.70 (m, 2 H), 5.24-5.40 (m, 2 H), 5.89-6.02 (m, 1 H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 29.65, 30.68 (d, J_{CCCP} = 1.6 Hz), 38.25 (d, J_{CP} = 120 Hz), 40 99, 41.03, 44.17 (d, J_{CCP} = 8.1 Hz), 66.71 (d, J_{COP} = 7.1 Hz), 71.59 (d, J_{COP} = 6.0 Hz), 118.13, 132.92 (d, J_{CCOP} = 5.9 Hz); EIMS *m/z* (rel. intensity) 559 (4), 515 (45), 245 (100), 189 (31), 147 (32),107 (19), 57 (42); HRMS Calcd for $C_{12}H_{22}O_3P$ (M-HgI) 245.1307, found 245.1305.

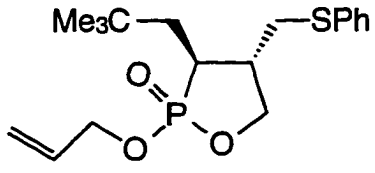
Allyl (2α,3α,4α)-3-(2,2-dimethylpropyl)-4-(phenylthiomethyl) propylphostonate (49)



(NOE favored structure)

The product was isolated as a colorless liquid.^{1}H NMR ($CDCl_3$, 300MHz) δ 0.94 (s, 9 H), 1.43 (ddd, J_{HCCP} = 21.9, J = 14.4, 4.5 Hz, 1H), 1.80 (ddd, J_{HCCP} = 18, J = 14.4, 7.6 Hz, 1 H), 2.16 (dddd, J_{HCP} = 19.2, J = 7.2, 7.2, 4.5 Hz, 1 H), 2.40-2.58 (m, 1 H), 3.01 (dd, J = 13.5, 12 Hz, 1H),3.20 (dd, J = 13.5, 3.5 Hz, 1 H), 4.01 (dddd, J = 9.6, 4.5, J_{HCOP} = 2.7, J_{HCCCP} = 1.5 Hz, 1 H), 4.42 (ddd, J_{HCOP} = 19.5, J = 9.6, 2.4 Hz, 1 H), 4.54-4.61 (m, 2 H), 5.22-5.38 (m, 2 H), 5.87-6.00 (m, 1 H), 7.18-7.37 (m, 5 H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 29.24, 30.79 (d, J_{CCCP} = 5.4 Hz), 32.07 (d, J_{CCP} = 3.1 Hz), 32.25 (d, J_{CP} = 122 Hz), 36.78, 41.71 (d, J_{CCP} = 5.9 Hz), 66.73 (d, J_{cop} = 7.0 Hz), 68.79 (d, J_{COP} = 7.5 Hz), 118.16, 126.73, 129.09, 130.07, 132.92 (d, J_{CCOP} = 5.7 Hz), 134.95; EIMS m/z (rel. intensity) 354 (M^+, 8), 339 (4), 313 (4), 232 (15), 245 (6), 149 (100), 109 (10), 57 (9); HRMS Calcd for C18H27O3PS 354.1419, found 354.1421.

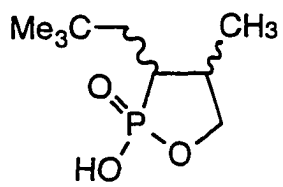
Allyl (2α,3α,4β)-3-(2,2-dimethylpropyl)-4-(phenylthiomethyl) propylphostonate (50)



(NOE favored structure)

The product was isolated as a colorless liquid.^{1}H NMR(CDCl3, 300MHz) δ 0.94 (s, H), 1.20 (ddd, J_{HCCP} =27, J = 14.4, 2.1Hz, 1H), 1.67-1.82(m, 1H), 2.00 (ddd, J_{HCCP} = 20.4, 14.1, 9 Hz, 1H), 2.30-2.43 (m, 1H), 2.79 (ddd, J = 13.5, 9.6 Hz, J_{HCCCP} = 1.8 Hz, 1H), 3.27(dd, J = 13.5, 3.9 Hz, 1H), 3.72 (ddd, J_{HCOP} = 9.6, J = 9.6, 3.3 Hz, 1H), 4.35 (ddd, J_{HCOP} = 21, J = 9.3, 6.6 Hz, 1H), 4.54-4.62 (m, 2H), 5.23-5.39 (m, 2H), 5.88-6.00 (m, 1H), 7.23-7.37 (m, 5 H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 29.12, 30.61(d, J_{CCCP} = 2.4 Hz), 33.2 (d, J_{CP} = 123 Hz), 35.78 (d, J_{CCP} = 16.3 Hz), 40.83 (d, J_{CCCP} = 1.4 Hz), 44.12 (d, J_{CCP} = 8.7 Hz), 66.77 (d, J_{COP} = 7.2 Hz), 69.30 (d, J_{COP} = 6.7 Hz), 118.2, 127.0, 129.2, 130.3, 132.8 (d, J_{CCOP} = 6.3 Hz), 134.7; EIMS *m/z* (rel.intensity) 354 (M^+, 21), 297 (4), 245 (23), 149 (100), 57 (19); HRMS Calcd for $C_{18}H_{27}O_3PS$, 354.1419, Found 354.1411.

3-(2,2-Dimethylpropyl)-4-methylpropylphostonate (56)

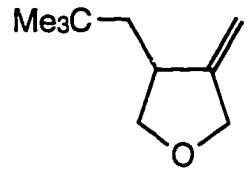


cis : *trans* = 1 : 1

Both ^{1}H NMR and ^{13}C NMR showed the isolated colorless liquid to be a mixture of *cis* and *trans* isomers in 1 : 1 ratio. ^{1}H NMR ($CDCl_3$, 300MHz) δ 0.977 (s, 9 H) and 0.984 (s, 9 H), 1.040 (d, J = 6.6 Hz, 3 H) and 1.142 (d, J = 7.2 Hz, 3 H), 1.238-1.924 (m, 5 H), 2.018-2.209 (m, 2 H), 2.424-2.590 (m, 1 H), 3.603 (ddd, J_{HCOP} =11.1, 9.0, 2.1 Hz, 1 H) and

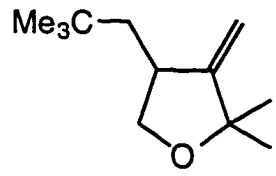
3.895 (ddd, J_{HCOP} = 18.6, 9.0, 2.1 Hz, 1 H), 4.134-4.255 (m, 2 H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 14.109 (d, J_{CCCP} = 2.8 Hz) and 15.369 (d, J_{CCCP} = 15.3 Hz), 29.373 and 29.394, 30.422 (d, J_{CCCP} = 1.2 Hz) and 30.750 (d, J_{CCCP} = 6.8 Hz), 32.194 (d, J_{CP} = 122.6 Hz) and 35.352 (d, J_{CP} = 124.7 Hz), 36.472 (d, J_{CCP} = 6.2 Hz) and 36.990(d, J_{CCP} = 1.6 Hz), 39.155 (d, J_{CCP} = 8.0 Hz) and 40.800 (d, J_{CCP} = 1.8 Hz), 71.520 (d, J_{COP} = 7.9 Hz) and 72.955 (d, J_{COP} = 9.9 Hz); EIMS *m/z* (rel.intensity) 207 (M^++1, 39), 206 (M^+, 12), 191 (31), 149 (49), 109 (55), 84 (40), 57 (45), 41 (100); HRMS Calcd for $C_9H_{19}O_3P$ 206.1072, found 206.1072.

3-Methylene-4-(2,2-dimethylpropyl)tetrahydrofuran (58)



The product was isolated as a colorless liquid. ^1H NMR ($CDCl_3$) δ 0.93 (s, 9 H), 1.29 (dd, *J* = 14.4, 9.6 Hz, 1 H), 1.62 (dd, *J* = 14.4, 2.4 Hz, 1 H), 2.58-2.68 (m, 1 H), 3.38 (t, *J* = 8.4 Hz, 1 H), 4.18-4.26 (m, 2 H), 4.35-4.41 (m, 1 H), 4.88-4.95 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 29.84, 30.55, 40.46, 46.66, 71.06, 75,75, 102.75, 153.47; EIMS *m/z* (rel. intensity) 154 (M^+, 5), 139 (9), 121 (4), 97 (10), 83 (24), 57 (100); HRMS Calcd for $C_{10}H_{18}O$ 154.1358, found 154.1358.

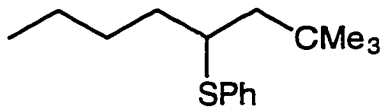
2,2-Dimethyl-3-methylene-4-(2,2-dimethylpropyl)tetrahydrofuran (60)



The product was isolated as a colorless liquid.^1H NMR ($CDCl_3$) δ 0.92 (s, 1 H), 1.24 (s, 3 H), 1.30 (dd, *J* = 14.4, 9.6 Hz, 1 H), 1.32 (s, 3 H), 1.58 (dd, *J* = 14.4, 2.4 Hz, 1 H), 2.68-

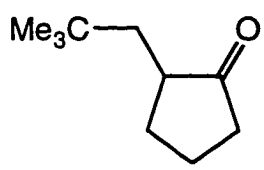
2.79 (m, 1 H), 3.40 (t, J = 8.7 Hz, 1 H), 4.14 (dd, J = 8.1, 8.1 Hz, 1 H), 4.81 (t, J = 2.4 Hz, 2 H); ^{13}C NMR ($CDCl_3$) δ 27.30, 28.73, 29.87, 30.58, 40.82, 47.48, 71.96, 81.33, 102.47, 161.83; EIMS *m/z* (rel.intensity) 182 (M^+, 1.4), 167 (100), 125 (3), 111 (25), 57 (40); HRMS Calcd for $C_{12}H_{22}O$ 182.1671, found 182.1667.

2,2-Dimethyl-4-(phenylthio)octane (62)



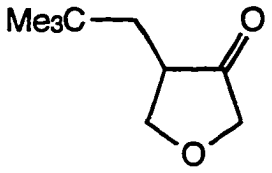
The product was isolated as a colorless liquid.^{1}H NMR ($CDCl_3$) δ 0.86 (t, J = 7.3 Hz, 3 H), 0.93 (s, 9 H), 1.21-1.61 (m, 8 H), 3.08 (p, J = 5.7 Hz, 1 H), 7.16-7.40 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 14.01, 22.60, 28.79, 29.92, 31.07, 36.73, 45.00, 48.16, 126.42, 128.69, 131.71, 136.33; EIMS *m/z* (rel. intensity) 250 (M^+, 31), 193 (4), 179 (8), 141 (9), 123 (9), 110 (100), 85 (26), 71 (27), 57 (74), 43 (33); HRMS Calcd for $C_{16}H_{26}S$ 250.1755, found 250.1759.

2-(2,2-Dimethylpropyl)cyclopentanone (63)



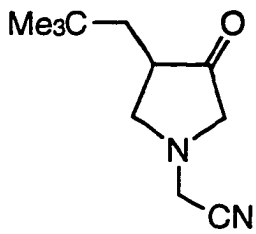
The product was isolated as a colorless liquid.^{1}H NMR ($CDCl_3$) δ 0.92 (s, 9 H), 1.05 (dd, J = 14.1, 9.0 Hz, 1 H), 1.43-1.57 (m, 1 H), 1.68-1.82 (m, 1H), 1.88 (dd, J = 14.1, 2.4 Hz, 1 H), 1.92-2.12 (m, 3 H), 2.25-2.43 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 20.80, 29.77, 30.47, 32.74, 37.37, 44.13, 46.77, 221.85; IR (neat) 2958, 2868, 1742cm^{-1}; EIMS *m/z* (rel.intensity) 154 (M^+, 7), 139 (14), 125 (11), 112 (28), 97 (29), 83 (32), 57 (100); HRMS Calcd for $C_{10}H_{18}O$ 154.1358, found 154.1361.

3-(2,2-Dimethylpropyl)tetrahydrofuran-4-one (64)



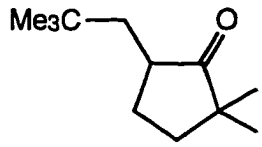
The product was isolated as a colorless liquid. ^{1}H NMR ($CDCl_3$) δ 0.91 (s, 9 H), 1.16 (dd, *J* = 14.4, 9.6 Hz, 1 H), 1.87 (dd, *J* = 14.4, 2.4 Hz, 1 H), 2.39-2.50 (m, 1 H), 3.69 (dd, *J* = 9.9, 9.6 Hz, 1 H), 3.74 (dd, *J* = 17.1, 0.6 Hz, 1 H), 4.08 (dd, *J* = 17.7, 1.2 Hz, 1 H), 4.60 (dd, *J* = 9.0, 9.0 Hz, 1 H); EIMS *m/z* (rel.intensity) 310 (2M-2, 4), 156 (M^+, 4), 155 (6), 141 (3), 114 (5), 83 (23), 57 (100), 41 (31); HRMS Calcd for $C_9H_{16}O_2$ 156.1150, found 156.1148.

***N*-(Cyanomethyl)-4-(2,2-dimethylpropyl)β–pyrrolidone (65)**



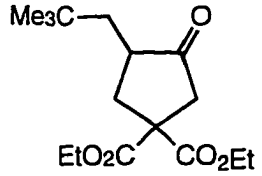
The product was isolated as a colorless liquid. ^{1}H NMR($CDCl_3$, 300MHz) δ 0.92 (s, 9 H), 1.22 (dd, *J* = 14.4, 9.6 Hz, 1 H), 1.87(dd, *J* = 14.1, 2.4 Hz, 1 H), 2.42-2.52 (m, 1 H), 2.59 (dd, *J* = 9.6, 8.8 Hz, 1 H), 2.91 (d, *J* = 16.5 Hz, 1 H), 3.36 (d, *J* = 16.5 Hz, 1 H), 3.49 (t, *J* = 8.1 Hz, 1 H), 3.76 (s, 2 H); ^{13}C NMR($CDCl_3$, 75MHz) δ 29.54, 30.36, 42.12, 42.37, 46.61, 58.17, 58.21, 113.94, 213.91; EIMS *m/z* (rel intensity) 194 (M^+, 13), 179 (28), 166 (15), 151 (13), 109 (28), 69 (64), 57 (100); HRMS Calcd for $C_{11}H_{18}N_2O$ 194.1419, found 194.1417.

2,2-Dimethyl-5-(2,2-dimethylpropyl)cyclopentanone (66)



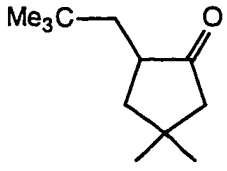
The product was isolated as a colorless liquid.^{1}H NMR ($CDCl_3$) δ 0.92 (s, 9 H), 0.94 (s, 3 H), 1.08 (dd, *J* = 13.8, 9.3 Hz, 1 H), 1.08 (s, 3 H), 1.46-1.70 (m, 2 H), 1.78-1.85 (m, 1 H), 1.89 (dd, *J* = 14.1, 2.4 Hz, 1 H), 2.02-2.12 (m, 1 H), 2.20-2.30 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 23.76, 24.70, 28.98, 29.84, 30.64, 36.84, 44.36, 45.55, 46.11, 225.12; EIMS *m/z* (rel.intensity) 182 (M^+, 26), 167 (16), 125 (58), 112 (22), 111 (19), 83 (22), 57 (100); HRMS Calcd for $C_{12}H_{22}O$ 182.1671, found 182.1669.

2-(2,2-Dimethylpropyl)-4,4-bis(ethoxycarbonyl)cyclopentanone (67)



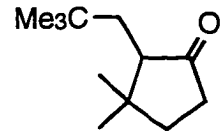
The product was isolated as a colorless liquid.^{1}H NMR($CDCl_3$, 300MHz) δ 0.92 (s, 9 H), 1.08 (dd, *J* = 14.1, 9.3 Hz, 1 H), 1.28 (t, *J* = 7.2 Hz, 6 H), 1.92 (dd, *J* = 14.1, 2.4 Hz, 1 H),1.96 (t, *J* = 12.6 Hz, 1 H), 2.24-2.35 (m, 1 H), 2.73 (d, *J* = 19.2 Hz, 1 H), 2.92-3.05 (m, 2 H), 4.19-4.30 (m, 4 H); ^{13}C NMR($CDCl_3$, 75MHz) δ 13.94, 29.67, 30.36, 39.08, 44.16, 44.25, 45.32, 55.06, 61.97, 170.75, 171.03, 215.94; EIMS *m/z* (rel intensity) 298 (M^+, 15), 283 (14), 253 (11), 241 (18), 200 (100), 154 (93), 69 (92), 57 (55); HRMS Calcd for $C_{16}H_{26}O_5$ 298.1780, found 298.1787.

2-(2,2-Dimethylpropyl)-4,4-dimethylcyclopentanone (68)



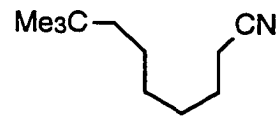
The product was isolated as a colorless liquid.^{1}H NMR($CDCl_3$, 300MHz) δ 2.33-1.95 (m, 4 H), 1.89 (dd, *J* = 13.8, 2.4 Hz, 1 H), 1.49-1.41 (m, 1 H), 1.17 (s, 3 H), 1.07 (s, 3 H), 1.07 (dd, *J* = 13.8, 9.6 Hz, 1H), 0.91 (s, 9 H); ^{13}C NMR($CDCl_3$, 75MHz) δ 221.96, 52.49, 47.23, 45.65, 45.31, 34.10, 30.53, 29.78, 29.74, 27.92; EIMS *m/z* (rel intensity) 182 (M^+, 16), 167 (13), 125 (85), 111 (22), 98 (17), 83 (26), 69 (29), 57 (100); HRMS Calcd for $C_{12}H_{22}O$ 182.1671, found 182.1675.

2-(2,2-Dimethylpropyl)-3,3-dimethylcyclopentanone (69)



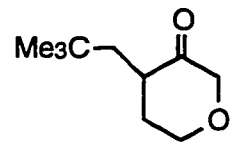
The ketone was isolated as a white solid, mp 42-44 ° C. ^{1}H NMR($CDCl_3$, 300MHz) δ 2.32 (dddd, *J* = 19.2, 8.4, 3.3, 1.2 Hz, 1 H), 2.14 (ddd, *J* = 19.2, 10.8, 8.7 Hz, 1 H), 1.82-1.72 (m, 3 H), 1.52 (dd, *J* = 13.8, 6.9 Hz, 1 H), 1.12 (s, 3 H), 0.98 (dd, *J* = 13.8, 1.5 Hz, 1 H), 0.88 (s, 9 H), 0.71 (s, 3 H); ^{13}C NMR($CDCl_3$, 75MHz) δ 219.63, 57.04, 39.55, 36.33, 35.54, 34.75, 30.24, 29.45, 27.99, 21.22; EIMS *m/z* (rel intensity) 182 (M^+, 7), 167 (59), 153 (16), 125 (66), 111 (53), 70 (40), 57 (100); HRMS Calcd for $C_{12}H_{22}O$ 182.1671, found 182.1670.

8,8-Dimethylnonanenitrile (71)



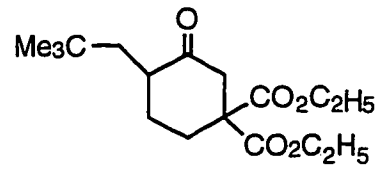
The product was isolated as a colorless liquid.^{1}H NMR($CDCl_3$, 300MHz) δ 2.34 (t, *J*=7.5 Hz, 2H), 1.12-1.76 (m, 10H), 0.86 (s, 9H); ^{13}C NMR($CDCl_3$, 75MHz) δ 119.86, 44.04, 30.25, 29.66, 29.36, 28.70, 25.37, 24.22, 17.12.

4-(2,2-Dimethylpropyl)-3-(2*H*)pyranone (72)



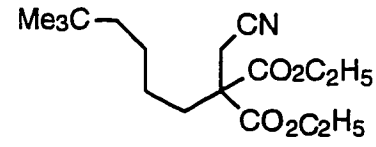
The product was isolated as a colorless liquid.^{1}H NMR($CDCl_3$, 300MHz) δ 0.90 (s, 9 H), 0.94 (dd, J = 14.1, 4.8 Hz, 1 H), 1.76-1.89 (m, 1 H), 2.17-2.28 (m, 2 H), 2.44-2.57 (m, 1 H), 3.81-3.98 (m, 2 H), 4.02 (ab, J = 20.7 Hz, 2 H); ^{13}C NMR($CDCl_3$, 75MHz) δ 29.45, 30.65, 34.34, 41.46, 43.82, 66.07, 74.60, 209.35;IR (neat) 2959, 2869, 1724, 1476, 1367, 1183 cm^{-1}; EIMS *m/z* (rel intensity) 170 (M^+, 8), 169 (8), 155 (10), 113 (25), 73 (20), 69 (15), 57 (100); HRMS Calcd for $C_{10}H_{17}O_2$ 169.1228, found 169.1224.

2-(2,2-Dimethylpropyl)-5,5-bis(ethoxycarbonyl)cyclohexanone (74)



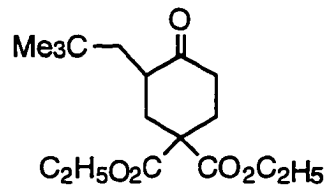
The material was isolated as a colorless liquid.^{1}H NMR($CDCl_3$, 300MHz) δ 0.86 (s, 9 H), 1.15-1.32 (m, 7 H), 1.48-1.61 (m, 1 H), 2.02-2.28 (m, 4 H), 2.36-2.44 (m, 1 H), 2.62 (dd, J = 14.1, 0.9 Hz, 1 H), 2.97 (dd, J = 14.1, 2.1 Hz, 1 H),4.11-4.29 (m, 4 H); ^{13}C NMR($CDCl_3$, 75MHz) δ 13.87, 29.32, 29.92, 30.53, 31.30, 41.68, 45.04, 46.11, 57.70, 61.67, 61.71, 170.18, 170.30, 207.52; EIMS *m/z* (rel intensity) 312 (M^+, 10), 297 (27), 255 (54), 239 (27), 211 (24), 181 (44), 175 (58), 138(43), 57(100); HRMS Calcd for $C_{17}H_{28}O_5$ 312.1937, found 312.1928.

3,3-Bis(ethoxycarbonyl)-8,8-dimethylnonanenitrile (75)



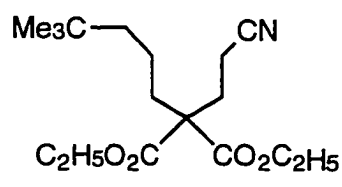
The material was isolated as a colorless liquid.^{1}H NMR($CDCl_3$, 300MHz) δ 0.87 (s, 9 H), 1.15-1.35 (m, 12 H), 2.06-2.12 (m, 2 H), 2.95 (s, 2 H), 4.25 (q, *J* = 7.2 Hz, 4 H); ^{13}C NMR($CDCl_3$, 75MHz) δ 13.88, 21.72, 24.51, 24.87, 29.24, 30.16, 32.69, 43.66, 55.30, 62.23, 116.31, 168.82; EIMS *m/z* (rel intensity) 311 (M^+, 7), 296 (86), 254 (20), 238 (32), 199 (84), 182(88), 154 (45), 97 (30), 57(100); HRMS Calcd for $C_{17}H_{29}NO_4$ 311.2096, found 311.2087.

2-(2,2-Dimethylpropyl)-4,4-bis(ethoxycarbonyl)cyclohexanone (76)



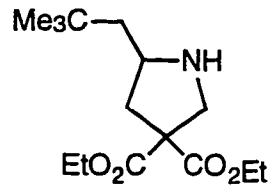
The material was isolated as a colorless liquid.^{1}H NMR($CDCl_3$, 300MHz) δ 4.32 (dq, *J* = 7.2, 2.4 Hz, 2 H), 4.19 (q, *J* = 7.2 Hz, 2 H), 2.75-2.37 (m, 5 H), 2.25 (dd, *J* = 14.1, 4.8 Hz, 1 H), 2.11 (dt, *J* = 13.2, 5.1 Hz, 1 H), 1.87 (t, *J* = 13.2 Hz, 1 H), 1.32 (t, *J* = 7.2 Hz, 3 H), 1.26 (t, *J* = 7.2 Hz, 3 H), 0.86 (s, 9 H), 0.76 (dd, *J* = 14.4, 4.5 Hz, 1 H); ^{13}C NMR($CDCl_3$, 75MHz) δ 210.06, 170.81, 170.47, 61.75, 61.72, 54.75, 43.07, 40.67, 40.33, 38.21, 31.94, 30.53, 29.27, 14.07, 13.92; EIMS *m/z* (rel intensity) 312 (M^+, 18), 297 (26), 296 (28), 255 (61), 181 (49), 173 (100), 140 (20), 108 (23), 69 (80), 57 (83); HRMS Calcd for $C_{17}H_{28}O_5$ 312.1936, found 312.1941.

4,4-Bis(ethoxycarbonyl)-8,8-dimethylnonanenitrile (77)



The material was isolated as a colorless liquid.^{1}H NMR($CDCl_3$, 300MHz) δ 4.28-4.14 (m, 4 H), 2.43-2.38 (m, 2 H), 2.27-2.22 (m,2 H), 1.87-1.82 (m, 2 H), 1.27 (t, *J* = 7.2 Hz, 6 H), 1.26-1.15 (m, 4 H), 0.86 (s, 9 H); ^{13}C NMR($CDCl_3$, 75MHz) δ 170.52, 119.12, 61.60, 56.72, 44.23, 34.14, 30.31, 29.25, 28.87, 19.13, 14.02, 13.03; EIMS *m/z* (rel intensity) 311 (M^+, 2), 296 (35), 266 (16), 254 (19), 181 (17), 173 (100), 108 (25), 57 (61); HRMS Calcd for $C_{17}H_{29}NO_4$ 311.2097, found 311.2094.

2-(2,2-Dimethylpropyl)-4,4-bis(ethoxycarbonyl)pyrrolidine (78)



The material was isolated as a colorless liquid.^{1}H NMR($CDCl_3$, 300MHz) δ 4.26-4.16 (m, 4H), 3.63 (d, *J*=12.6Hz, 1H), 3.21-3.11 (m, 1H), 3.13 (d, *J*=12.3 Hz, 1H), 2.67 (dd, *J*=13.2, 6.6 Hz, 1H), 2.08 (br, 1H), 1.77 (dd, *J*=13.5, 9.3 Hz, 1H), 1.57 (dd, *J*=13.8, 5,4 Hz, 1H), 1.41 (dd, *J*=14.1, 6.6 Hz, 1H), 1.26 (t, *J*=7.2 Hz, 6H), 0.95 (s, 9H); ^{13}C NMR($CDCl_3$, 75MHz) δ 172.25, 171.25, 61.57, 61.49 (two carbons), 57.73, 54.70, 49.29, 43.33, 30.33, 30.03, 13.99, 13.97; EIMS *m/z* (rel intensity) 285 (M^+, 1), 270 (2), 240 (9), 214 (100), 194 (7), 140 (14), 68 (10); HRMS Calcd for $C_{15}H_{27}NO_4$ 285.1940, found 285.1940.

CHAPTER III. HOMOLYTIC AROMATIC ALKYLATIONS OF ELECTRON-DEFICIENT AROMATICS BY *TERT*-BUTYLMERCURY HALIDES

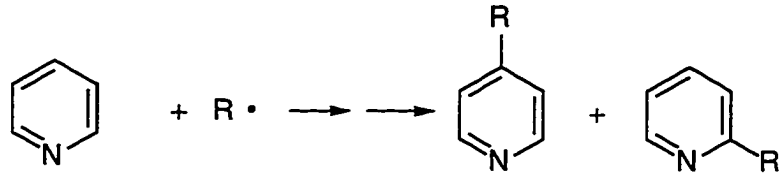
Introduction

Electron-deficient heteroaromatic bases such as pyridines and quinolines undergo homolytic alkylation. Alkyl radicals attacking the bases are simple radicals including $\bullet CH_3$, $\bullet C_2H_5$, $\bullet CMe_2$, $\bullet CH_2CH_2CH_2CH_3$, $\bullet CMe_3$, and $\bullet c\text{-}C_6H_{11}$. The radical sources typically used are: 1) RCOOH/$Ag^+/S_2O_8^{2-}$; 2) alkyl iodides/H_2O_2-Fe(II); 3) RCOOH/$Pb(OAc)_2$. [59a,b,c,d] The reactions are accelerated significantly by protonating the substrates.

$$2Ag^+ + S_2O_8^{2-} \longrightarrow 2Ag^{2+} + 2SO_4^{2-}$$

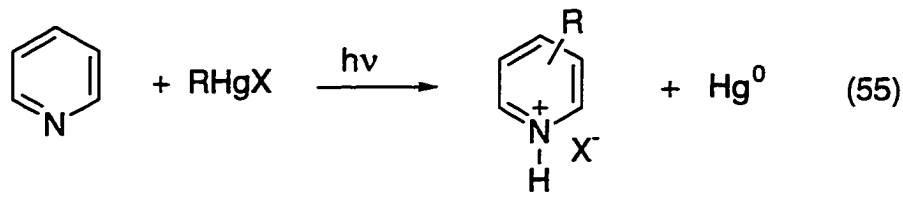
$$RCOOH + Ag^{2+} \longrightarrow RCOO\bullet + H^+ + Ag^+$$

$$RCOO\bullet \longrightarrow R\bullet + CO_2$$



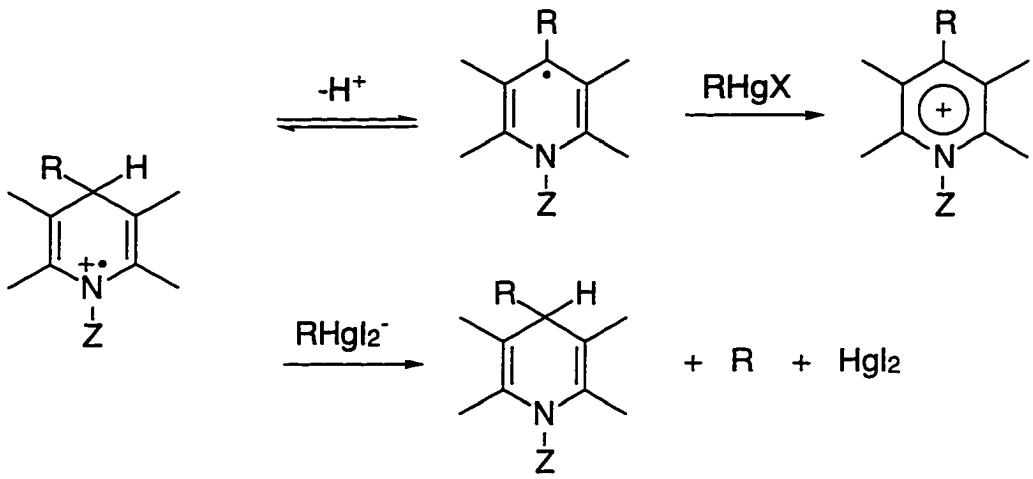
Alternative alkylation of pyridines and quinolines was achieved recently by using the alkylmercury halide methodology.[7e,9e,f,10a] The alkylation may involve the attack of *t*-Bu• upon free pyridine, upon a complex of the pyridine with *t*-BuHgX [60] or upon the pyridinium ion. Photolysis of *t*-BuHgX in DMSO gives 2-and 4-alkylated pyridines. Both protonation and complexion of the heteroaromatics are known to activate the substrates toward radical additions.[59d] The feature of the mercury method is that reductive alkylation competes with oxidative alkylation in some cases. A example is given below (Scheme 32).[61] The adduct

radical can either be reduced to the reductive product or lose the proton and then be oxidized by RHgX.

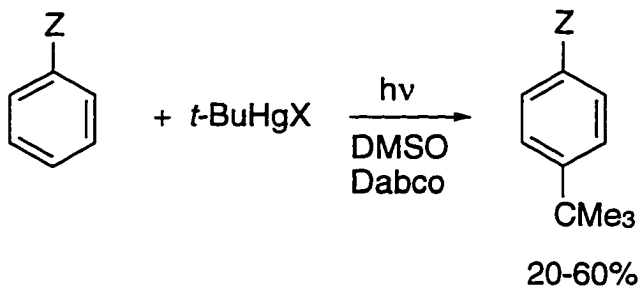


(55)

Scheme 32



Similarly, the benzenes bearing an electron-withdrawing group Z (Z=CHO, COCH3, COPh, COBu-*t*)were found to react with *t*-BuHgX to afford alkylated products.[62] Because of reversibility of the additions and the steric factor, only 4-substituted products were obtained.



(56)

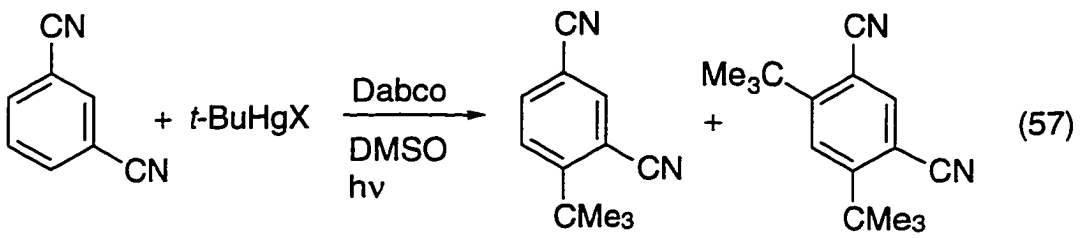
Group Z contributes to a reduce energy of the transition states by a polar effect and stabilizes the adduct radicals by resonance.

Results and Discussion

In the presence of a base such as Dabco, electronegatively disubstituted benzenes, including 1,2-,1,3-, and 1,4-disubstitited benzenes, react with *t*-BuHgX to give alkylated products. The activating groups are -CN, -CHO and $-CO_2Et$. The ractions proceed via a radical chain mechanism and an electron transfer is involved in the propagation step. Eletron-donating group such as OCH_3 deactivates the substrates and no reaction is observed for 3- or 4-methoxybenzonitrile. The presence of a nitro group probably inhibits the chain reaction. Consequently no reaction occurs for 3-nitrobenzonitrile.

t-BuHgX serves as a radical source and an electron acceptor. Since *t*-BuHgI is labile, *t*-BuHgCl was used for most reactions. For the more reactive substrates, facile reactions can also be achieved with *t*-BuHgI and I^- in tha dark.

Of the three kinds of the disubstituted benzenes, 1,3-disubstituted benzenes are the most reactive toward alkylation. For 1,3-dicyanobenzene the reaction does not stop at the mono-alkylated product. An essentially quantitative yield of the 1,5-bis(1,1-dimethylethyl)-2,4-dicyanobenzene is obtained with an excess of *t*-BuHgCl for 4.5 h (Table 25). In the dark, a



79 **80** (57)

reaction with *t*-BuHgI/KI also gave a high yield of the dialkylated product. This dark reaction occurs even in the absence of Dabco, but at a much slow rate and lower yield.

The mechanism is depicted in Scheme 33. The adduct radical and the radical anion are stabilized by both cyano groups. Polar effect may play an important role in forming the radical adduct. The initial kinetic chain length measured by $(t\text{-Bu})_2NO\bullet$ inhibition method was 22 (Table 26 and Figure 10).

Table 25. Alkylation of 1,3-Dicyanobenzene with *t*-BuHgX[a]

	Mol equiv.			%Yield[b]	
Entry	*t*-BuHgX	Dabco, KI	Condition	**79**	**80**
1	Cl (4)	4, 0	hv, 4.5 h	0	99
2	Cl (1)	4, 0	hv, 20 min	26	1
3	Cl (1)	4, 0	hv, 1.5 h	44	27
4	I (4)	4, 4	dark, 19 h	0	99
5	I (2)	4, 2	dark, 3 h	48	46
6	I (2)	4, 2	dark, 5.5 h	31	66
7	I (4)	0, 4	dark, 20 h	20	3

[a] Reaction of 1,3-Dicyanobenzene (0.05 mmol) with *t*-BuHgX in 0.6 mL of DMSO-d_6 at 35-40 °C with sunlamp irradiation or at room temperature in the dark.

[b] NMR yield with toluene as an internal standard.

Scheme 33

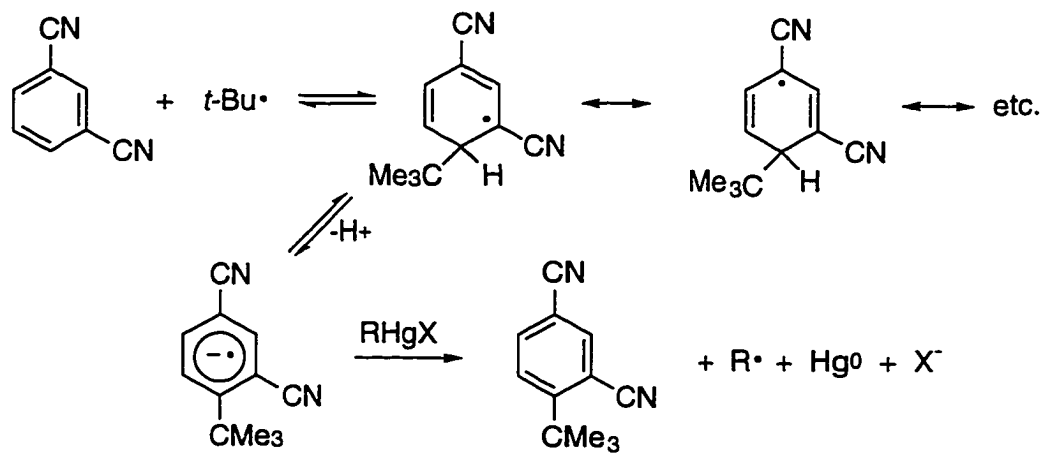


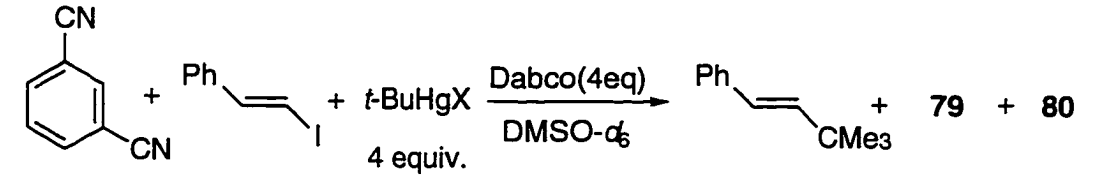
Table 26. Alkylation of 1,3-dicyanobenzene in DMSO-d_6[a]

		%Yield without DTBN[b]		%Yield with DTBN	
Entry	Time (min)	**79**	**80**	**79**	**80**
1	4	4	0	0	0
2	10	13	0	0	0
3	20	38	4	0	0
4	30	44	14	0	0
5	45	51	27	0	0
6	60	46	48	0	0
7	95	-	-	0	0
8	115	-	-	30	4
9	120	-	-	41	6
10	130	-	-	47	13

a Reaction of 1,3-dicyanobenzene (0.05 mmol) with *t*-BuHgCl(2 equiv) and Dabco(4 equiv) in 0.6 mL of DMSO-d_6 with sunlamp irradiation at 35-40 °C.

b ^{1}H NMR yield with toluene as an internal standard.

The reactivity of 1,3-dicyanobenzene was also compared with *(E)*-β-iodostyrene with respect to radical addition. A competition reaction between the two compounds gives a relative reactivity of 1,3-dicyanobenzene vs. *(E)*-β-iodostyrene. The ratio measured is 1.90 based on the kinetic calculation method.[62]



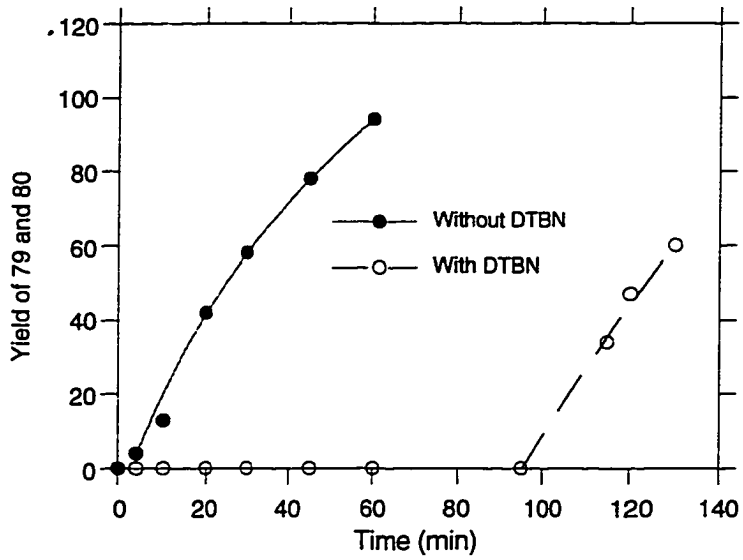
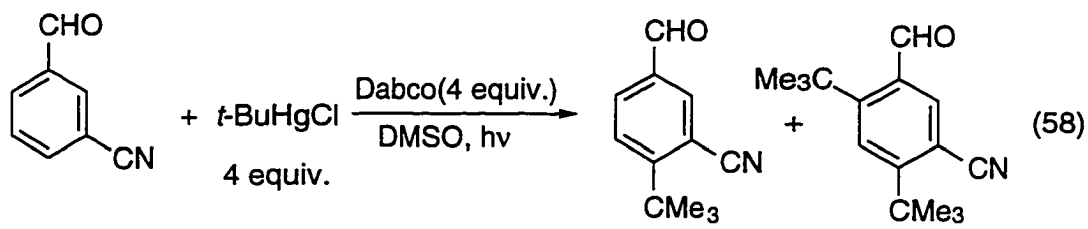
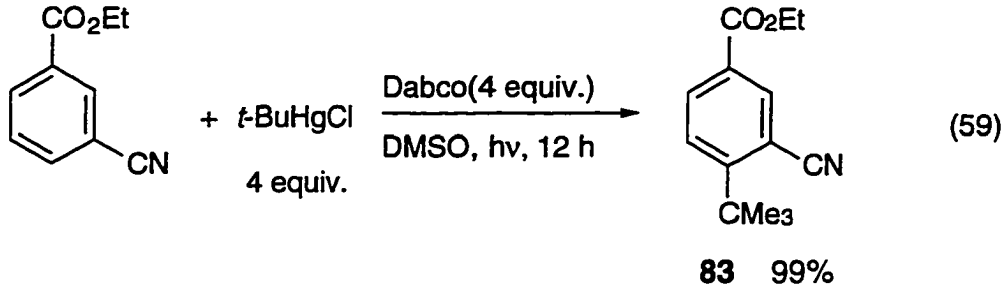


Figure 10. Yield of **79** and **80** with Time.

Similarly, 3-cycanobenzaldehyde undergoes a facile alkylation. The difference is that the second step alkylation is slow as shown (Eq 58). Within 15 h the dialkylated product is formed in only 24% while 42% of the monoalkylated product is still present. This can be explained by steric hindrance of the formyl group. This explanation is confirmed by the reaction of ethyl 3-cyanobenzoate which gives only the mono-alkylated product **83** in 99% yield without any dialkylated product (Eq 59). Apparently, the -CO_2Et group has a bigger steric hindrance than the -CHO group.

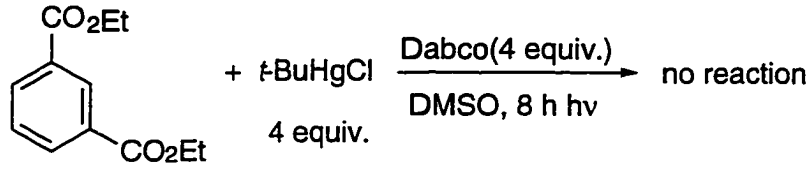


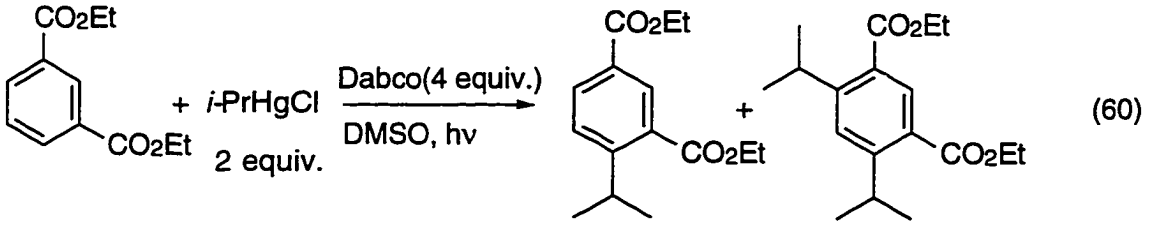
	81	**82**
3 h	84%	12%
15 h	42%	24%



83 99% (59)

An extreme example involving steric hindrance is diethyl isophthalate. No reaction was observed with *t*-BuHgCl/Dabco and the starting material was quantitatively recovered. However, if *t*-Bu• is replaced with *i*-Pr•, a fairly good alkylation occurs (Eq 60). In this condition, even the dialkylated product is formed, indicating that steric congestion is greatly relieved by changing *t*-Bu• to *i*-Pr•.



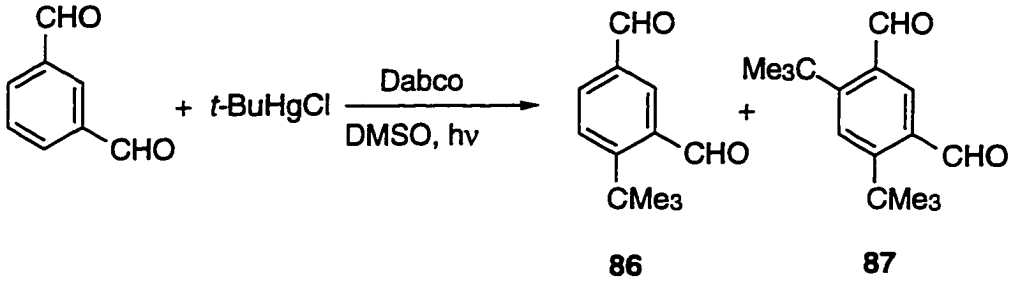


(60)

84 **85**

11 h	67%	12%
20 h	70%	20%

As a 1,3-disubstituted benzene, isophthalaldehyde is also studied. Compared with 1,3-dicyanobenzene, the reaction of this substrate is somewhat slower and not very clean. Longer photolysis causes decomposition of the monoalkylated product without increasing the yield



86 **87** (61)

Table 27. Alkylation of Isophthalaldehyde with *t*-BuHgCl[a]

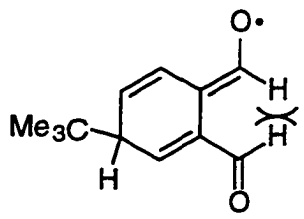
	Mol equiv.			%Yield[b]	
Entry	*t*-BuHgCl	Dabco	Condition	**86**	**87**
1	4	4	hv, 6 h	36	20
2	4	4	hv, 18 h	14	20
3	2	4	hv, 1.5 h	36	3
4	2	4	hv, 4 h	46	12

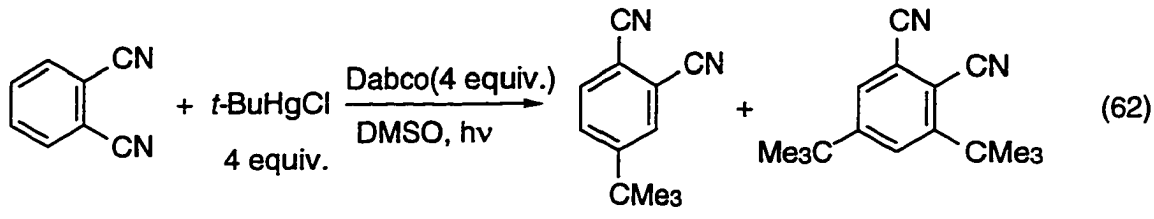
[a] Reaction of isophthalaldehyde(0.05 mmol) with *t*-BuHgCl in 0.6 mL of DMSO-*d*6 at 35-40 °C with sunlamp irradiation.

[b] ^{1}H NMR yield with toluene as an internal standard.

of dialkylated product. The problem may arise from the formyl group participating in other processes (Eq 61 and Table 27).

1,2-dicyanobenzene and phthalimide[61] undergo this type of alkylation reaction similarly (Eq 62, 63, 64 and Table 27). However, phthalaldehyde, ethyl phthalate or phthalic anhydride fail to react with *t*-BuHgCl/Dabco/hv. For the aldehyde and ester, resonance stabilization may be lost because of steric congestion from interaction of the two carbonyl groups. For the latter, the lack of reactivity may be related to the ease of reduction. Phthalic anhydride has a more negative reduction potential (-1.16 V)than phthalimide (-0.70 V).[62] and therefore can not

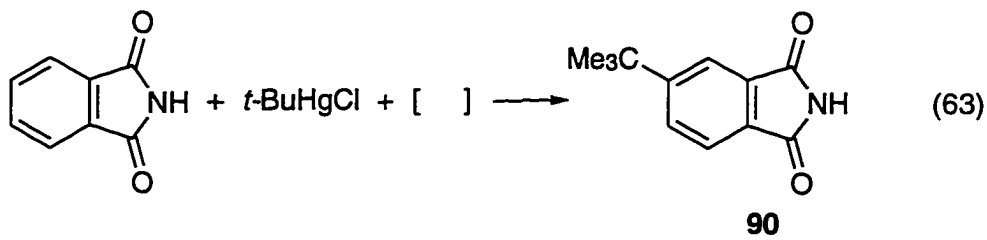




	88	89
3 h	90%	10%
10 h	84%	16%

(62)

Table 28. Alkylation of phthalimide with *t*-BuHgX[a]



(63)

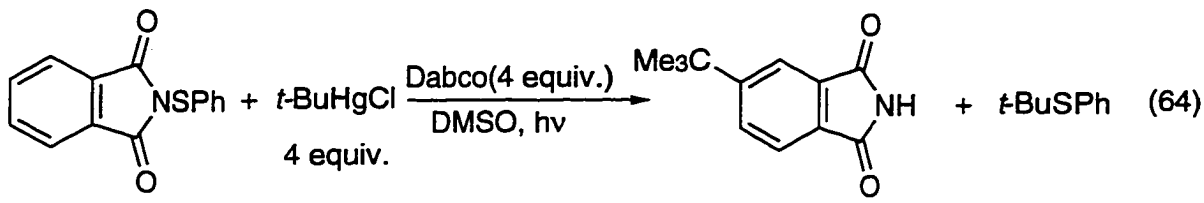
Entry	*t*-BuHgX	Dabco	Condition	%Yield of **90**[b]
1	Cl (2)	0	hv, 5 h	tr.
2	I (2)	4	hv, 5 h	63
3	Cl (2)	4	hv, 21 h	91
4	I (2), KI (4)	4	drak, 35 h	60
5	I (4)	4	hv, 7 h	78

a Reaction of phthalimide (0.05 mmol) in 0.6 mL of DMSO-d_6.

b see Table 27.

stabilize the transition state t-Bu^{+}--$ArX^{\bullet-}$ as efficiently as phthalimide.

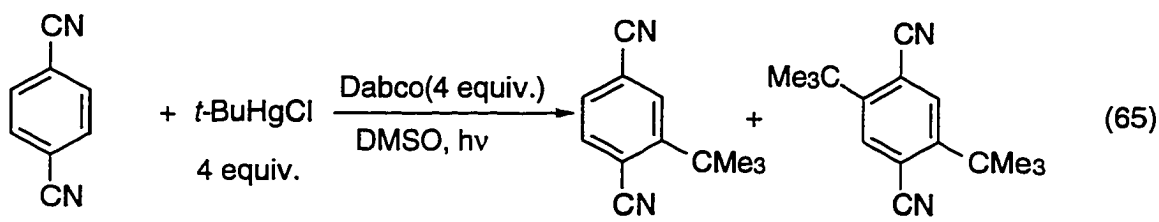
A related compound, *N*-phenylthiophthalimide, was also studied. The products observed are **90** and t-BuSPh. No direct alkylation product is observed but phthalimide is found. Obviously the substitution of hydrogen for -SPh is fater than alkylation of the substrate. The source of hydrogen is from t-BuHgCl.



90

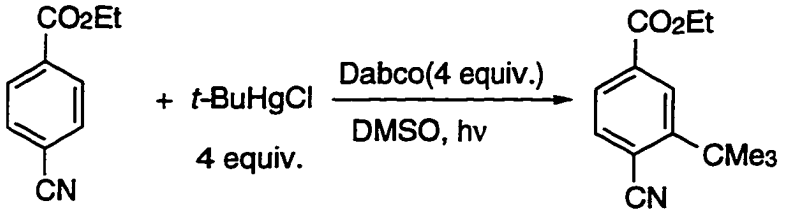
4 h	26%	61%
9 h	50%	65%

The 1,4-disubstituted benzenes are less reactive than the 1,3-derivatives. No reaction was observed for terephthalaldehyde. However, 1,4-dicyanobenzene gives monoalkylated product **91** in 58% yield and dialkylated product **92** in 11% yield after 3 h of photolysis. The conversion of **91** to **92** occurs slowly. Ethyl 4-cyanobenzoate is even less reactive and only a 24% yield of **93** is obtained in 6 h. It takes 45 h to reach 80% yield. No dialkylated product is formed in this case.



91 **92**

3 h	58%	11%
6.5 h	61%	30%

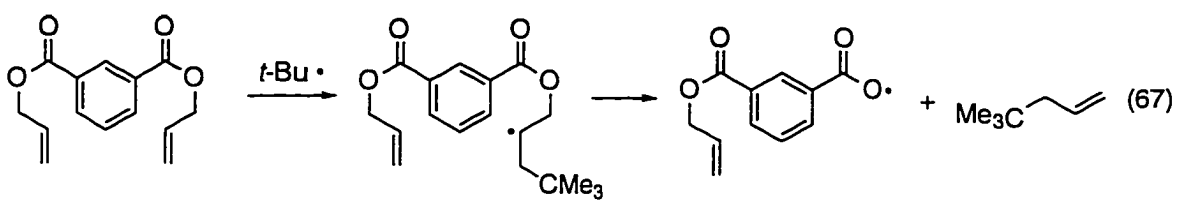


(66)

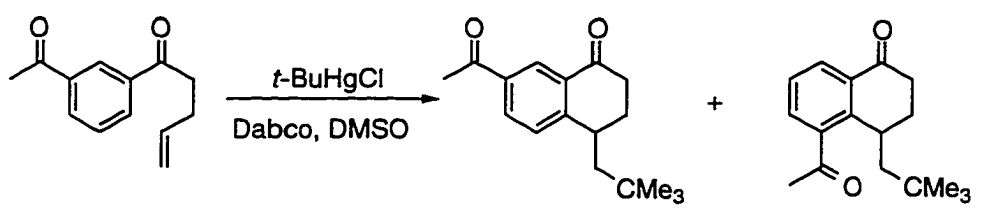
93

6 h	24%
18 h	46%
45 h	80%

Intramolecular radical addition leads to cyclized products. Three substrates have been investigated. Diallyl isophthalate does not give any cyclized compound since the adduct radical undergoes a rapid β-elimination (Eq 67). Such problem is avoided by using 1-(3-acetylphenyl)-4-penten-1-one which affords two cyclized products. Introduction of the acetyl group was expected to increase the reactivity of the substrate relative to the cyclization of 1-phenyl-4-penten-1-one previously reported.[63] However the formation of isomer **95** was unexpected (Eq 68 and Table 29). The reason is not clear. This result indicates that intramolecular alkylation is different from intermolecular alkylation. In this case, steric requirement is reduced to such an extent that there is no discrimnation between 1 and 3 position.



(67)



(68)

94 **95**

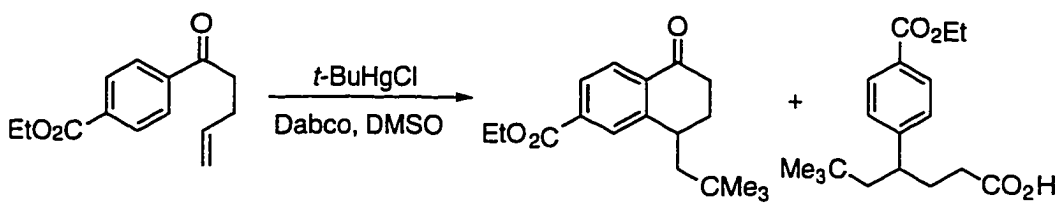
Table 29. Cyclization of 1-(3-acetylphenyl)-4-penten-1-one[a]

	Molar equiv.			%Yield[b]	
Entry	*t*-BuHgX	Dabco	Condition	**94**	**95**
1	Cl (3)	4	hv, 8 h	22	25
2	Cl (3)	4	hv, 18 h	31	32
3	I (4)	4	hv, 13 h	23	30

a Photolysis of the substrate (0.05 mmol) with *t*-BuHgX in 0.6 mL of DMSO-d_6.

b See Table 25.

The symmetric substrate 1-(4-ethoxycarbonylphenyl)-4-penten1-1-one, after photolysis with 4 equivalent of *t*-BuHgCl and Dabco, gives only one cyclized product **96** together with the side product **97** which is formed by a rearrangement process shown below in Scheme 34. In the absence of Dabco, the reaction still gives a 1:1 mixture of **96** and **97** (total 44% yield) after 26 h photolysis with 4 equivalent of *t*-BuHgCl. The rearrangement involves a 1,4 aryl shift for which there is literature precedence.[66] The uncyclized adduct radical undergoes an intramolecular addition ($Ar_{1,5}$ process) leading to the spiro ring which gives the acyl

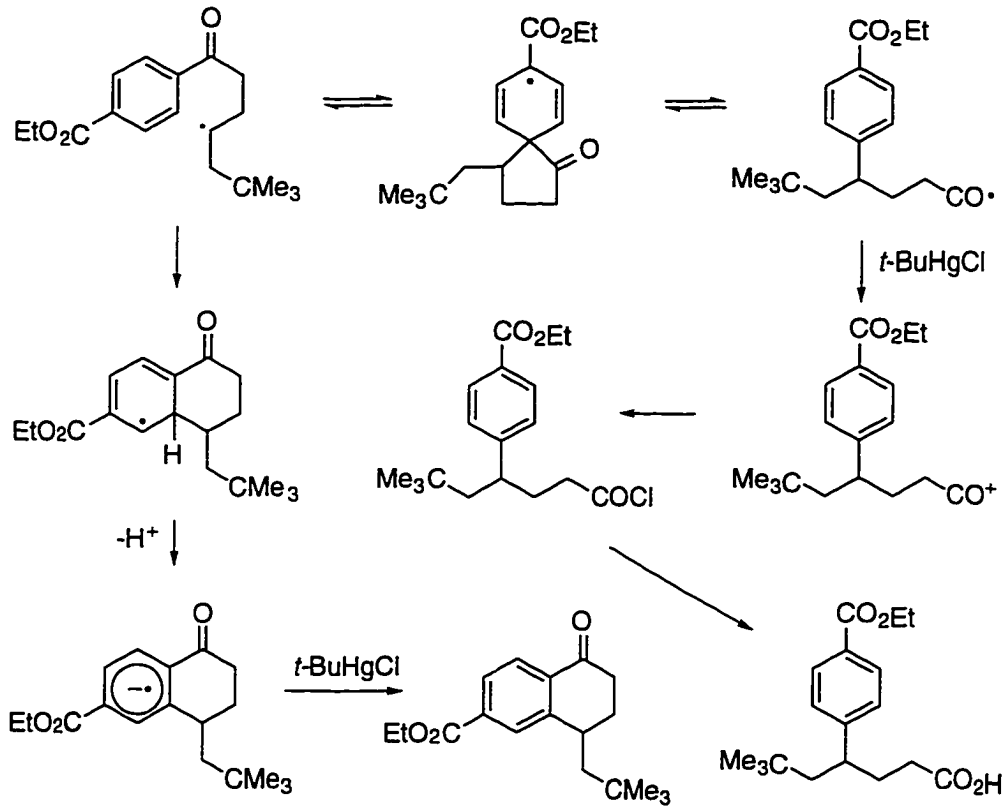


(69)

	96	**97**
6 h	25%	20%
18 h	40%	33%

radical upon ring opening. An electron transfer from the acyl radical to *t*-BuHgCl occurs and the acyl cation is formed. The proposed mechanism is supported by trapping of the intermediate with diethyl amine to give the corresponding amide which was identified by GCMS.

Scheme 34



Conclusion

tert-Alkylmercury halides are suitable reagents for alkylation of electronegatively disubstituted benzenes in photostimulated reactions in DMSO. Typical substituents are CN, CHO and CO_2Et. A base, such as Dabco, promotes the reactions efficiently. 1,3-

Dicyanobenzene is the most reactive species although 1,2- and 1,4-disubstituted benzenes also give the satisfactory yields of the alkylated products. Dialkylated products are very common. However, they are often avoided when one of the substituents is an ester function. Cyclizations are achieved by intramolecular alkylations leading to tetralones.

Experimental Section

General Consideration

See Experimental Section, Chapter I for instrumentation and other details.

Solvents and Reagents

See Experimental Section, Chapter I for description of solvents. Chemical reagents were purchased mostly from Aldrich Chemical Co. They were used without further purification. *tert*-Butylmercury chloride and iodide were prepared as previously described (see Chapter I).

Materials

Preparations are described below for the reagents which are not commercially available.

1. Ethyl 3-Cyanobenzoate

This compound was prepared by the reaction of 3-cyanobenzoyl chloride with ethanol in the presence of triethylamine in CH_2Cl_2 at 0-25 °C. ^1H NMR ($CDCl_3$, 300MHz) δ 8.34-8.33 (m, 1H), 8.28 (dt, J=8.1, 1.5 Hz, 1H), 7.84 (dd, J=7.8, 1.5 Hz, 1H), 7.59 (t, J=7.8 Hz, 1H), 4.42 (q, J=7.2 Hz, 2H), 1.42 (t, J=7.2 Hz, 3H).

2. Diethyl Isophthalate

This compound was prepared by the reaction of isophthaloyl dichloride with ethanol in the presence of triethylamine in CH_2Cl_2 at 0-25 °C ^1H NMR ($CDCl_3$, 300MHz) δ 8.69-8.68 (m, 1H), 8.23 (dd, *J*=7.8, 1.8 Hz, 2H), 7.53 (t, *J*=7.5 Hz, 1H), 4.42 (q, *J*=7.2 Hz, 4H), 1.42 (t, *J*=7.2 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 165.72, 133.58, 130.81, 130.52, 128.42, 61.23, 14.23.

3. *N*-Phenylthiophthalimide

The compound was prepared according to a literature procedure.[64] A mixture of 0.965 g of N-bromophthalimide (4.2 mmol) and 0.456 g of PhSSPh (2.1 mmol) was refluxed in 5 mL of benzene for 30 min. 30 mL of hexane was used to precipitate the product which was then washed with 5 mL of hexane. Purification by recrystallization from ethanol gave the pure product. ^1H NMR ($CDCl_3$, 300MHz) δ 7.93 (dd, *J*=5.4, 3.0 Hz, 2H), 7.78 (dd, *J*=5.4, 3.0 Hz, 2H), 7.62-7.59 (m, 2H), 7.35-7.30 (m, 3H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 167.71, 145.08, 135.02, 134.68, 131.99, 130.94, 129.32, 124.05.

4. 3-butenyl 3-acetylphenyl ketone

This compound was prepared using a literature method.[65] To a mixture of 7 mmol of KH (Aldrich product, 38% dispersion in mineral oil; washed with dry THF for three times and the THF removed and evaporated before weighing) and 10 mL of THF was added a solution of 1,3-diacetylbenzene (6 mmol) in 2 mL of THF at room temperature. 8 mmol of Et_3B(1M solution in THF) was added at one time and allyl bromide(9 mmol) was added dropwise. After 3 h of stirring, the reaction was quenched with $NaOH/H_2O_2$ solution and the mixture was extracted with ether. The organic layer was washed twice with $NaHCO_3$ and brine and dried over $MgSO_4$. Evaporation of the solvent and purification by passing through silica gel afforded the product in the yield of 30%.^1H NMR ($CDCl_3$, 300MHz) δ 8.53 (t, *J*=1.5 hz, 1H), 8.18-

8.14 (m, 2H), 7.59 (t, *J*=7.8 Hz, 1H), 5.98-5.84 (m, 1H), 5.14-5.01 (m, 2H), 3.14 (t, *J*=7.2 Hz, 2H), 2.67 (s, 3H), 2.56-2.48 (m, 2H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 198.62, 197.28, 137.37, 137.21, 136.95, 132.39, 132.22, 129.02, 127.71, 115.50, 37.84, 27.93, 26.68.

5. 3-Butenyl 4-Ethoxycarbonylphenyl Ketone

This compound was prepared in the same manner as above and isolated as a white solid, mp 50-51 °C. ^1H NMR ($CDCl_3$, 300MHz) δ 8.14-8.10 (m, 2H), 8.02-7.99 (m, 2H), 5.97-5.84 (m, 1H), 5.13-5.00 (m, 2H), 4.40 (q, *J*=7.2 Hz, 2H), 3.11 (t, *J*=7.2 Hz, 2H), 2.55-2.47 (m, 2H), 1.42 (t, *J*=7.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 198.77, 165.61, 139.92, 136.91, 134.07, 129.68, 127.78, 115.40, 61.32, 37.99, 27.87, 14.17.

General Procedures for *tert*-Butylation and Cyclization

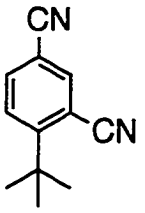
The substrate (0.05 mmol) and reagents were dissolved in 0.6 mL of DMSO-d_6 in a NMR tube and exposed to a 275W sunlamp at a distance of *ca.* 25 cm at 35-40 °C. Yields are based on toluene (0.1 mmol) as an internal standeard.

Isolation of Products

The substrate(1-2 mmol) and reagents were dissolved in 4 mL of DMSO in a Pyrex test tube and irradiated for a period of time. After the reaction was completed, the mixture was poured into 50 mL of aq. $Na_2S_2O_3$ and extracted with methylene chloride (20 mL) for three times. The combined organic layer was washed with brine (20 mL) for three times to remove DMSO. The solution was dried with MgSO4. Isolation was performed on TLC plates after the solvent was evaporated. The eluent used was a hexane:ethyl acetate mixture. The ratio depended on individual samples.

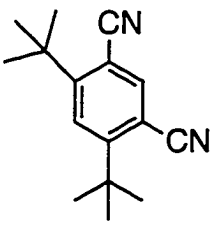
Characterization of Products

2,4-Dicyano-1-(1,1-dimethylethyl)benzene (79)



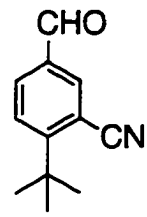
The compound was isolated as a white solid, mp 56-57 °C. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.95 (d, *J*=1.8Hz, 1H), 7.80 (dd, *J*=8.4, 1.8Hz, 1H), 7.65 (d, *J*=8.4Hz, 1H), 1.55 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 158.80, 138.50, 135.70, 127.64, 118.04, 116.71, 112.48, 110.98, 36.31, 29.75; EIMS m/z (rel.intensity) 184 (M^+, 21), 169 (100), 141 (26), 69 (12), 57 (4); HRMS calcd for $C_{12}H_{12}N_2$ 184.1001, found 184.1005; Anal. calcd for $C_{12}H_{12}N_2$: C, 78.23; H, 6.57; N, 15.20, found C, 78.19; H, 6.78; N, 15.18.

2,4-Dicyano–1,5-bBis(1,1-dimethylethyl)benzene (80)[67]



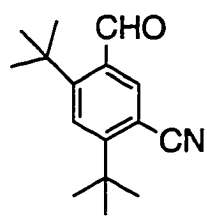
The compound was isolated as a white solid, mp 170-172 °C (lit.[67] 189-190 °C). ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.94 (s, 1H), 7.63 (s, 1H), 1.53 (s, 18H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 158.15, 141.61, 124.88, 118.22, 109.35, 36.55, 29.81; EIMS m/z (rel.intensity) 240 (M^+, 14), 225 (100), 210 (12), 197 (15), 57 (14); HRMS Calcd for $C_{16}H_{20}N_2$ 240.1626, found 240.1630.

3-Cyano-4-(2,2-dimethylethyl)benzaldehyde (81)



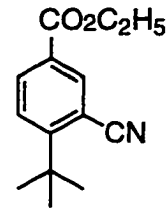
The compound was isolated as a white solid, mp 112-115 °C. ^{1}H NMR ($CDCl_3$, 300MHz) δ 10.01 (s, 1H), 8.18 (d, *J*=1.8Hz, 1H), 8.02 (dd, *J*=8.4, 1.8Hz, 1H), 7.70 (d, *J*=8.4Hz, 1H), 1.57 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 189.68, 160.00, 136.74, 134.27, 132.96, 127.33, 119.02, 111.95, 36.30, 29.90; EIMS m/z (rel.intensity) 187 (M^+, 16), 172 (100), 144 (16), 57 (4); HRMS calcd for $C_{12}H_{13}NO$ 187.0997, found 187.0991; Anal. Calcd for $C_{12}H_{13}NO$: C, 76.98; H, 7.00; N, 7.48, found C, 76.49; H, 7.22; N, 7.35.

5-Cyano-2,4-bis(1,1-dimethylethyl)benzaldehyde (82)



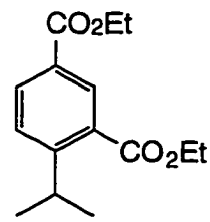
The compound was isolated as a white solid, mp 119-122 °C. ^{1}H NMR ($CDCl_3$, 300MHz) δ 10.75 (s, 1H), 8.22 (s, 1H), 7.62 (s, 1H), 1.542 (s, 9H), 1.539 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 190.11, 158.14, 156.25, 137.50, 133.40, 124.83, 119.24, 109.17, 36.67, 36.42, 32.58, 29.91; EIMS m/z (rel.intensity) 243 (M^+, 11), 228 (100), 210 (12), 186 (9), 154 (5), 57 (21); HRMS calcd for $C_{16}H_{21}NO$ 243.1623, found 243.1623; Anal. Calcd for $C_{16}H_{21}NO$: C, 78.97, H, 8.70; N, 5.76, found C, 78.46; H, 9.09; N, 5.56.

Ethyl 3-cyano-4-(1,1-dimethylethyl)benzoate (83)



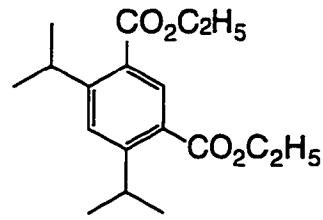
The compound was isolated as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.34 (d, *J*=2.1Hz, 1H), 8.15 (dd, *J*=8.4, 2.1Hz, 1H), 7.58 (d, *J*=8.4Hz, 1H), 4.40 (q, *J*=7.2Hz, 4H), 1.55 (s, 9H), 1.41 (t, *J*=7.2Hz, 3H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 164.59, 158.24, 136.56, 133.43, 128.76, 126.58, 119.38, 111.07, 61.46, 35.97, 29.91, 14.20; EIMS m/z (rel.intensity) 231 (M^+, 21), 216 (100), 188 (36), 115 (11), 43 (12); HRMS calcd for $C_{14}H_{17}NO_2$ 231.1259, found 231.1259. Anal. calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06, found C, 72.95; H, 7.51; N, 6.01.

Diethyl 4-isopropylisophthalate (84)



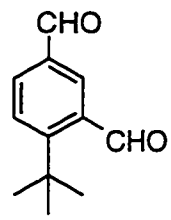
The compound was isolated as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.38 (d, *J*=2.1 Hz, 1H), 8.10 (dd, *J*=8.4, 2.1Hz, 1H), 7.48 (d, *J*=8.4 Hz, 1H), 4.39 (q, *J*=7.2 Hz, 2H), 4.38 (q, *J*=7.2 Hz, 2H), 3.76 (h, *J*= 6.9 Hz, 1H), 1.41 (t, *J*=7.2 Hz, 3H), 1.40 (t, *J*=7.2 Hz, 3H), 1.28 (d, *J*=6.9 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 167.61, 165.75, 154.36, 132.20, 130.84, 130.54, 127.82, 126.33, 61.14, 60.96, 29.74, 23.60, 14.22, 14.15; EIMS m/z (rel.intensity) 264 (M^+, 76), 235 (26), 219 (92), 218 (84), 217 (100), 203 (30), 115 (15); HRMS calcd for $C_{15}H_{20}O_4$ 264.1362, found 264.1361; Anal. calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63, found C, 67.43; H, 7.77.

Diethyl 4,6-diisopropylisophthalate (85)



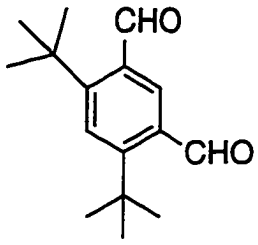
The compound was isolated as a colorless liquid. ^1H NMR ($CDCl_3$, 300MHz) δ 8.16 (s, 1H), 7.44 (s, 1H), 4.37 (q, *J*=7.2 Hz, 4H), 3.80 (h, *J*=6.9 Hz, 2H), 1.39 (t, *J*=7.2 Hz, 6H), 1.27 (d, *J*=7.2Hz, 12H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 167.48, 153.17, 131.74, 127.42, 124.09, 60.92, 29.65, 23.67, 14.19; EIMS m/z (rel.intensity) 306 (M^+, 52), 277 (21), 261 (76), 260 (100), 259 (67), 245 (20); HRMS calcd for $C_{18}H_{26}O_4$ 306.1831, found 306.1827; Anal. calcd for $C_{18}H_{26}O_4$: C, 70.56; H, 8.55, found C, 69.94; H, 8.71.

4-(1,1-Dimethylethyl)isophthalaldehyde (86)



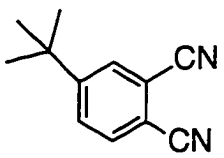
The compound was isolated as a white solid, mp 42-44 °C. ^1H NMR ($CDCl_3$, 300MHz) δ 10.88 (s, 1H), 10.06 (s, 1H), 8.40 (d, *J*=1.8Hz, 1H), 8.02 (dd, *J*=8.1, 1.8Hz, 1H), 7.68 (d, *J*=8.1Hz, 1H)1.57 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 191.44, 191.02, 158.36, 136.13, 134.51, 132.49, 132.46, 127.43, 36.39, 32.67; EIMS m/z (rel.intensity) 190 (M^+, 11), 175 (100), 157 (24), 129 (39), 91 (16), 43 (40); HRMS Calcd for $C_{12}H_{14}O_2$ 190.0994, found 190.0994; Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42, fonud C, 75.75; H, 7.51.

4,6-Bis(1,1-dimethylethyl)isophthalaldehyde (87)



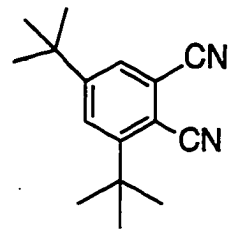
The compound was isolated as a white solid, mp 130-132 °C.^{1}H NMR ($CDCl_3$, 300MHz) δ 10.74 (s, 2H), 8.45 (s, 1H), 7.63 (s, 1H), 1.54 (s, 18H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 191.47, 156.61, 134.42, 133.57, 125.22, 36.65, 32.39; EIMS m/z (rel.intensity) 246 (M^+, 3), 245 (8), 231 (100), 213 (16), 115 (12), 57 (20); HRMS Calcd for $C_{16}H_{22}O_2$ 246.1620, found 246.1604; Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00, fonud C, 77.34; H, 9.07.

1,2-Dicyano-4-(1,1-dimethylethyl)benzene (88)[68]



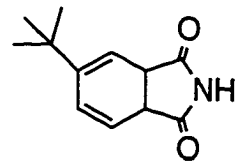
The compound was isolated as a white solid, mp 59-60 °C (lit.[68] 56-57 °C). ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.84 (dd, *J*=1.5, 0.9 Hz, 1H), 7.81-7.75 (m, 2H), 1.38 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 157.65, 133.28, 130.78, 130.41, 115.74, 115.52, 115.49, 112.58, 35.48, 30.55; EIMS m/z (rel.intensity) 184 (M^+, 18), 169 (100), 141 (59), 114 (9); HRMS calcd for $C_{12}H_{12}N_2$ 184.1001, found 184.1004.

2,3-Dicyano-1,5-bis(1,1-dimethylethyl)benzene (89)[68]



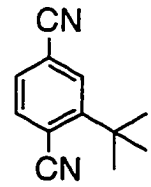
The compound was isolated as a white solid, mp 127-129 °C (lit.[68] 131-132 °C). ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.75 (d, *J*=1.8Hz, 1H), 7.65 (d, *J*=1.8Hz, 1H), 1.55 (s, 9H), 1.35 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 156.88, 155.38, 128.26, 127.74, 118.58, 116.82, 116.54, 111.06, 36.30, 35.69, 30.75, 30.00; EIMS m/z (rel.intensity) 240 (M^+, 13), 225 (100), 210(11), 197 (10), 57 (13); HRMS Calcd for $C_{16}H_{20}N_2$ 240.1626, found 240.1628.

4-(1,1-Dimethylethyl)phthalimide (90)[69]



The compound was isolated as a white solid, mp 131-132 °C (lit.[69] 131-132 °C). ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.58 (br. 1H), 7.91 (t, *J* = 1.2Hz, 1H), 7.82-7.76 (m, 2H), 1.39 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 168.97, 168.57, 158.94, 132.82, 131.32, 129.92, 123.37, 120.68, 35.72, 31.08.

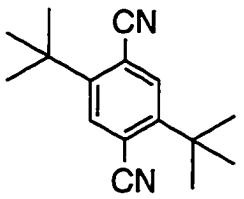
1,4-Dicyano-3-(1,1-dimethylethyl)benzene (91)



The compound was isolated as a white solid, mp 150-151 °C. ^{1}H NMR ($CDCl_3$, 300MHz) δ 7.81-7.78 (m, 2H), 7.60 (dd, *J*=7.8, 1.5Hz, 1H), 1.55 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz)

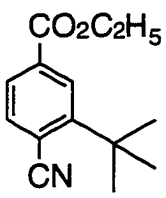
δ 155.05, 135.95, 130.16, 129.53, 118.45, 117.54, 116.31, 115.13, 35.91, 29.75; EIMS m/z (rel.intensity) 184 (M^+, 17), 169 (100), 141 (30), 114 (8), 57 (5); HRMS calcd for $C_{12}H_{12}N_2$ 184.1001, found 184.1001; Anal. calcd for $C_{12}H_{12}N_2$: C, 78.23; H, 6.57; N, 15.20, found C, 78.06, H, 6.78; N, 15.11.

1,4-Dicyano-2,5-bis(1,1-dimethylethyl)benzene (92)[67]



The compound was isolated as a white solid, mp 177-180 °C (lit.172-174 °C [67]). ^1H NMR ($CDCl_3$, 300MHz) δ 7.75 (s, 2H), 1.52 (s, 18H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 151.52, 133.34, 119.01, 114.67, 35.29, 29.78; EIMS m/z (rel.intensity) 240 (M^+, 12), 225 (100), 197 (11), 182 (7), 155 (6), 57 (7); HRMS Calcd for $C_{16}H_{20}N_2$ 240.1626, found 240.1633.

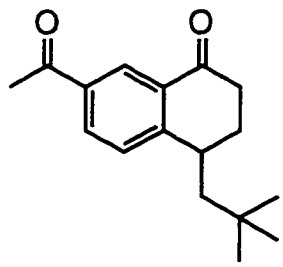
Ethyl 4-cyano-3-(1,1-dimethylethyl)benzoate (93)



The compound was isolated as a colorless liquid. ^1H NMR ($CDCl_3$, 300MHz) δ 8.16 (d, *J*=1.5Hz, 1H), 7.94 (dd, *J*=7.8, 1.5Hz, 1H), 7.75 (d, *J*=8.1Hz, 1H), 4.42 (q, *J*=7.2Hz, 4H), 1.56 (s, 9H), 1.42 (t, *J*=7.2Hz, 3H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 165.38, 154.08, 135.53, 133.84, 127.29, 126.90, 119.46, 114.58, 61.63, 35.74, 30.01, 14.21; EIMS m/z (rel.intensity) 231 (M^+, 14), 216 (100), 188 (30), 144 (9); HRMS calcd for $C_{14}H_{17}NO_2$

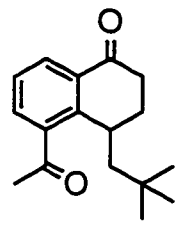
231.1259, found 231.1260. Anal. calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06, found C, 71.64; H, 7.40; N, 5.93.

7-Actyl-4-(2,2-dimethylpropyl)-α-tetralone (94)



The compound was isolated as a white solid, mp 39-41 °C. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.54 (d, *J*=2.1Hz, 1H), 8.11 (dd, *J*=8.1, 2.1Hz, 1H), 7.38 (d, *J*=8.1Hz, 1H), 3.12 (m, 1H), 2.86 (ddd, *J*=17.7, 12.3, 5.1Hz,1H), 2.64 (s, 3H), 2.64 (dt, *J*=18, 5.1Hz, 1H), 2.29 (tt, *J*=12.6, 4.5Hz, 1H), 2.19-2.09 (m, 1H), 1.77 (dd, *J*=14.4, 7.8Hz, 1H), 1.48 (dd, *J*=14.4, 2.7Hz, 1H), 1.06 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 197.72, 197.30, 155.36, 135.40, 132.40, 131.63, 129.12, 127.74, 47.85, 34.83, 34.35, 31.53, 29.86, 28.00, 26.63; EIMS m/z (rel.intensity) 258 (M^+, 57), 243 (58), 188 (84), 187 (100), 115 (30); HRMS calcd for $C_{17}H_{22}O_2$ 258.1620, found 258.1622.

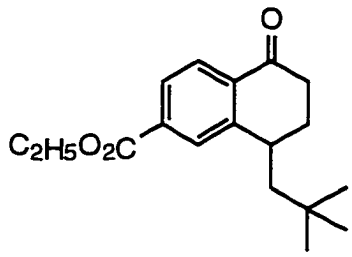
5-Acetyl-4-(2,2-dimethylpropyl)-α-tetralone (95)



The compound was isolated as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300MHz) δ 8.15 (dd, *J*=7.8, 1.5Hz, 1H), 7.76 (dd, *J*=7.5, 1.5Hz, 1H), 7.37 (t, *J*=7.5Hz, 1H), 3.93 (dq, *J*=10.8, 3.0Hz, 1H), 2.87 (ddd, *J*=18.6, 14.4, 5.7Hz, 1H), 2.60 (ddd, *J*=18.6, 5.4, 2.1Hz, 1H),

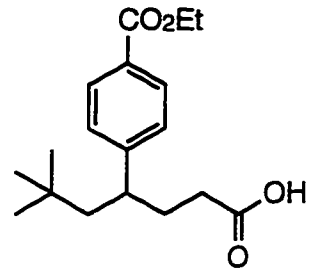
2.33 (m, 1H), 2.13 (tt, *J*=14.4, 4.2Hz, 1H), 1.61 (dd, *J*=14.4, 11.4Hz, 1H), 1.32 (dd, *J*=14.7, 2.7Hz, 1H), 1.02 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 201.98, 198.26, 149.78, 137.78, 133.36, 133.18, 130.51, 125.95, 46.29, 32.88, 31.23, 30.75, 30.60, 24.96, 30.25; EIMS m/z (rel.intensity) 258 (M^+, 39), 243 (6), 201 (100), 187 (21), 147 (14), 115 (16); HRMS calcd for $C_{17}H_{22}O_2$ 258.1620, found 258.1620.

6-(Ethoxycarbonyl)-4-(2,2-Dimethylpropyl)-α-tetralone (96)



The compound was isolated as a colorless liquid. ^1H NMR ($CDCl_3$, 300MHz) δ 8.04 (d, *J*=8.1Hz, 1H), 7.95 (s, 1H), 7.91 (dd, *J*=8.1, 1.8Hz, 1H), 4.40 (q, *J*=7.2Hz, 2H), 3.13 (m, 1H), 2.85 (ddd, *J*=17.7, 12.4, 5.1Hz, 1H), 2.62 (dt, *J*=17.7, 4.8Hz, 1H), 2.27 (tt, *J*=13.5, 4.5Hz, 1H), 2.19-2.10 (m, 1H), 1.75 (dd, *J*=14.7, 8.1Hz, 1H), 1.53 (dd, *J*=14.7, 3.0Hz, 1H), 1.41 (t, *J*=7.2Hz, 3H), 1.06 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 198.03, 165.91, 150.24, 145.06, 134.58, 129.85, 127.19, 127.00, 61.37, 48.05, 34.70, 34.54, 31.45, 29.91, 28.13, 14.23; EIMS m/z (rel.intensity) 288 (M^+, 35), 243 (14), 232 (14), 218 (74), 217 (100), 177 (18), 115 (24); HRMS calcd for $C_{18}H_{24}O_3$ 288.1725, found 288.1721.

4-(4'-Ethoxycarbonylphenyl)-6,6-dimethylheptanoic acid (97)



The compound was isolated as a colorless liquid. ^{1}H NMR ($CDCl_3$, 300MHz) δ 10.5 (b, 1H), 7.98-7.94 (m, 2H), 7.25-7.22 (m, 2H), 4.36 (q, *J*=7.2Hz, 2H), 2.78-2.69 (m,1H), 2.18-1.72 (m, 5H), 1.56 (dd, *J*=14.1, 3.3Hz, 1H), 1.38 (q, *J*=7.2Hz, 3H), 0.76 (s, 9H); ^{13}C NMR ($CDCl_3$, 75MHz) δ 178.97, 166.59, 151.75, 129.81, 128.52, 127.87, 60.81, 50.42, 41.95, 33.97, 31.92, 31.34, 30.03, 14.33; EIMS m/z (rel.intensity) 306 (M^+, 48), 261 (28), 249 (65), 203 (64), 189 (92), 177 (100), 149 (39), 131 (39), 117 (34), 57 (64); HRMS calcd for $C_{18}H_{26}O_4$ 306.1831, found 306.1827.

GENERAL SUMMARY

α,β-Unsaturated nitriles such as acrylonitrile, fumaronitrile, crotononitrile react with *t*-BuHgX in the presence of KI via a radical chain process. The addition of *t*-BuHgX to the double bonds forms 1:1 adducts (e.g., *t*-$BuCH_2CH(HgI)CN$) in essentially quantitative yields. The reactions are promoted by iodide ion and in the presence of I^- proceed readily in the dark in DMSO for acrylonitrile. Sunlamp irradiation speeds up the reactions. Ammonium iodide leads to the fromation the reductive alkylation products, e.g., *t*-$BuCH_2CH_2CN$, through two routes:1) ionic cleavage of the adduct mercurial; 2) protonation of the adduct radicals followed by transfer of an electron from *t*-$BuHgI_2^-$. RHgI with R=*t*-BuCH2CHCN undergoes comproportionation to give R_2Hg, which upon photolysis gives the dimer R-R. The intermediate *t*-$BuCH_2CH(CN)$• can be trapped with a variety of reagents such as allyl bromide, I_2, NBS, PhSeSePh to form the three-component condensation products.

Photostimulated reactions of *t*-BuHgX with of 1,6-dienes leads to 5-exo radical cyclization to give high yields of the cyclopentylmethylmercury compounds. *Cis* isomers are favored with *cis/trans* ratios ranging from 3 to 6. Diallyl phosphonate and allyl phosphonate demonstrate higher reactivities but the stereoselectivity is lost. With a proton donor present, unsaturated nitriles upon reaction with t-BuHgX/HI undergo 5-exo cyclization to form cyclopentanones. The *t*-BuHgI/HI system provides the radical source, proton, and the ate complex *t*-$BuHgI_2^-$, which are required for protonation and electron transfer in the chain reactions. PTSA and NH_4I are less efficient in protonating iminyl radicals than HI in DMSO. Geminal disubstitution increases the yield of cyclized products. Thus for 3,3-bis(ethoxycarbonyl)-5-hexenenitrile an 80% yield of the cyclized ketone is observed. The 6-exo mode cyclization of unsaturated nitriles is slow. With gem-diester substitution 5-exo cyclization was also achieved for olefinic *S*-phenyl thioesters with *t*-BuHgCl and for olefinic azides with *t*-$BuHgI/NH_4I$.

Benzenes with two electron-withdrawing groups such as -CN, -CHO, and -CO_2Et react with *t*-BuHgX/Dabco to give alkylation products by a radical chain process. 1,3-Disubstituted benzenes are the most reactive owing to resonance stabilization of the intermediate adduct radicals. A steric factor plays an important role in the addition of *t*-Bu• to the benzene rings. For the cyano group, dialkylated products are easily formed. A good radical chain pathway is established in which substituted cyclohexadienyl radical anions transfer an electron to *t*-BuHgX to regenerate *t*-Bu•. Several α-tetralones were made based on this method involving an intramolecular radical cyclization. Acyl radicals formed by $Ar_{1,5}$ cyclization followed by ring opening, are oxidized by *t*-BuHgX to form the acyl cation which can be converted to the acid or amide.

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