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2H-Cyclohepta[b]furan-2-ones: preparation by flash vacuum pyrolysis of aryl propiolates and possible utility in the synthesis of hydroazulenic sesquiterpene lactones

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IOWA STATE UNIVERSITY, PH.D., 1979

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by

Andrew Shu-tsung Lee

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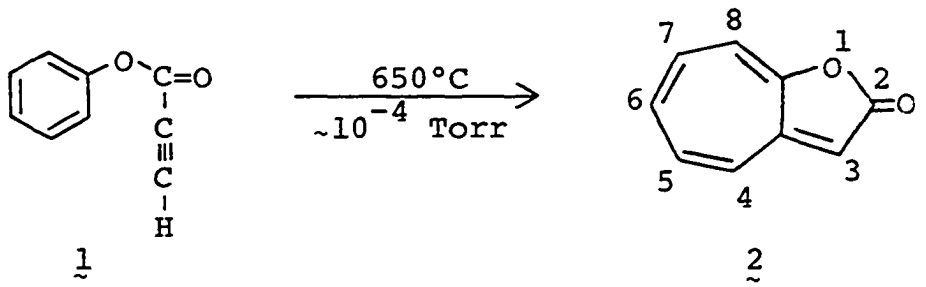
INTRODUCTION

Flash pyrolysis of organic compounds has long been used for generating thermolabile compounds and reactive intermediates. There are basically two different ways that substrates are introduced into the hot zone (1). One method involves the application of a stream of inert gas to carry the substrate into the reactor. In the other method molecular distillation or sublimation is used to introduce the sample. This latter form of pyrolysis is also called flash vacuum pyrolysis (FVP) or very low pressure pyrolysis (VLPP). In most of the FVP studies the starting compounds usually undergo fragmentation reactions which produce smaller molecules; only a small portion of FVP work deals with rearrangements.

This project is concerned with the investigation of the unusual rearrangement observed in the flash vacuum pyrolysis of phenyl propiolate (1) (2) (Eq. 1). The product 2H-cyclohepta[b]furan-2-one and its numbering system is shown in Equation 1.



1 2 (1)

This work also deals with the possibility of incorporating the basic principles of the above pyrolysis reaction in the synthesis of pseudoguaianolides and guaianolides, two important classes of hydroazulenic sesquiterpene lactones.

HISTORICAL

Flash Vacuum Pyrolysis

Pyrolysis reactions (reactions effected by heat alone) were important in the early development of organic chemistry because it was one of the principal ways to obtain new compounds. Now, after a period of obscurity it has resurfaced in the light of the FVP technique (1,3,4,5,6).

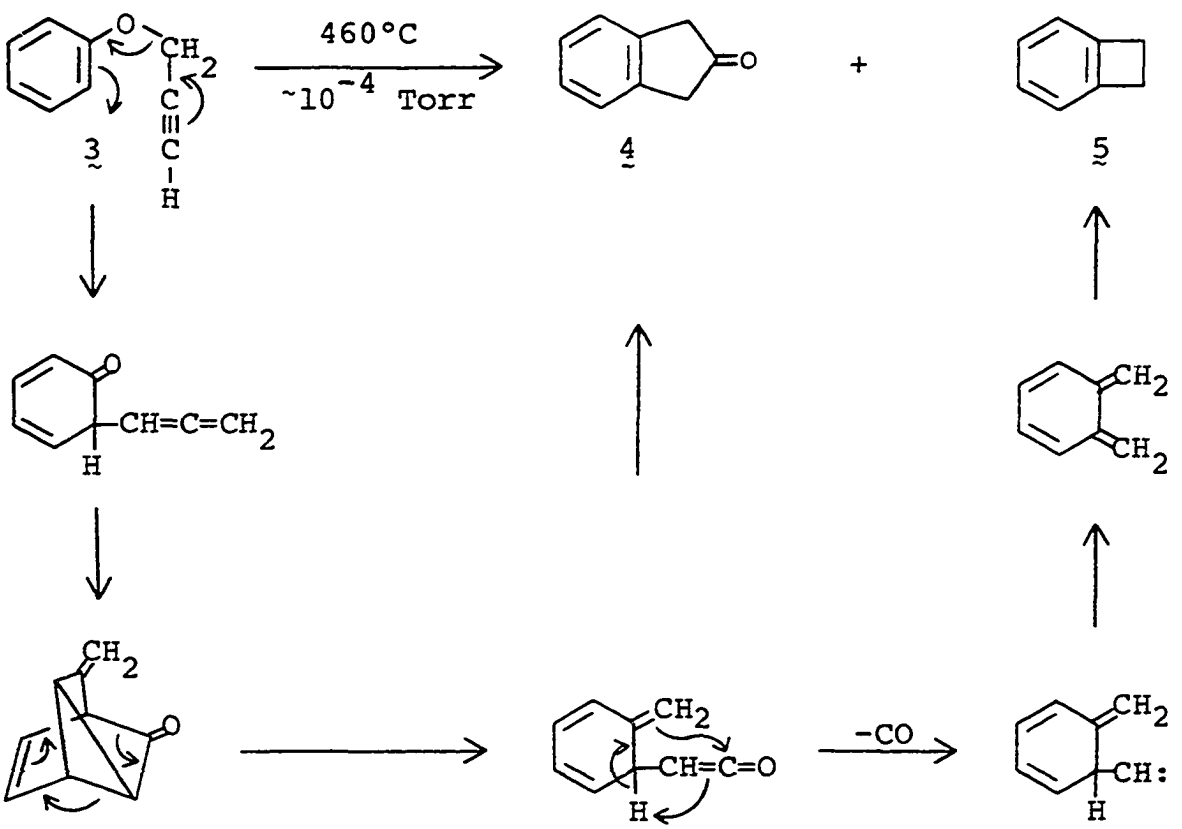
High temperature, short contact time (1-20 ms), low pressure, molecule-wall collisions for excitation, unimolecular reactions, and the absence of secondary reactions are all characteristics of flash vacuum pyrolysis. The technique of FVP has been used to generate very reactive species some of which have still not been prepared by conventional methods.

FVP has been used to eliminate N_2, CO_2, CO, SO_2, and HX from organic substrates. Retro-diene and -ene reactions have also been observed. Cleavage of dimer molecules have been effected and rearrangements of the starting materials have also been studied. However, rearrangement studies constitute a smaller segment of FVP research since conventional pyrolysis techniques are sufficient in many cases.

There are no previous investigations of flash vacuum pyrolysis of aryl propiolates. However in 1972 Trahanovsky and Mullen (7) reported the mechanistic studies of FVP of

phenyl propargyl ether (3). The mechanism they proposed for the formation of the products 2-indanone (4, 26%) and 1,2-dihydrobenzocyclobutene (5, 31%) is depicted in Scheme I.

Scheme I

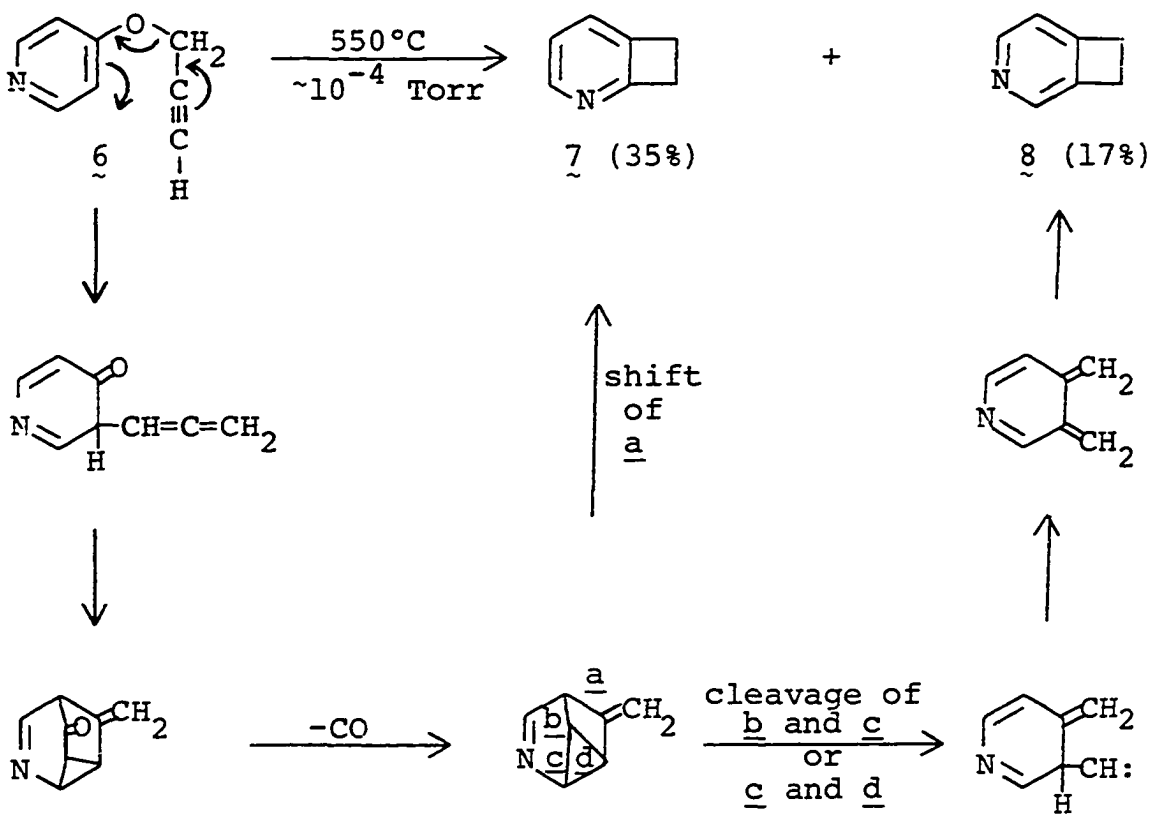


The mechanism for the formation of (4) is supported by the work of Zsindely and Schmid (8), Hansen and Schmid (9), and the deuterium kinetic labelling work performed by Al-Sader and Al-Fekri (10) in 1978.

In 1977 Reimann and Trahanovsky (11) studied the FVP of o-, m-, and p-tolyl propargyl ethers. They found the

results corresponded very well with the mechanism proposed earlier for the FVP of phenyl propargyl ether. Also in 1977 Reimann and Trahanovsky (12) reported the FVP of propargyl 4-pyridyl ether (6). The results and mechanism are shown in Scheme II.

Scheme II

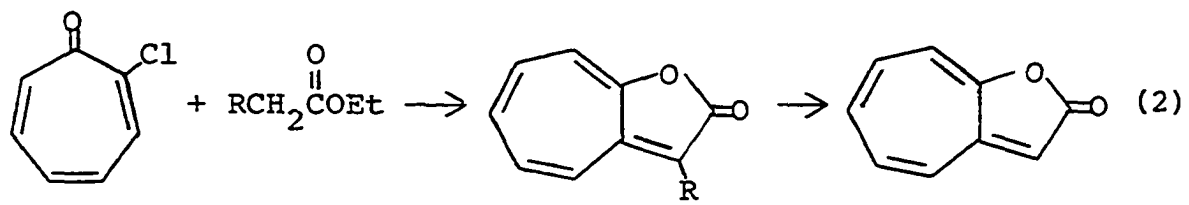


This FVP work prompted the investigation of the pyrolysis of phenyl propiolate and the unexpected product obtained, 2H-cyclohepta[b]furan-2-one (2), stimulated further studies of this pyrolysis reaction.

2H-Cyclohepta[b]furan-2-ones (2CHF's)

2H-Cyclohepta[b]furan-2-one and many of its derivatives have been synthesized since the 1950's. Sasada (13) obtained the X-ray structure of 2 in 1959.

Three basic methods have been reported for obtaining 2 and/or its derivatives. The most widely used route (14,15) involves the conversion of 2-chlorotropone (9) and ethyl acetoacetate (10) or diethyl malonate (11) to 3-acetyl-2H-cyclohepta[b]furan-2-one (12) or 3-carboethoxy-2H-cyclohepta-[b]furan-2-one (13), respectively. Both of these compounds can be hydrolyzed to 2 (Eq. 2).



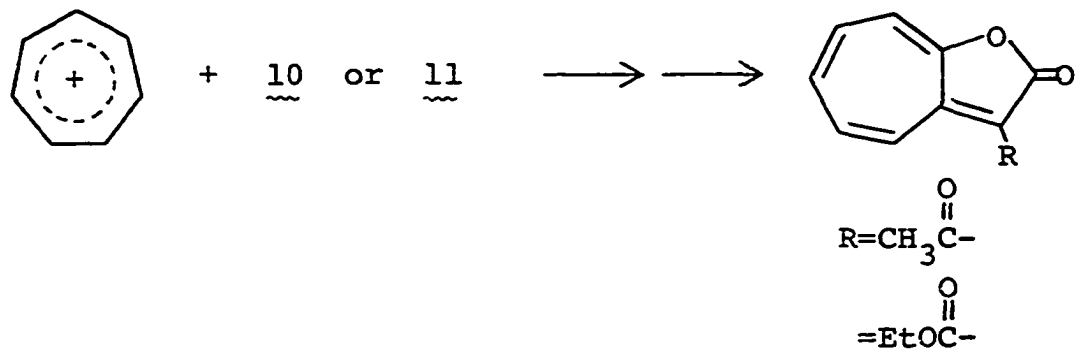
(2)

9 10, R=CH_3CO- 12, R=CH_3CO- 2
11, R-EtOOC- 13, R=EtOOC-

Products with isopropyl (16,17,18), methyl (19,20,21,22), phenyl (23), hydroxy (24,25,26), or combinations of these substituents on the seven-membered ring have been obtained by starting with appropriately substituted tropones (see Table I for some examples).

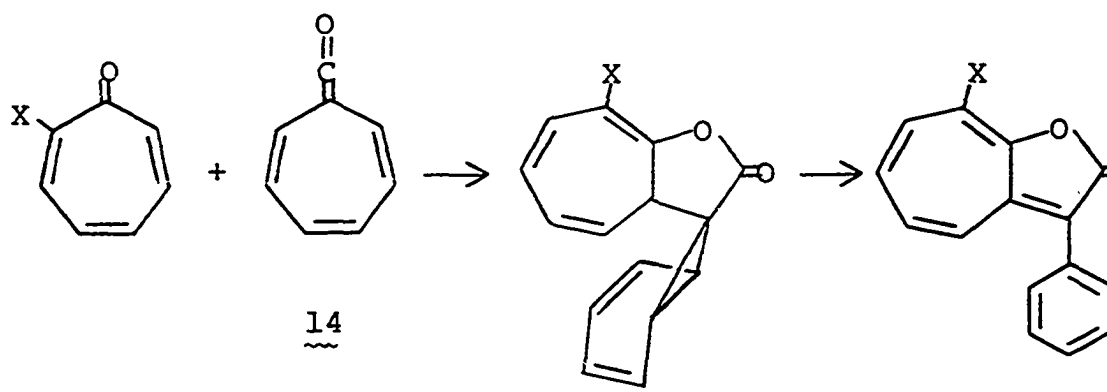
Another method used in the synthesis of 2 involves the reaction of tropylium ion with activated methylene compounds

such as 10 or 11 (27) (Eq. 3). The substituent pattern in the products is dependent on the substituent pattern of the tropylium ion used.



(3)

The third method used to produce these lactone compounds involves the use of [8+2] reactions between tropones and 8-oxoheptafulvene (14) (28,29) (Eq. 4) or ketenes (30) (Eq. 5). This method has its limitations since only compounds with substituents at the 3 position can be synthesized.



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(4)

X=Cl, CH_3, H

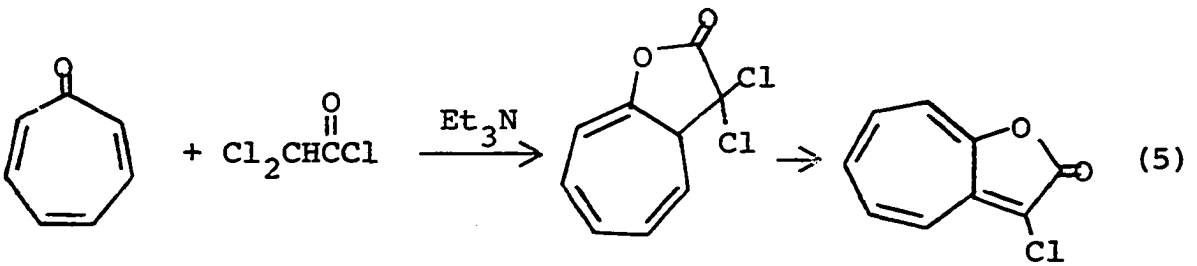
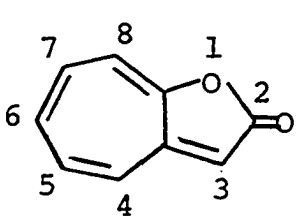


Table I shows some of the known derivatives of 2.

Table I. Examples of previously prepared derivatives of 2H-cyclohepta[b]furan-2-one

Substituents[a]	Reference
7-Methyl-	20
3-Carboethoxy-6-isopropyl-	16
3-Cyano-8-phenyl-	23
7-Methyl-8-acetoxy-	24
3-Tropyl-5-isopropyl-	18
3-Benzoyl-8-hydroxy-	25
3-Phenyl-8-bromo-	31
3,4-(3,6-Cyclohexa-1,4-diene)-	31

[a]The numbering system is shown on the following structure.

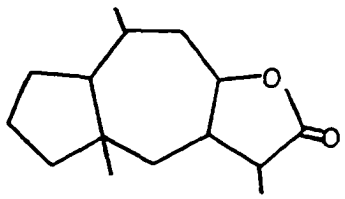


Hydroazulenic Sesquiterpene Lactones

Pseudoguaianolides and guaianolides are two classes of hydroazulenic sesquiterpene lactones (32,33). Many of these compounds have been isolated from plants, chiefly from species of Compositae. It was not until recently that synthesis of these compounds became popular. The impetus for these efforts may have been due to the anti-tumor activities many of these compounds have exhibited (34,35). Besides the anti-tumor activities, pseudoguaianolides and guaianolides have also been demonstrated to inhibit microbial and plant growth, to be useful as chemoprophylaxis in schistosomiases, to cause allergic contact dermatitis in humans, and to cause livestock-poisoning.

However, because of the stereochemical complexities of their structures not many of them have been synthesized. There are no reported total syntheses of a guaianolide. Furthermore, there were no reported total syntheses of a pseudoguaianolide before 1976. Since then, the total syntheses of eight different pseudoguaianolides have been reported.

The difference between the pseudoguaianolides and guaianolides lies in the basic carbon skeleton. The two pseudoguaianolide systems. 15 and 16, have quaternary methyl groups; whereas, the two guaianolide systems, 17 and 18, have no quarternary methyl groups.



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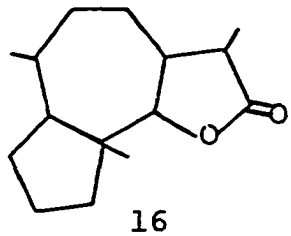

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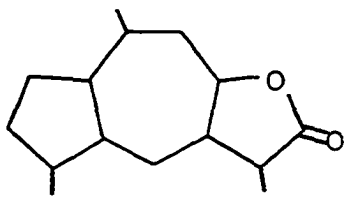

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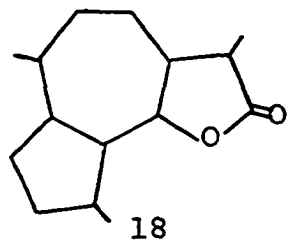

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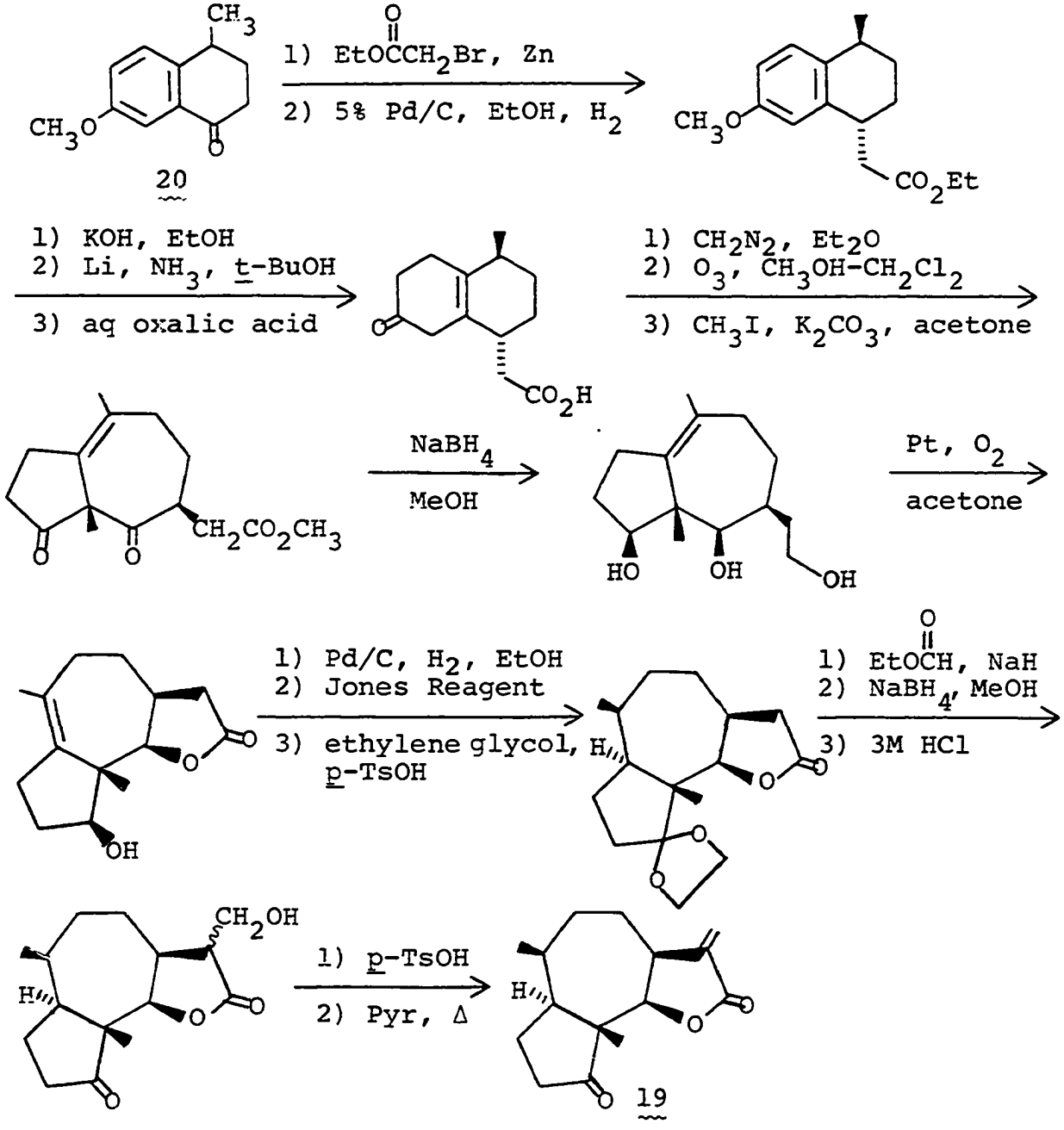
Table II lists the pseudoguaianolides that have been synthesized thus far.

Table II. Reported total syntheses of pseudoguaianolides

Pseudoguaianolide	Structure Number	Principal Researcher	Reference
(±)-Damsin	19	Kretchmer Vandewalle Grieco	36 37 38
(±)-Confertin	23	Marshall Semmelhack Wender	39 40 41
(±)-Ambrosin	26	Grieco	38
(±)-Helenalin	27	Grieco	42
(±)-Stramonin-B	28	Grieco	43
(±)-Neoambrosin	30	Vandewalle	44
(±)-Parthenin	31	Vandewalle	44
(±)-Hymenin	32	Vandewalle	44

Damsin (19) was the first pseudoguaianolide to be synthesized. In 1976 Kretchmer and Thompson (36) synthesized (±)-damsin from 4-methyl-7-methoxytetralone (20) (Scheme III).

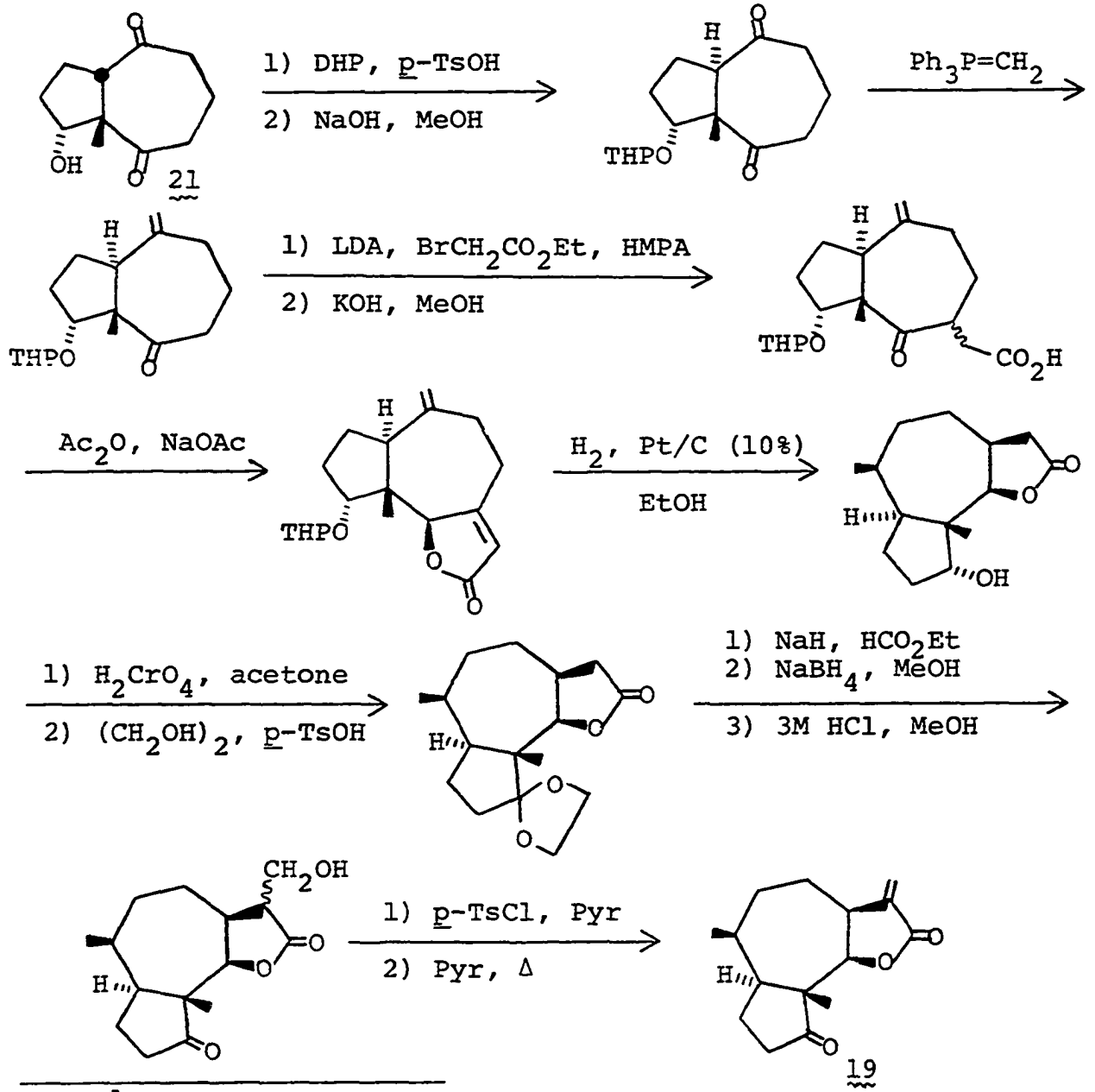
Scheme III[1]



[1]In reactions where isomers were formed, only the desired isomer is shown.

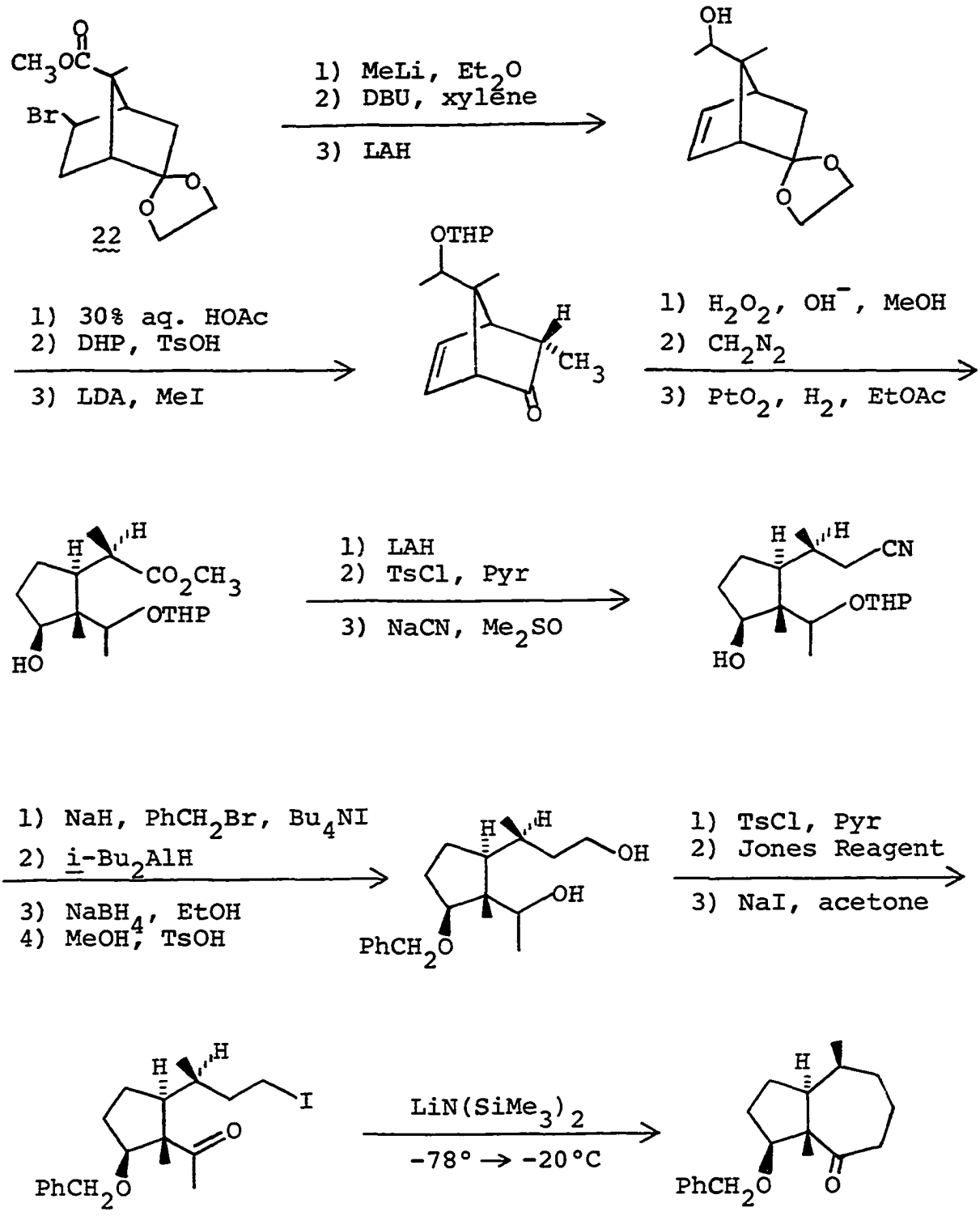
In 1977 De Clercq and Vandewalle (37) and Grieco and co-workers (38) both came out with their syntheses of (±)-damsin. Vandewalle performed the feat with starting synthon 21 (Scheme IV); whereas, Greico started with 22 (Scheme V).

Scheme IV[1]

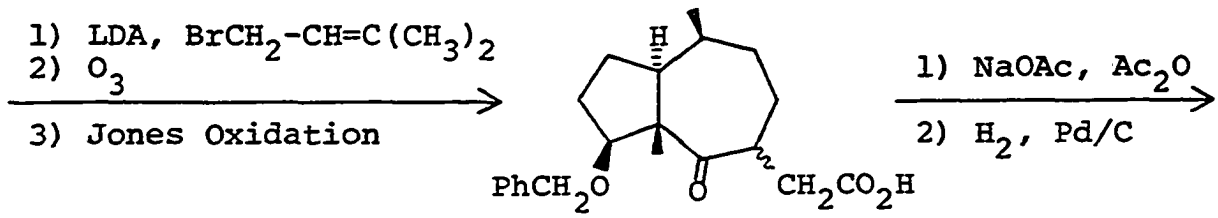


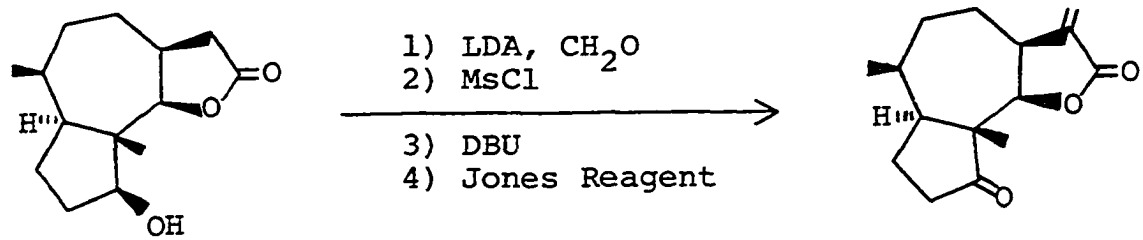
[1]In reactions where isomers were formed, only the desired isomer is shown.

Scheme V[1]



[1]In reactions where isomers were formed, only the desired isomer is shown.

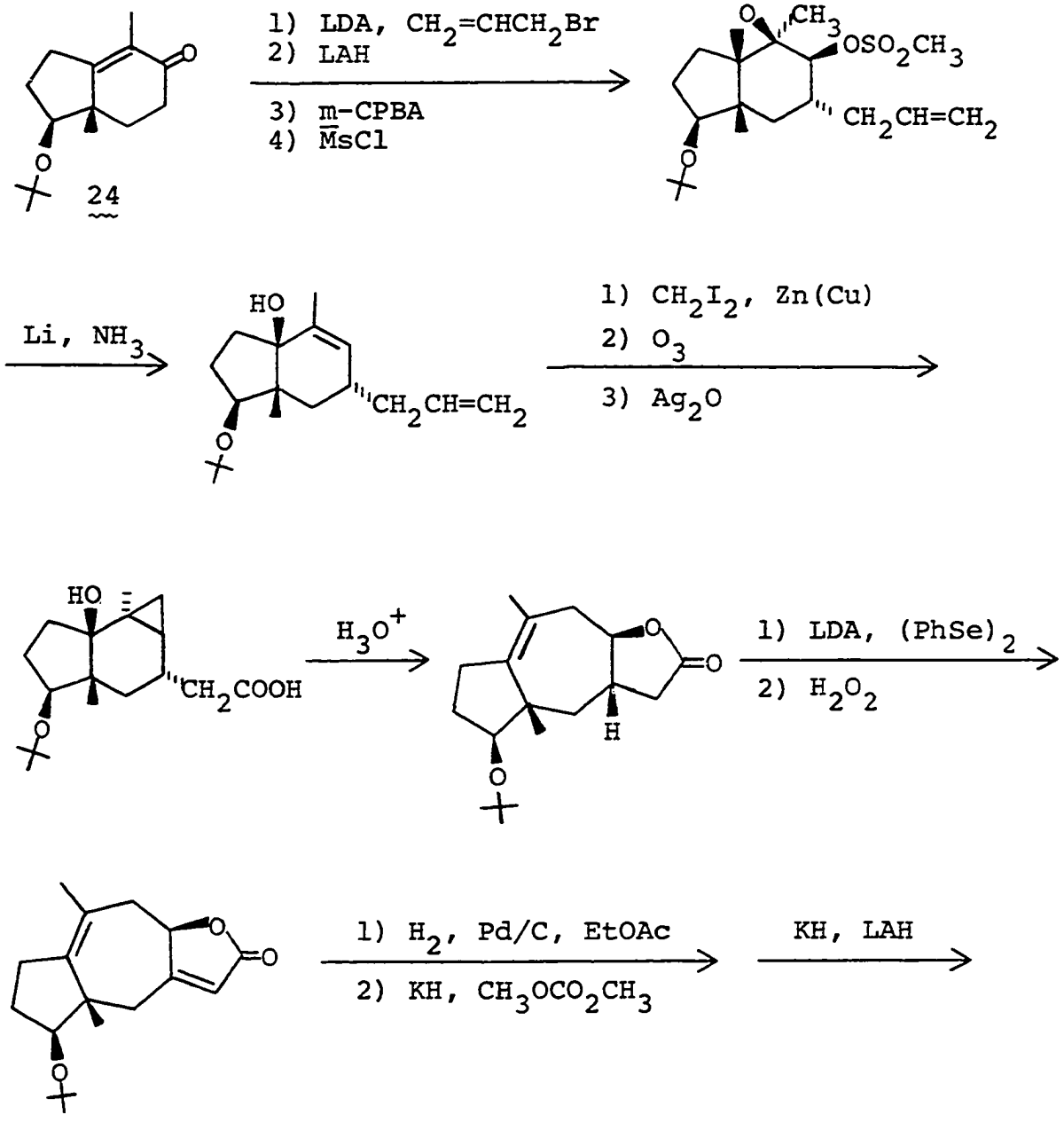

1) LDA, BrCH2-CH=C(CH3)2
2) O3
3) Jones Oxidation
H
PhCH2O
O
CH2CO2H
1) NaOAc, Ac2O
2) H2, Pd/C


H
O
O
OH
1) LDA, CH2O
2) MsCl
3) DBU
4) Jones Reagent
H
O
O
O

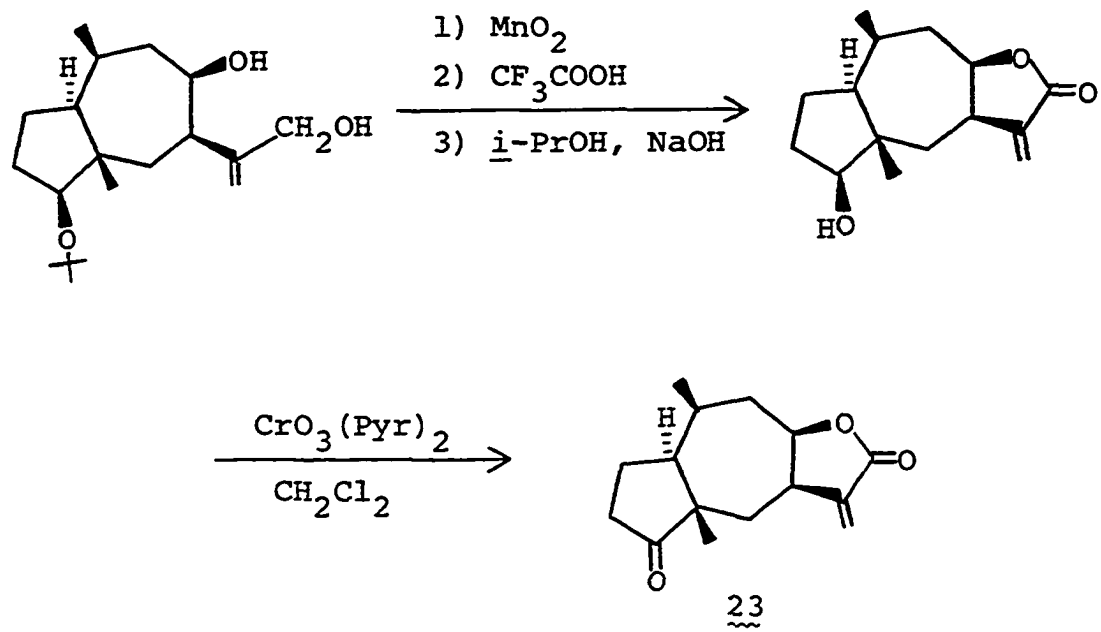
19

Confertin (23) was the second pseudoguaianolide to be synthesized. In 1976 Marshall and Ellison (39) synthesized it via ring expansion of 24 (Scheme VI).

Scheme VI[1]



[1]In reactions where isomers were formed, only the desired isomer is shown.

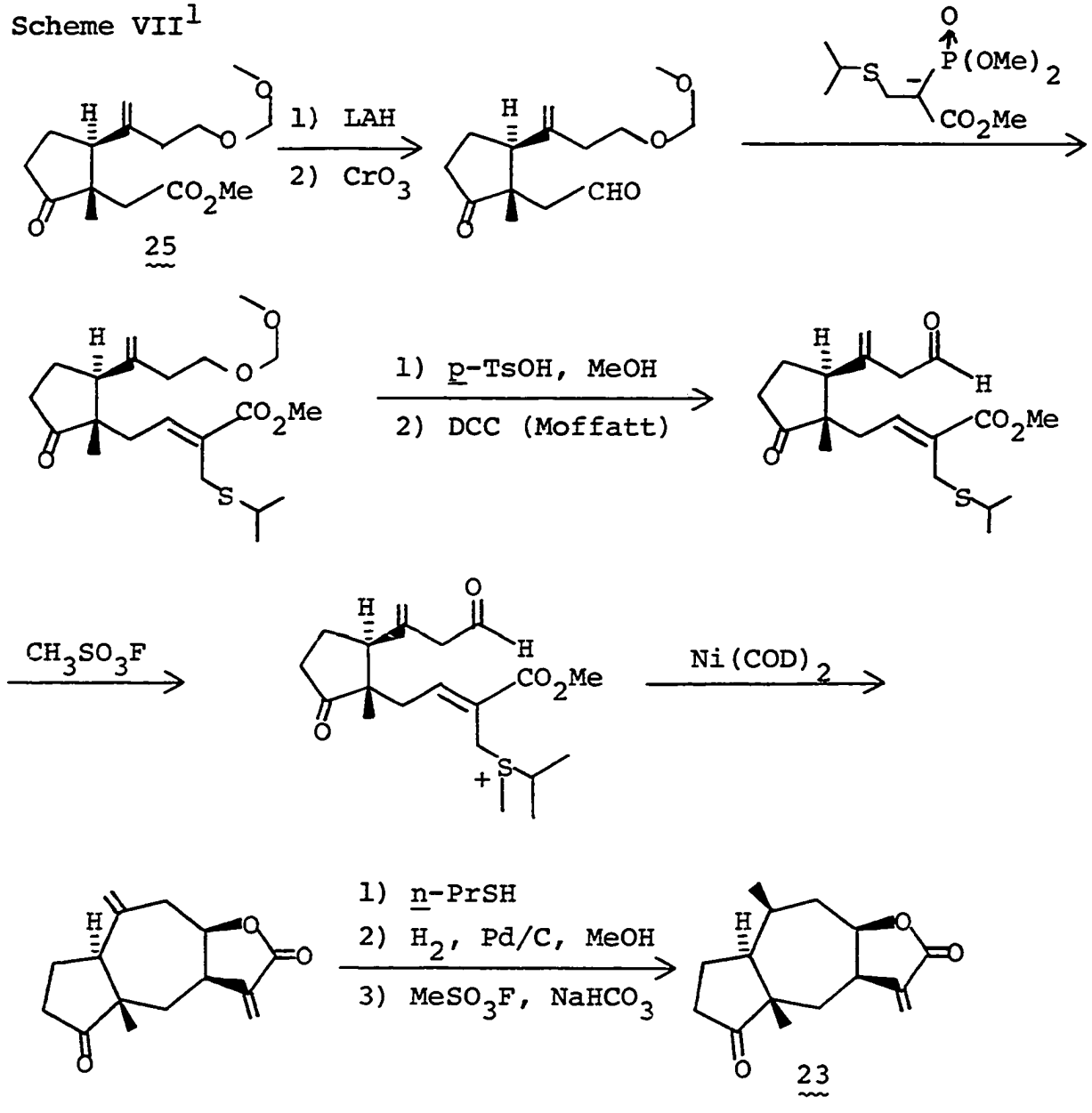

1) MnO_2
2) CF_3COOH
3) i-PrOH, NaOH
OH
CH_2OH
H
O
HO
O
O

$CrO_3(Pyr)_2$
CH_2Cl_2
H
O
O
O

23

In 1978 Semmelhack and co-workers (40) started with cyclopentanone derivative 25 and utilized nickel bis-cyclooctadiene, $Ni(COD)_2$, to promote the cyclization and lactonization to attain (±)-confertin (Scheme VII).

Scheme VII[1]



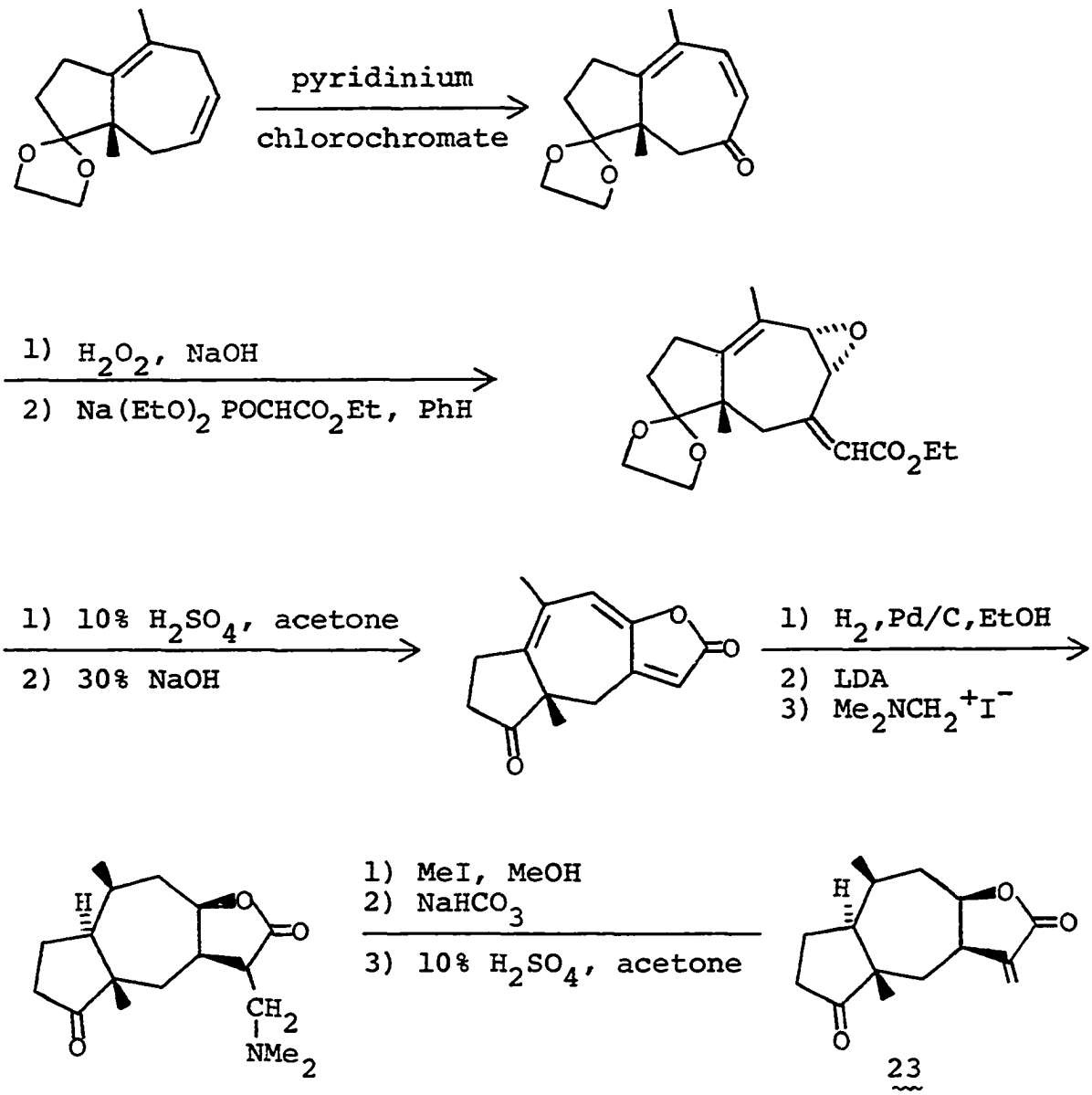
25

23

[1]In reactions where isomers were formed, only the desired isomer is shown.

In 1979 Wender and co-workers (41) synthesized (±)-confertin (Scheme VIII).

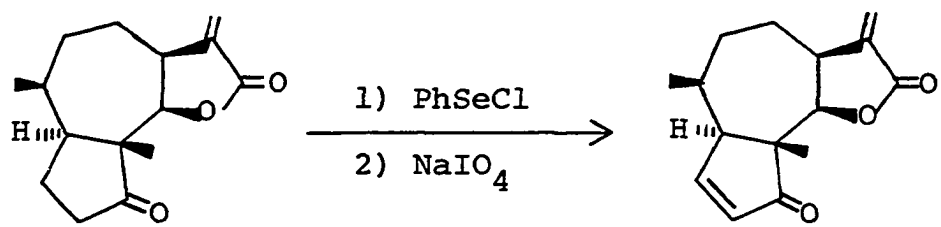
Scheme VIII[1]



23

[1]In reactions where isomers were formed, only the desired isomer is shown.

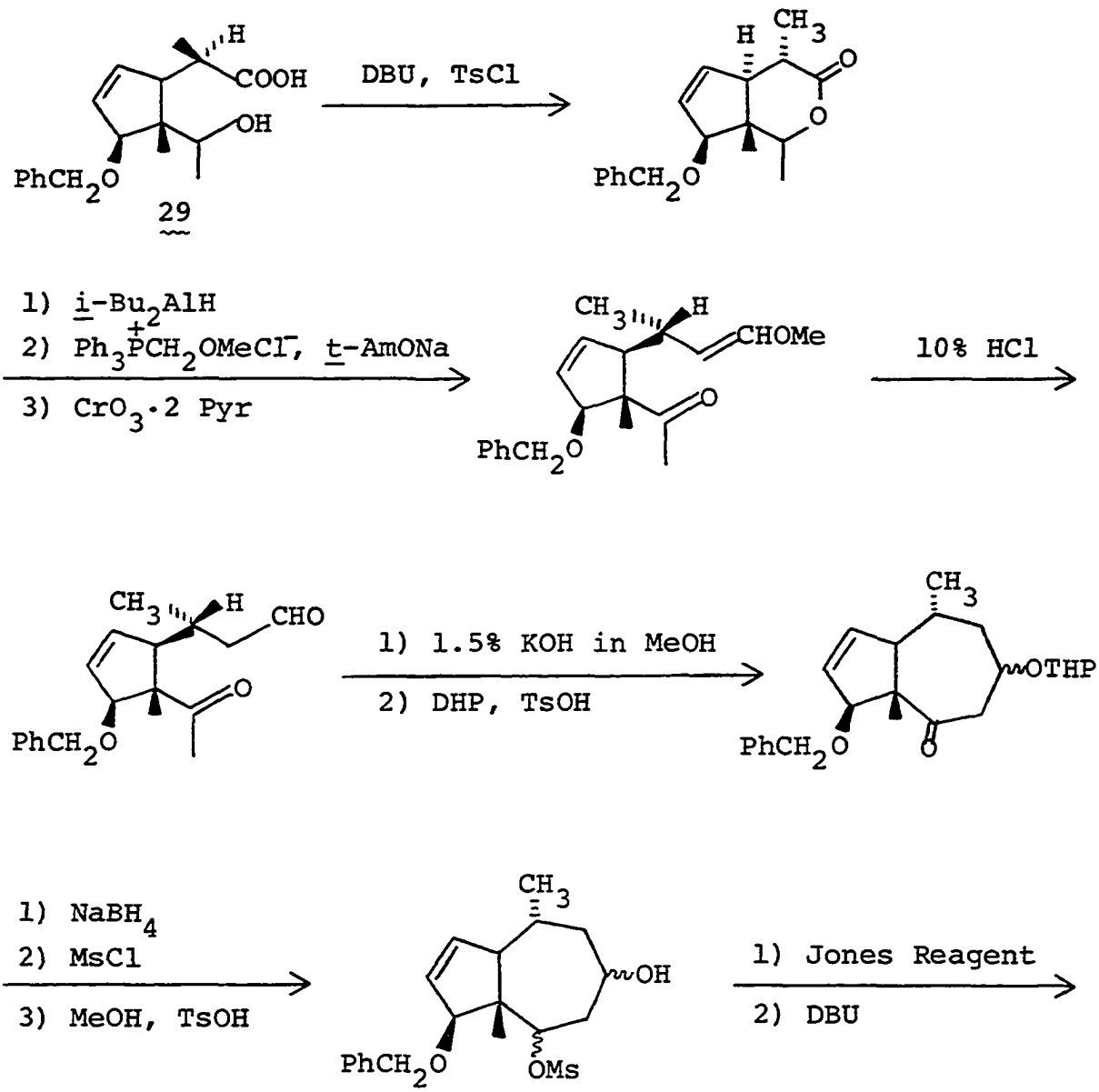
Grieco and co-workers (38,42,43) synthesized (±)-ambrosin (26) (Eq. 6) in 1977, (±)-helenalin (27) (Scheme IX), and (±)-stramonin-B (28) (Scheme X) both in 1978.



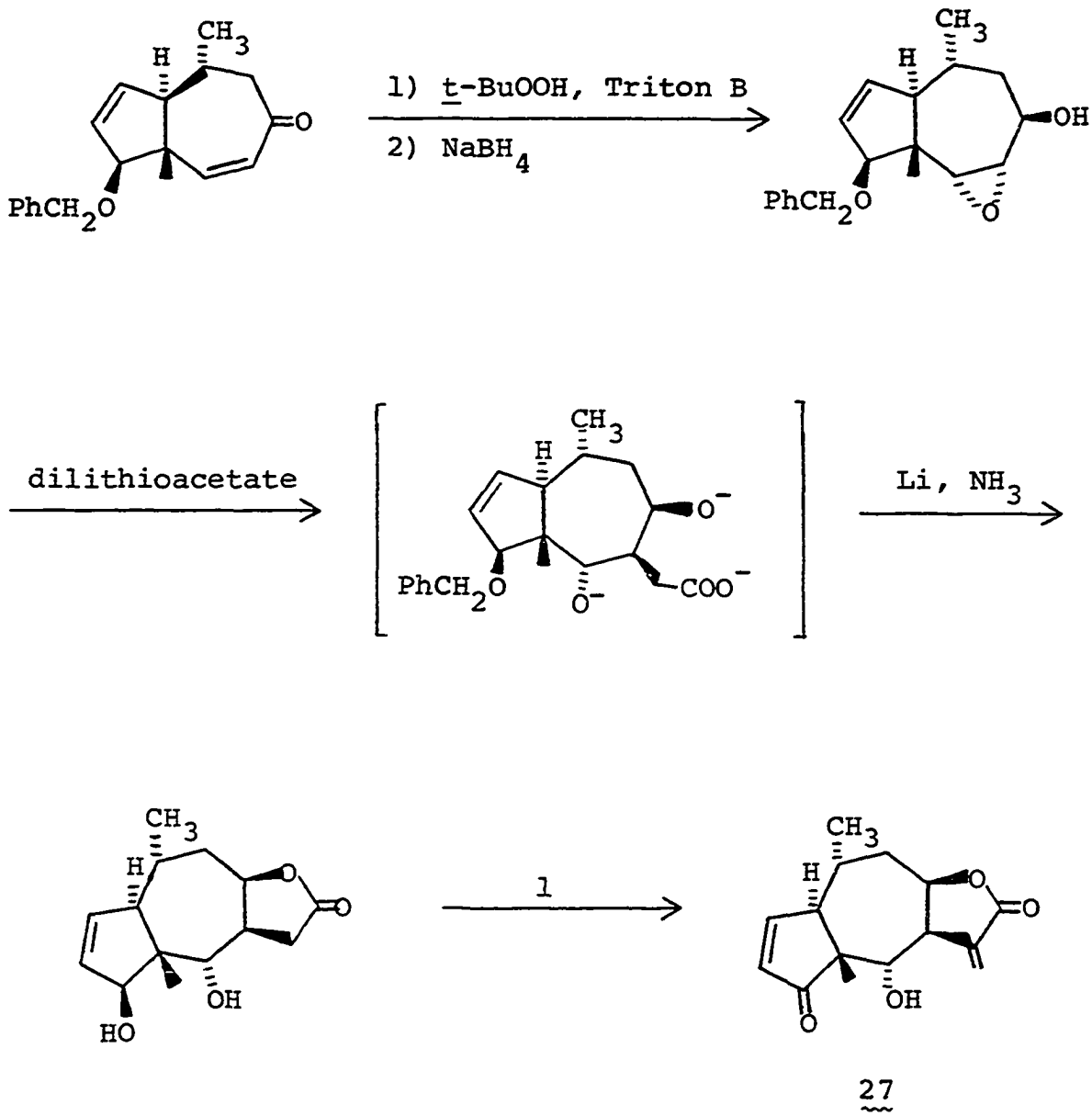
(6)

19 26

Scheme IX[1]



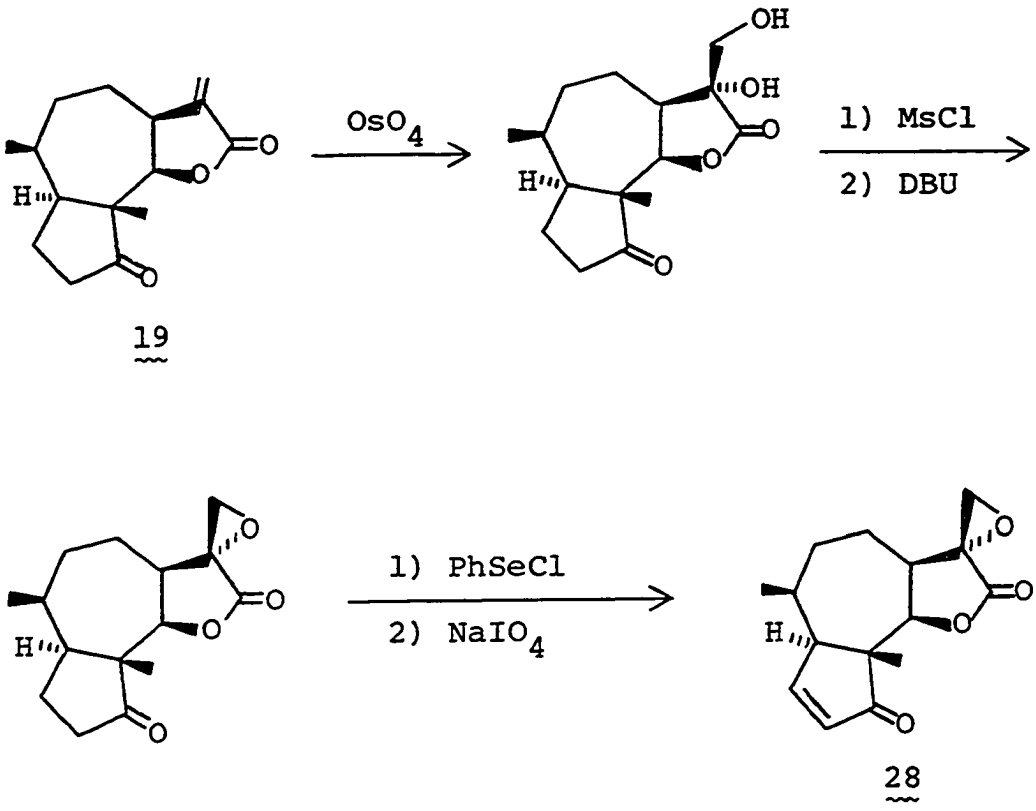
[1]In reactions where isomers were formed, only the desired isomer is shown.



27

[1] See Scheme V.

Scheme X

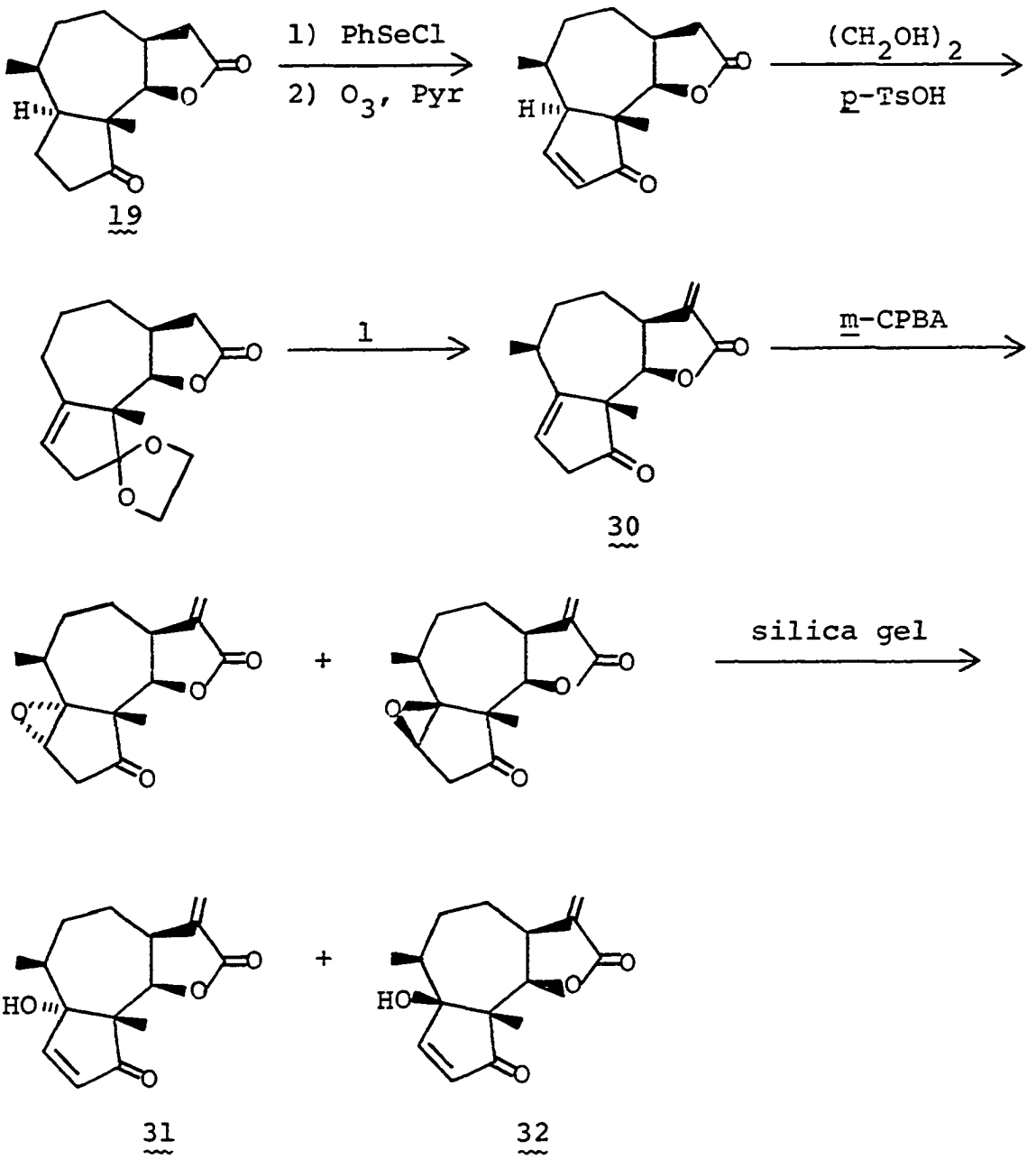


19

28

Recently, Kok and co-workers (44) synthesized (Scheme XI) (±)-neoambrosin (30), (±)-parthenin (31), and (±)-hymenin (32).

Scheme XI



[1]See Scheme IV.

Although the biological activites of confertin, neoambrosin, and hymenin have not been reported, ambrosin (35), damsin (34), parthenin (45), and stramonin-B (43) have all been demonstrated to be active against KB cells (cells from human carcinoma of the nasopharynx). Some of these compounds have also shown inhibitory activities against other tumor cells (46) and other biological activities.

RESULTS

With the discovery that FVP of phenyl propiolate produced 2H-cyclohepta[b]furan-2-one (1), a series of aryl propiolates was synthesized by Miller's general method (47) and then was pyrolyzed. Table III summarizes the results of the esterification of propiolyl chloride and the various phenol derivatives. Tables IV, V, and VII show the results of the pyrolyses of these aryl propiolates.

A schematic diagram of the pyrolysis apparatus (Figure 1) shows the main features of the apparatus. Most of the FVP work was done at ~650°C and at ~10^{-4} Torr with the hot zone packed with quartz chips; however, in some cases pyrolysis studies were performed at different temperatures and without packing. The products obtained varied from yellowish to reddish in appearance. Ironically, they are all thermally unstable at their melting points. In all cases the 2H-cyclohepta[b]furan-2-ones (2 CHF's) were deposited at region A (Figure 1); by-products were collected in the liquid nitrogen trap, region C.

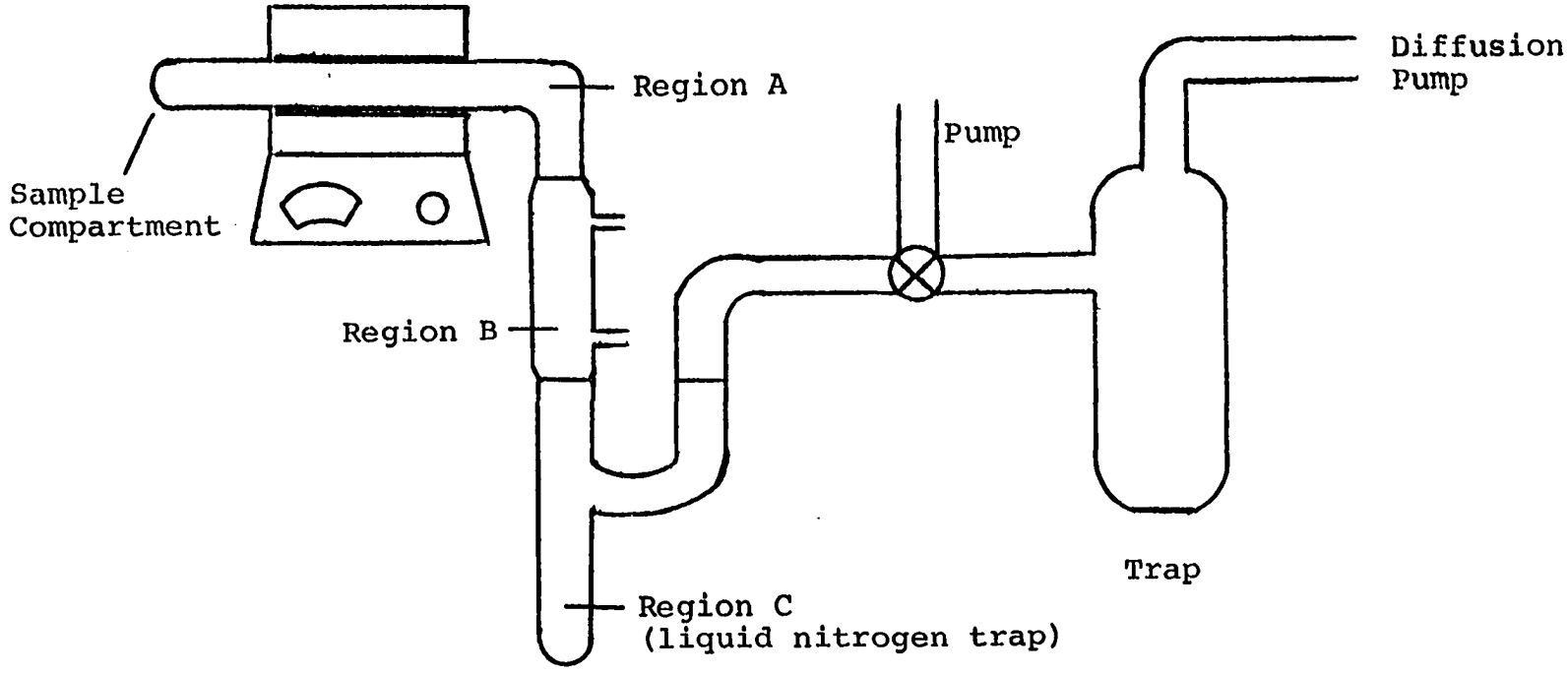
The products were identified mainly from their ^{1}H nuclear magnetic resonance (nmr), infrared (ir), and in a few cases ^{13}C nmr spectra. The hydrogen alpha to the lactone carbonyl served as the key ^{1}H nmr reference signal because of its unique chemical shift between δ6 and δ5. This signal served

Table III. Synthesis of aryl propiolates

Propiolate	Structure Number	Yield[a] (%)
Phenyl	1	69
2,6-Dimethylphenyl	33	29
2,4,6-Trimethylphenyl	34	34
o-Methylphenyl	35	53
o-Chlorophenyl	36	86
o-Bromophenyl	37	90
o-Isopropylphenyl	38	82
2,4-Dichlorophenyl	39	68
p-Chlorophenyl	40	94
p-Bromophenyl	41	60
p-Formylphenyl	42	38
p-Hydroxyphenyl	43	6
p-Acetoxyphenyl	44	42
p-Methoxyphenyl	45	61
5-Indanyl	46	45
4-Indanyl	47	87
5-(6-Chloroindanyl)	48	70
7-(1-Oxoindanyl)	49	73
7-(1-Oxo-4-methylindanyl)	50	41
6-(1-Oxoindanyl)	51	64
6-(1-Oxo-5-chloroindanyl)	52	37
6-(1-Oxo-4-methylindanyl)	53	56

[a]Based on the reaction between the phenol derivative and propiolyl chloride.

Figure 1. Diagram of the pyrolysis apparatus

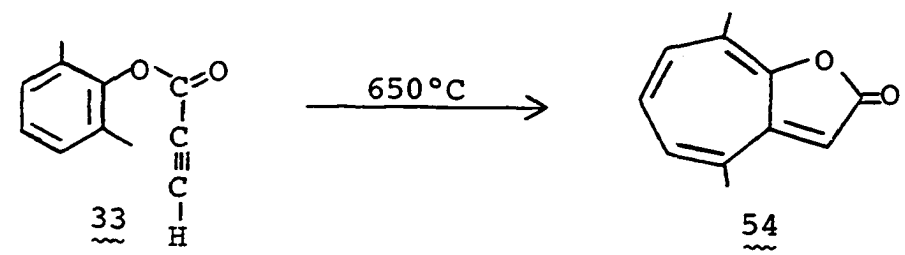

Region A
Sample
Compartment
Region B
Pump
Diffusion
Pump
Trap
Region C
(liquid nitrogen trap)

to indicate the presence of isomeric mixture of 2CHF's (Figures 2 and 3).

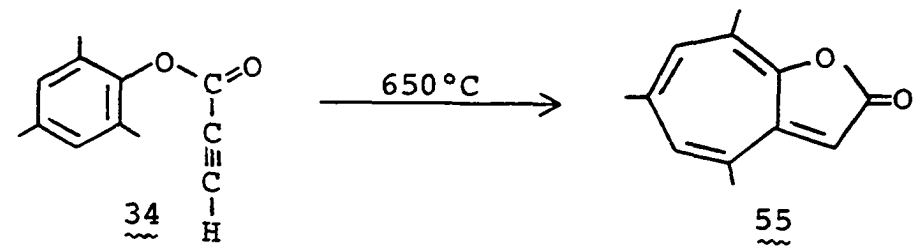
Pyrolysis of Symmetrical Aryl Propiolates

Table IV summarizes the results of the pyrolyses of the symmetrical propiolates. The FVP of all the propiolates in Table IV, except for p-hydroxyphenyl (43), p-acetoxyphenyl (44), and p-methoxyphenyl (45) propiolates, behaved as anticipated and yielded the corresponding 2CHF's. Pyrolysis of 43 yielded hydroquinone which was collected in the liquid nitrogen trap. The products from the FVP of 44 and 45 were found in the liquid nitrogen trap and were not identified. Varying the temperature of pyrolysis from 540°C to 700°C for 45 did not produce any corresponding 2CHF.

FVP of 33 and 34 produced products that were identified as 4,8-dimethyl-2H-cyclohepta[b]furan-2-one (54) and 4,6,8-trimethyl-2H-cyclohepta[b]furan-2-one (55), respectively (Eqs. 7 and 8). The positions of the methyl groups in



(7)



(8)

Figure 2. A-60 nmr spectrum of 2H-cyclohepta[b]furan-2-one in chloroform-d

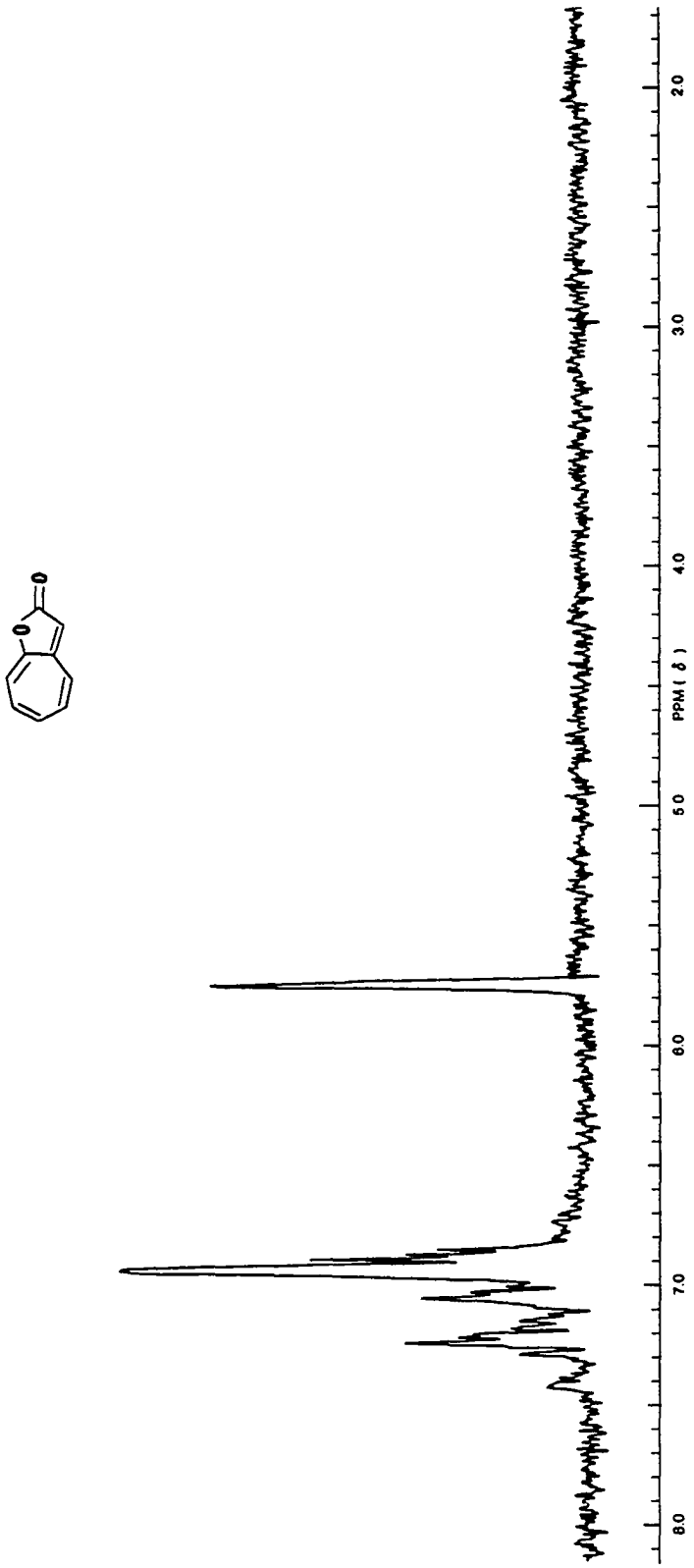

8.0
7.0
6.0
5.0
PPM (δ)
4.0
3.0
2.0

Figure 3. A-60 nmr spectra of 8-methyl-2H-cyclohepta[b]-furan-2-one (59) and 4-methyl-2H-cyclohepta[b]-furan-2-one (60) in chloroform-d

Top: Spectrum of a mixture of 59 and 60

Middle: Spectrum of 59

Bottom: Spectrum of 60

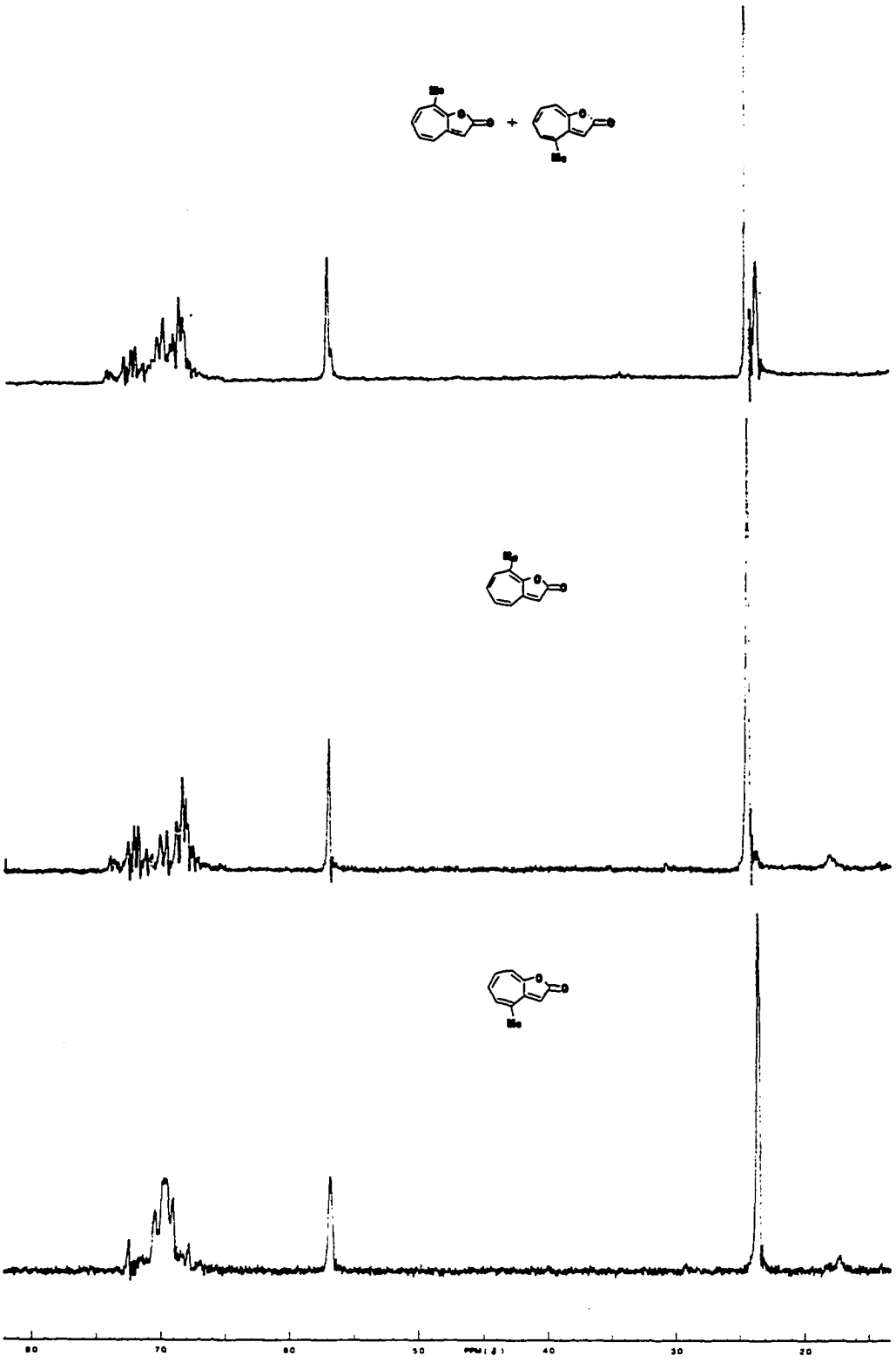

80
70
60
50
40
30
20

Table IV. Pyrolysis of symmetrical aryl propiolates

Propiolate	Pyrolysis Temp[a] (°C)	2H-Cyclohepta[b]furan-2-one	Structure Number	Yield[b] (%)
33	650	4,8-Dimethyl-	54	45
34	650	4,6,8-Trimethyl-	55	44
40	650	6-Chloro-	56	55
41	650	6-Bromo-	57	59
42	650	6-Formyl-	58	31
43[c]	650	--		
44[d]	650	--		
45[d,e]	660	--		

[a]The hot zone was packed with quartz chips.

[b]The remaining materials were in the forms of charred materials in the hot zone and by-products in the liquid nitrogen trap.

[c]Hydroquinone recovered in the liquid nitrogen trap, no products deposited in region A (Figure 1).

[d]No identifiable product deposited in region A (Figure 1).

[e]Pyrolysis was also carried out at 540°C, 600°C, and 700°C with similar results.

54 and 55 were established using the ^{13}C nmr coupling data of the methyl groups (Figures 4 and 5). The results suggested that no scrambling of the phenyl ring carbons occurred during the rearrangement. This hypothesis has held after considerably more work on the FVP of the aryl propiolate system.

The nmr spectra of 6-chloro- (56), 6-bromo- (57), and 6-formyl- (58) 2H-cyclohepta[b]furan-2-ones revealed an interesting fact about these lactone systems. The hydrogens at positions 3 and 8 are coupled (J=2 Hz) through the coplanar "w" coupling mode (48). In 56, 57, and 58 irradiating the hydrogen at position 3 caused the splitting pattern of the hydrogen at position 8 to collapse from a doublet of doublets to a doublet (Figures 6 and 7). Although the coplanar "w" coupling is very prominent in 56, 57, and 58, in other compounds this coupling is not as sharply defined. This coupling proved to be very useful in structure elucidation in later work.

Pyrolysis of Unsymmetrical Propiolates

Table V summarizes the results of the FVP of some of the unsymmetrical propiolates. In each case two isomers were formed as expected although at different ratios. Due to the similarities in their spectral data, conclusive identification of the major and minor isomers could not be made based on their spectral data alone.

Figure 4. HX-90 ^{13}C nmr spectra of 4,8-dimethyl-2H-cyclohepta[b]furan-2-one (54) in chloroform-d

Top: Broad band decoupled spectrum of 54

Middle: Gated decoupled spectrum of 54

Bottom: Gated decoupled spectrum of the methyl groups of 54

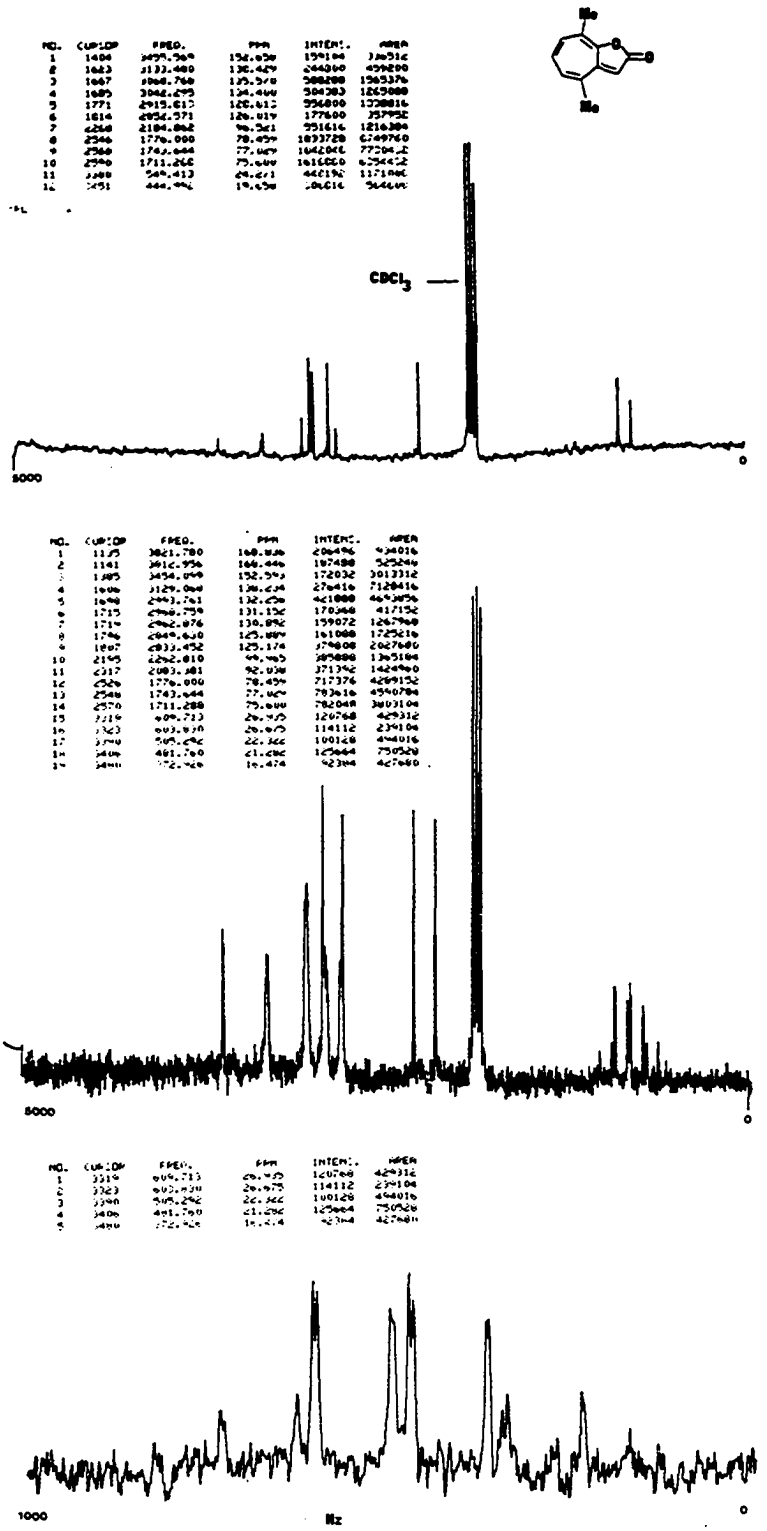

Me
O
O
Me
CDCl3
5000
0
5000
0
1000
Hz
0

Figure 5. HX-90 ^{13}C nmr spectra of 4,6,8-trimethyl-2H-cyclohepta[b]furan-2-one (55) in chloroform-d

Top: Broad band decoupled spectrum of 55

Middle: Gated decoupled spectrum of 55

Bottom: Gated decoupled spectrum of the methyl groups of 55

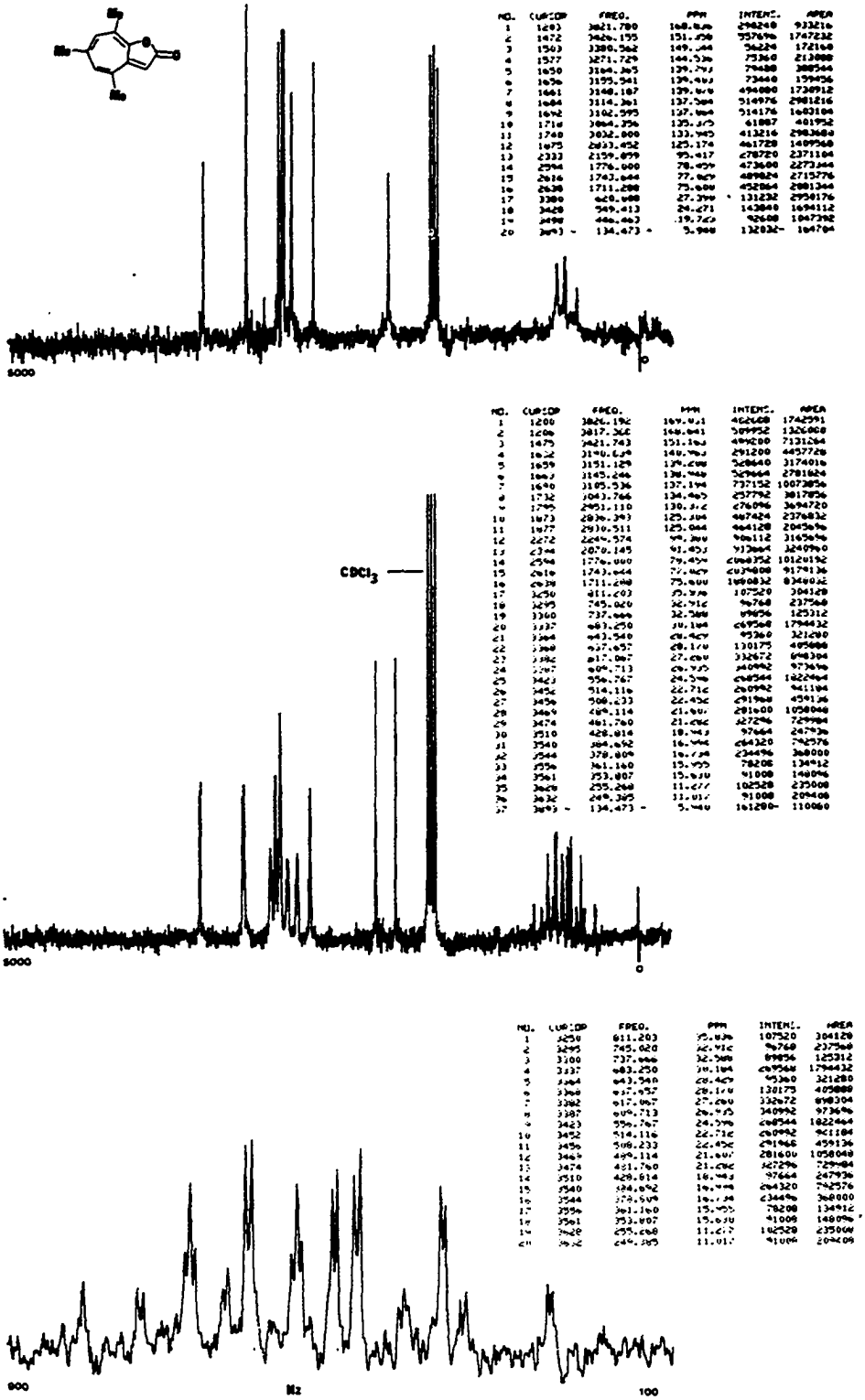

CDCl3
5000
0
900
100

Figure 6. HA-100 nmr spectra of 6-bromo-2H-cyclohepta[b]-furan-2-one (57) in chloroform-d

Top: Spectrum of 57

Second: Spectrum of 57 with the signal at δ5.83 decoupled

Third: Spectrum of 57 with the signal at δ6.64 decoupled

Bottom: Spectrum of 57 with the signal at δ6.64 decoupled

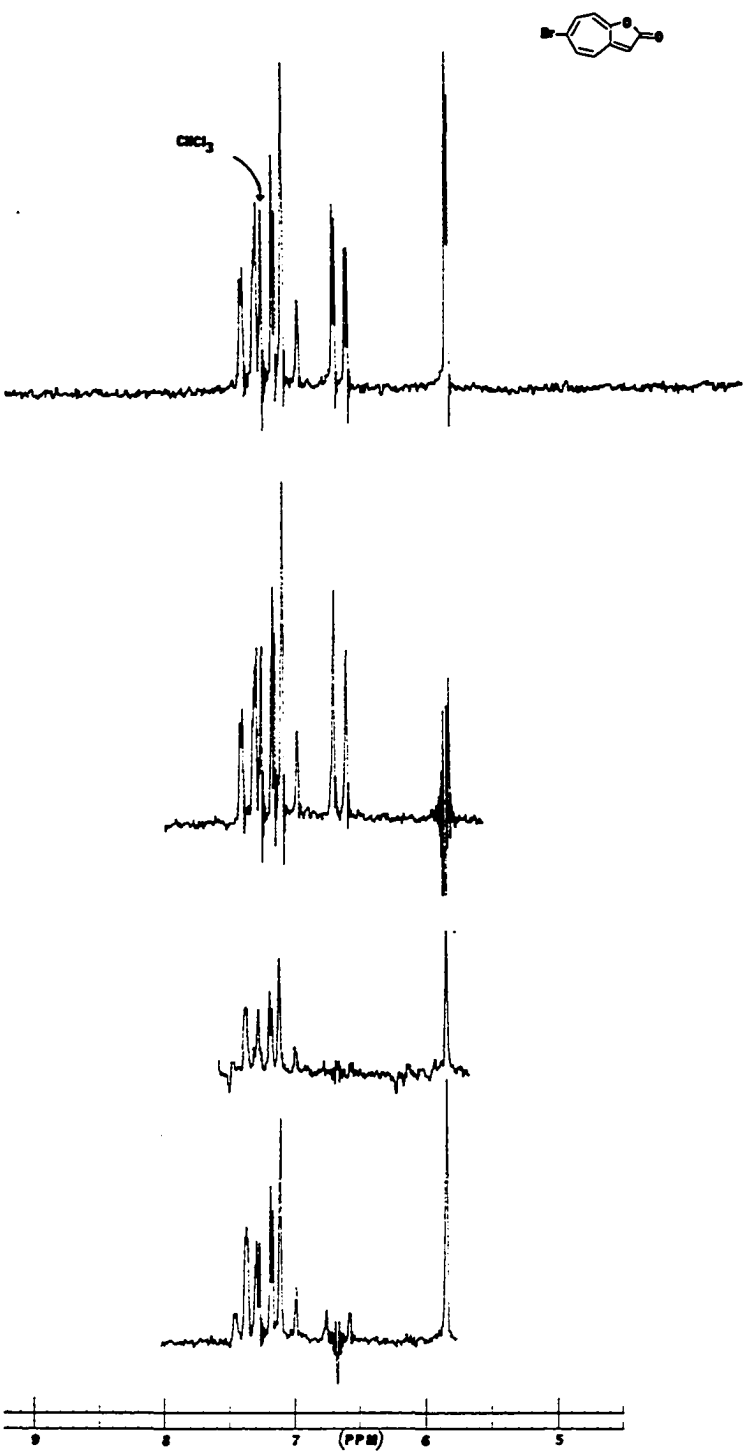

CHCl3
9
8
7
(PPM)
6
5

Figure 7. HA-100 nmr spectra of 6-formyl-2H-cyclohepta[b]-furan-2-one (58) in chloroform-d

Top: Spectrum of 58

Middle: Spectrum of 58 with the signal at δ5.99 decoupled

Bottom: Spectrum of 58 with the signal at δ7.05 decoupled

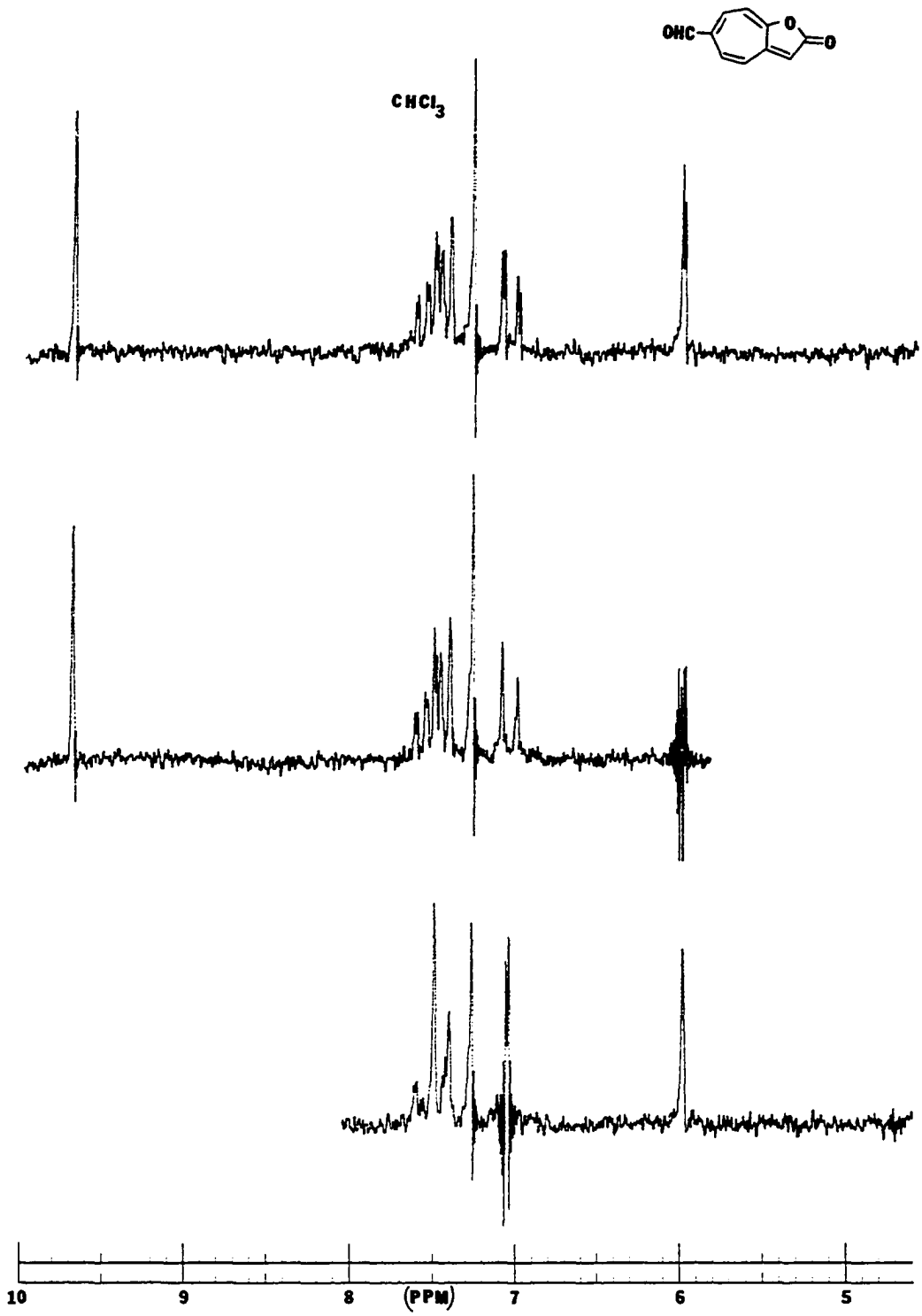

OHC
O
O
CHCl3
10
9
8
(PPM)
7
6
5

Table V. Pyrolysis of unsymmetrical aryl propiolates

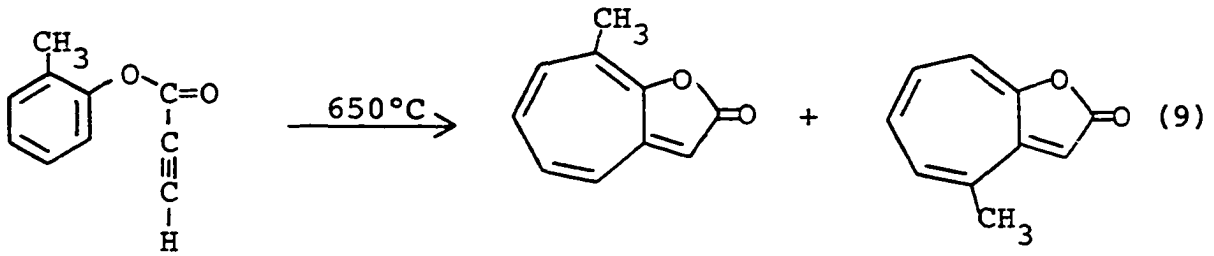
Propiolate	Pyrolysis Temp[a] (°C)	2CHF[b]	Structure Number	Yield (%)	2CHF	Structure Number	Yield (%)
35	650	8-Methyl-	59	44	4-Methyl	60	11
36	650	8-Chloro-	61	35	4-Chloro-	62	7
37[c]	650	8-Bromo-	63		4-Bromo-	64	
38	660	8-Isopropyl-	65	24	4-Isopropyl-	66	10
39	650	6,8-Dichloro-	67	30	4,6-Dichloro-	68	4

[a]Hot zone was packed with quartz chips.

[b]2CHF≡2H-Cyclohepta[b]furan-2-one.

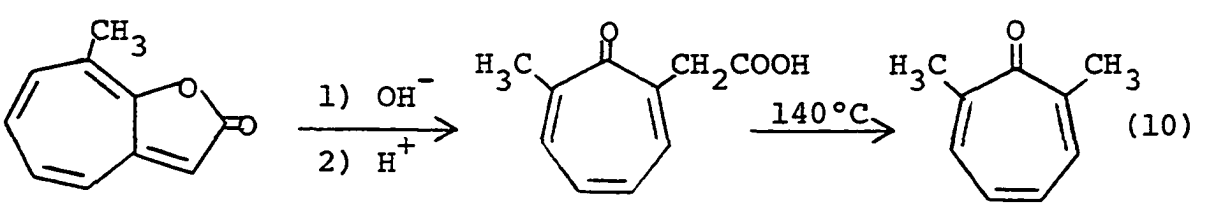
[c]Results were not reproducible.

Assignments of the isomeric products from the first unsymmetrical propiolate to be pyrolyzed, o-methylphenyl propiolate (35), were made after chemical degradation of each isomeric product (Eq. 9). The isomers were separated by a

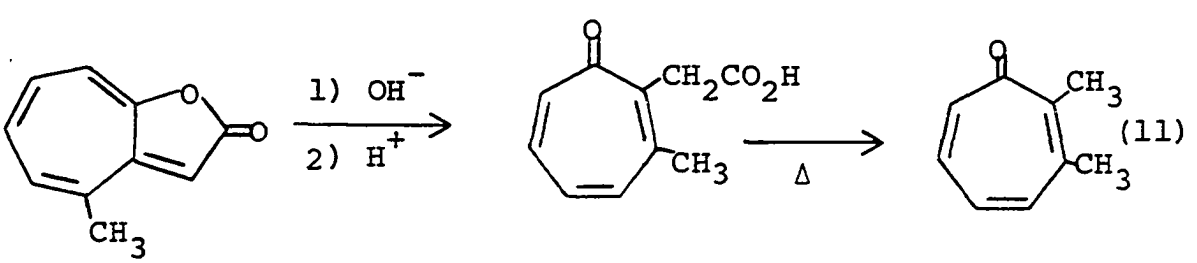


35 59 60

combination of column chromatography and fractional recrystallization. Then they were hydrolyzed to their corresponding troponylacetic acids; next, the acids were decarboxylated to their corresponding tropones. The tropones were then identified (Eqs. 10 and 11). The results indicated that the major



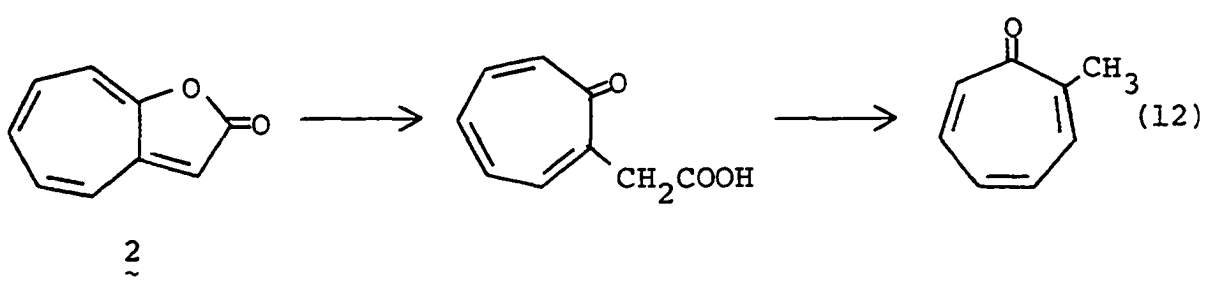
59



60

isomer is 59. The results also indicated that in the nmr spectrum the chemical shift of the hydrogen at position 4, δ7.25, is significantly lower than the rest of the ring hydrogens. The rest of the ring hydrogens have similar chemical shift, δ7.0 (Figure 3). These observed chemical shift differences were found to be valid only for compounds with alkyl substituents; substituents containing heteroatoms seemed to destroy the validity of these observations. These results plus the coplanar "w" coupling data were applied with discretion to identify the major and minor isomers from the pyrolyses of the ortho-substituted aryl propiolates. The findings indicated that the isomers with the substituent at position 8 is the major isomer in every case.

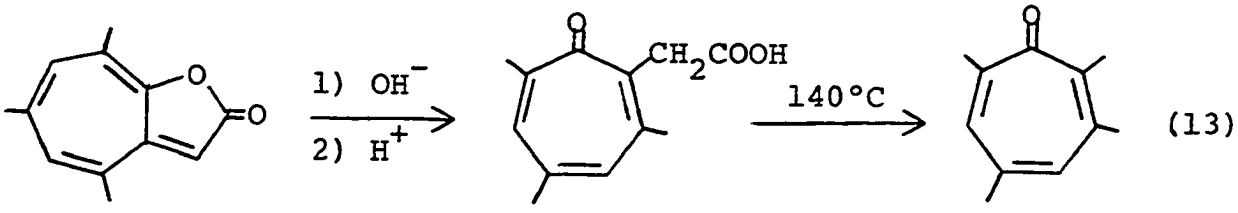
The hydrolysis of 59 and 60 to their corresponding troponylacetic acids required major modification of the procedures described by Seto (15). The procedure to hydrolyze 2 as described by Seto was repeated unsuccessfully many times. Working with 2 a procedure was developed that hydrolyzed 2 to 2-troponylacetic acid . Decarboxylation was also effected to give 2-methyltropone (Eq. 12).



2 (12)

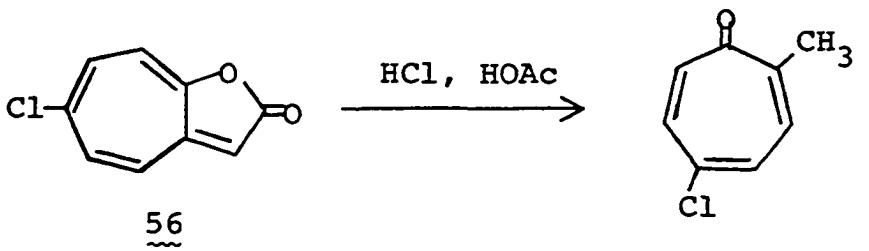
The hydrolysis procedure developed for 2 was modified and then used for the hydrolysis of 59 and 60. Compounds 59 and 60 were hydrolyzed to 2-(7-methyltroponyl)acetic acid and 2-(3-methyltroponyl)acetic acid, respectively. Then the acids were decarboxylated to 2,7-dimethyl- and 2,3-dimethyltropones, respectively.

Further studies were made to see whether FVP of aryl propiolates and subsequent hydrolysis and decarboxylation of the products could be used to obtain substituted tropones. Compound 55 was degraded to 2,3,5,7-tetramethyltropone by the procedure used for 59 and 60 (Eq. 13). Hydrolysis

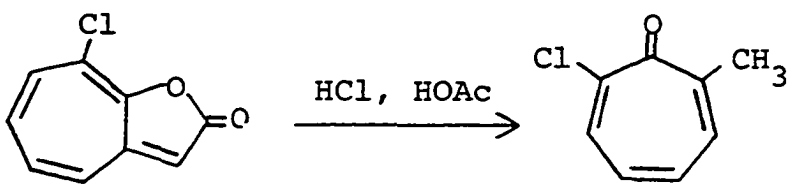


55 (13)

and decarboxylation of 6-chloro-2H-cyclohepta[b]furan-2-one (56) and 8-chloro-2H-cyclohepta[b]furan-2-one (61) to their respective tropones were accomplished using concentrated hydrochloric acid and acetic acid (Eqs. 14 and 15). These



56 (14)



61 (15)

results indicate that certain substituted tropones could be obtained from the FVP of aryl propiolates and subsequent hydrolysis and decarboxylation.

FVP of o-isopropylphenyl (38) and o-bromophenyl (37) propiolates were not as well-behaved. Pyrolysis of 38 yielded some brown decomposition product that co-deposited with the isomeric mixture of 8-isopropyl- (65) and 4-isopropyl- (66) 2H-cyclohepta[b]furan-2-ones in a 2.4:1 ratio. Attempts to separate 65 from 66 failed. Pyrolysis of 37 presented a unique problem; the results were not predictable. Table VI summarizes the results of seven runs carried out at the same experimental conditions.

Table VI. Pyrolysis of o-bromophenyl propiolate at 650°C

Pyrolysis	63[a]		64[b]
1	4	:	3
2	-[c]		
3	7	:	1
4	7	:	1
5	1	:	1
6	1	:	1
7	2	:	1

[a] 63≡8-Bromo-2H-cyclohepta[b]furan-2-one.

[b] 64≡4-Bromo-2H-cyclohepta[b]furan-2-one.

[c] Only 63 was obtained.

Pyrolysis of Indanyl Propiolates

To determine the feasibility of obtaining the carbon skeletons of hydroazulenic sesquiterpene lactones and of incorporating FVP of aryl propiolate as an intermediate step in the synthesis of a pseudoguaianolide, FVP of some indanyl propiolates were examined. Table VII summarizes the results of the FVP of the indanyl series of propiolates. Again two isomers were obtained from each propiolate. Some of these products have the same basic carbon skeletons as pseudoguaianolides and guaianolides.

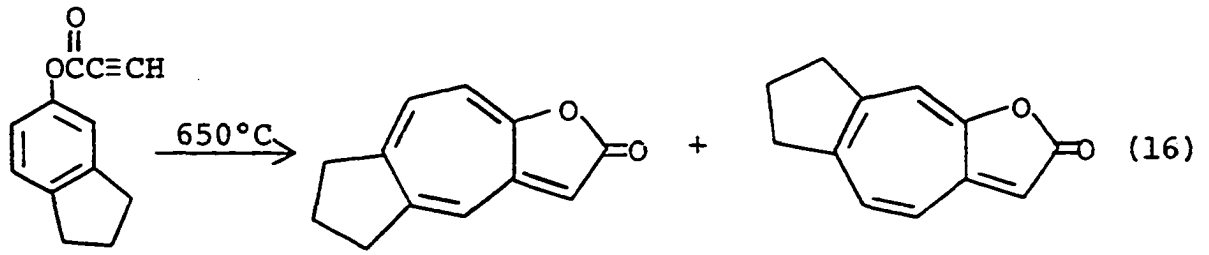
The pyrolysis of 5-indanyl propiolate (46) yielded a 1:1 ratio of isomeric 6,7-dihydro-azuleno[5,4-b]furan-2(5H)-

Table VII. Pyrolysis of indanyl propiolates

Propiolate	Pyrolysis Temp (°C)	Product	Structure Number	Yield (%)	Product	Structure Number	Yield (%)
46	650[a]	6,7-Dihydro-azuleno-[6,5-b]furan-2(5H)-one	69	20	7,8-Dihydro-azuleno-[5,6-b]furan-2(6H)-one	70	20
47	650[a]	8,9-Dihydro-azuleno-[4,5-b]furan-2(7H)-one	71	15	5,6-Dihydro-azuleno-[5,4-b]furan-2(4H)-one	72	13
48	650[a]	6,7-Dihydro-9-chloro-azuleno[6,5-b]furan-2(5H)-one	73	34	4-Chloro-7,8-dihydro-azuleno[5,6-b]furan-2(6H)-one	74	4
49	660[b]	7,8-Dihydro-azuleno-[4,5-b]furan-2,9-dione	75	14	5,6-Dihydro-azuleno-[5,4-b]furan-2,4-dione	76	14
50	760[b]	6-Methyl-7,8-dihydro-azuleno[4,5-b]furan-2,9-dione	77	22	5,6-Dihydro-7-methyl-azuleno[5,4-b]furan-2,4-dione	78	22
51	750[b]	6,7-Dihydro-azuleno-[6,5-b]furan-2,5-dione	79	48	6,7-Dihydro-azuleno-[5,6-b]furan-2,8-dione	80	14
52	720[b]	6,7-Dihydro-9-chloro-azuleno[6,5-b]furan-2,5-dione	81	51	4-Chloro-6,7-dihydro-azuleno[5,6-b]furan-2,8-dione	82	0
53	750[a]	6,7-Dihydro-8-methyl-azuleno[6,5-b]furan-2,5-dione	83	28	5-Methyl-6,7-dihydro-azuleno[5,6-b]furan-2,8-dione	84	14
53	720[b]	83	83	16	84	84	32

[a]Hot zone packed with quartz chips.
[b]Hot zone empty.

one (69) and 7,8-dihydro-azuleno[5,6-b]furan-2(6H)-one (70) (Eq. 16). Separation of 69 and 70 proved extremely difficult.

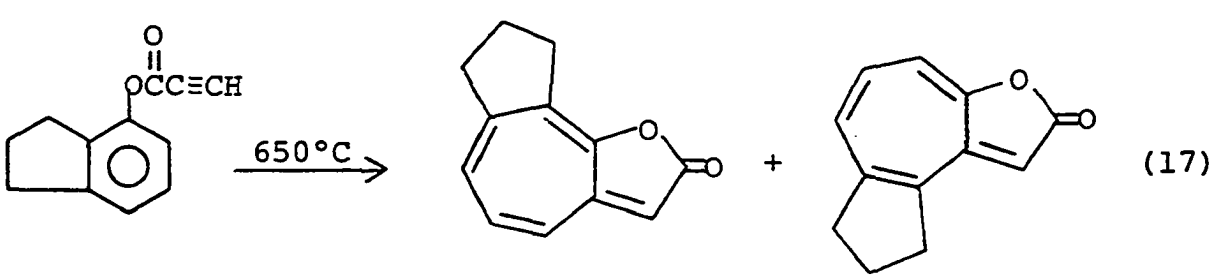


(16)

46 69 70

It required the use of preparative layer chromatographic plates with multiple elutions (ca. 10 times).

Pyrolysis of 4-indanyl propiolate (47) yielded a 6:5 ratio of isomeric products 8,9-dihydro-azuleno[4,5-b]furan-2(7H)-one (71) and 5,6-dihydro-azuleno[5,4-b]furan-2(4H)-one (72), the separation of which required the same separation technique used for the separation of 69 and 70. Although the separation was difficult, the pyrolysis itself went smoothly.

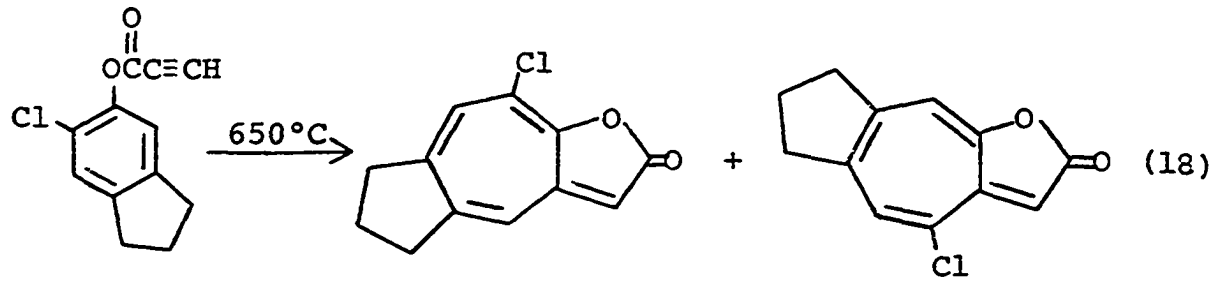


(17)

47 71 72

Pyrolysis of 5-(6-chloroindanyl) propiolate (48) at 650°C yielded 34% of 6,7-dihydro-9-chloro-azuleno[6,5-b]-

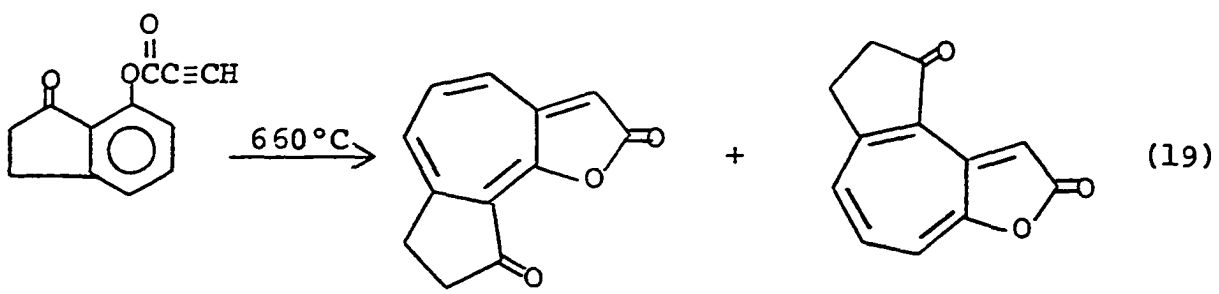
furan-2(5H)-one (73) and only 4% of 4-chloro-7,8-dihydro-azuleno[5,6-b]furan-2(6H)-one (74) (Eq. 18).



(18)

48 73 74

However, when carbonyl groups were added to the indanyl propiolates, problems were encountered. For 7-(1-oxoindanyl) propiolate (49) (Eq. 19), a drastic decrease in the yield was



(19)

49 75 76

observed; a third component was formed and was deposited in the same region of the apparatus as the two isomeric products; and it became more difficult to sublime the starting material. To improve the yield the pyrolysis temperature was varied from 550°C to 650°C. No improvement on the 7% yield of 7,8-dihydro-azuleno[4,5-b]furan-2,9-dione (75) or the 7% yield of 5,6-dihydro-azuleno[5,4-b]furan-2,4-dione (76) was observed. However, when the quartz chips were

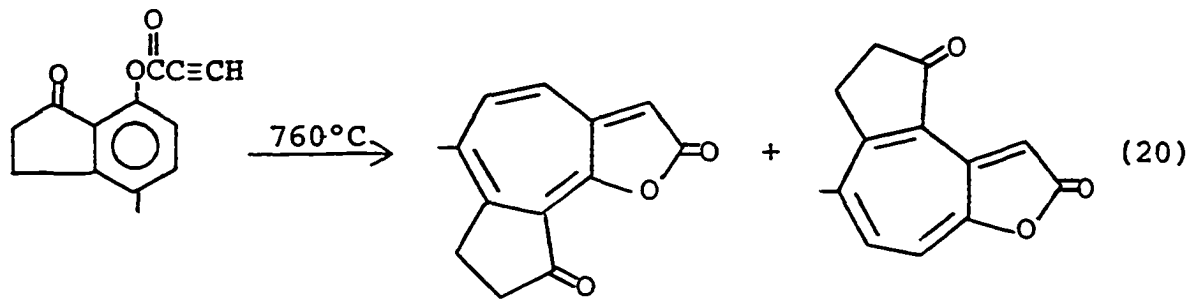
removed from the hot zone and with the temperature at 660°C, the yield of 75 and 76 increased to 14% for each compound. Although the absence of the quartz chips improved the yield, it created an additional problem. A small amount of the starting propiolate sublimed through the hot zone unchanged and deposited in the same region as the other compounds.

Purification of 75 and 76 required two column chromatographic separations (silica gel). The first column was to remove the unreacted propiolate. The second column provided the final separation of the remaining three components. Assignments of 75 and 76 proved easy due to the unique chemical shift of the hydrogen at position 3 in 76. The hydrogen lies in the deshielding cone of the ketonic carbonyl, and this shifted the hydrogen signal from its normal vinyl region to the aromatic region.

The problem of low volatility of 49 was never solved. Attempts to synthesize the ethylene glycol ketal of 49 and 7-hydroxy-1-indanone failed.

Problems similar to those encountered with 49 were also present in the FVP of 7-(1-oxo-4-methylindanyl) propiolate (50). Studies were made with an unpacked tube and with the temperature varied from 650°C to 770°C. The optimum temperature of 760°C yielded 22% of each of the isomeric products, 6-methyl-7,8-dihydro-azuleno[4,5-b]furan-2,9-

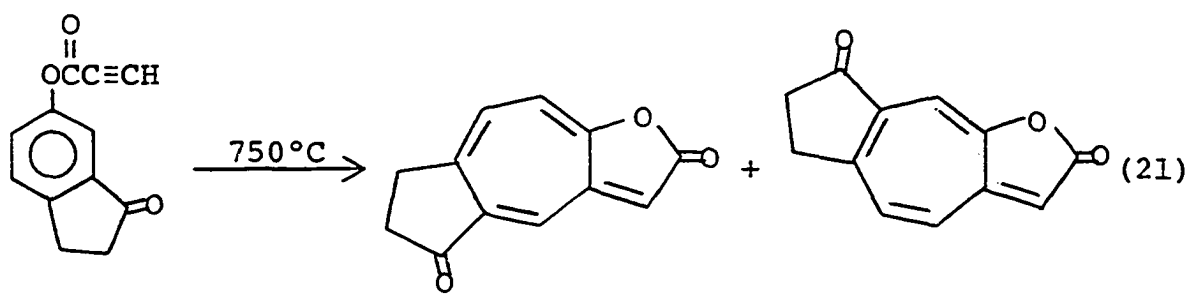
dione (77) and 5,6-dihydro-7-methyl-azuleno[5,4-b]furan-2,4-dione (78) and 11% of starting material 50 (Eq. 20).



50 77 78

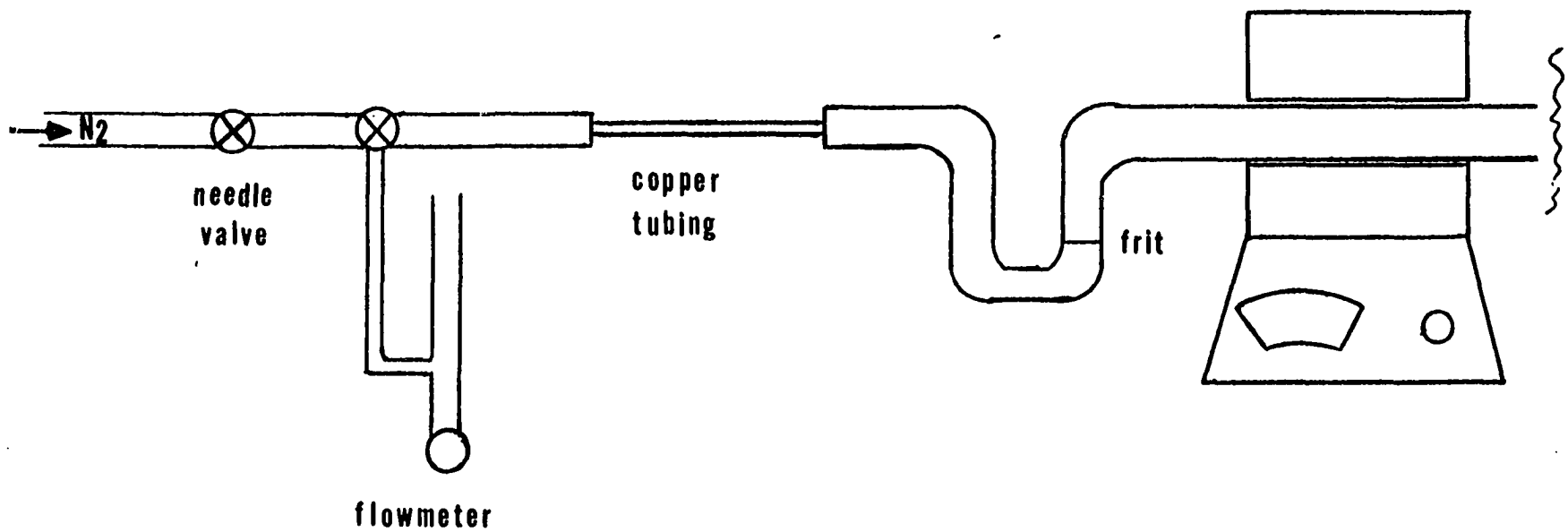
A nitrogen-flow pyrolysis system (Figure 8) was tried to circumvent the problem of the low volatility of the starting material. Pyrolysis temperatures of 520°C, 570°C, 620°C and 720°C were tried with 50 in this flow system; however, no improvement was observed.

Pyrolysis of 6-(1-oxoindanyl) propiolate (51) at 750°C provided surprising results. A 10:3 ratio instead of the expected 1:1 ratio of 6,7-dihydro-azuleno[6,5-b]furan-2,5-dione (79) (48%) to 6,7-dihydro-azuleno[5,6-b]furan-2,8-dione (80) (14%) was obtained (Eq. 21).

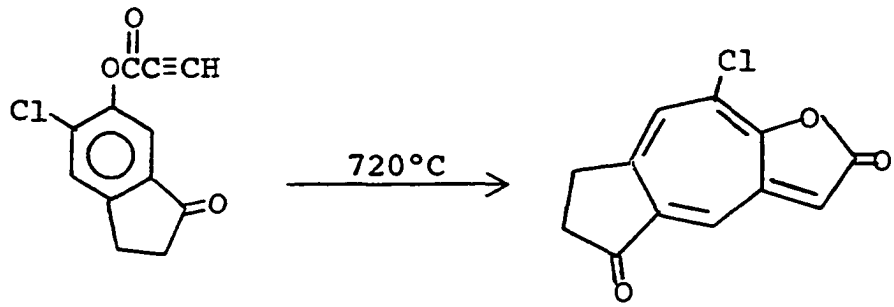


51 79 80

Figure 8. Diagram of the N_2-flow pyrolysis apparatus


N2
needle
valve
flowmeter
copper
tubing
frit

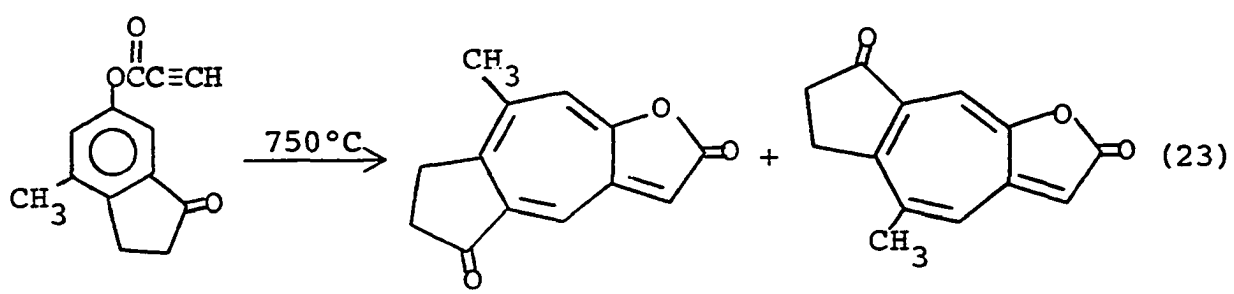
Only the 6,7-dihydro-9-chloro-azuleno[6,5-b]furan-2,5-dione (81) (51%) was formed when 6-(1-oxo-5-chloroindanyl) propiolate (52) was pyrolyzed at 720°C (Eq. 22).



(22)

52 81

FVP of 6-(1-oxo-4-methylindanyl) propiolate (53) also produced some very intriguing results. When 53 was pyrolyzed at 720°C with an unpacked tube, a 1:2 ratio of 6,7-dihydro-8-methyl-azuleno[6,5-b]furan-2,5-dione (83) to 5-methyl-6,7-dihydro-azuleno[5,6-b]furan-2,8-dione (84) was obtained. However, when 53 was pyrolyzed at 750°C with a packed tube, the ratio was reversed.



(23)

53 83 84

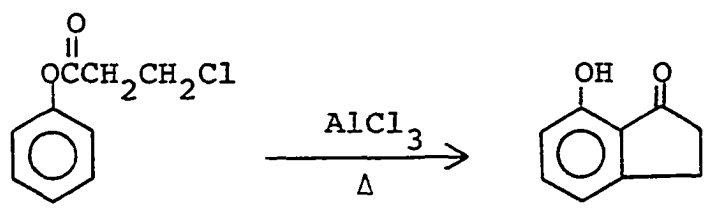
The separation of the isomers created many problems. Firstly, separations were difficult because of the similar-

ities of the compounds. And secondly, the separation procedures used inevitably required the use of silica gel which caused varying degrees of decomposition on all the products from the indanone series of propiolates.

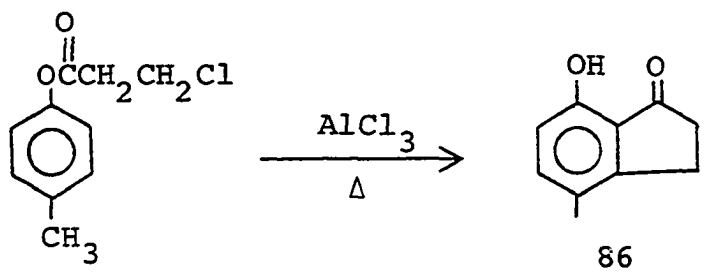
The isolated yields of 79, 80, 83, and 84 after column chromatographic separation using silica gel were 36%, 10%, 18%, and 3%, respectively.

Synthesis of Phenol Derivatives

Fries rearrangement of phenyl 3-chloropropionate and p-tolyl 3-chloropropionate produced 7-hydroxy-1-indanone (85) and 4-methyl-7-hydroxy-1-indanone (86), respectively (Eqs. 24 and 25).



85 (24)



86 (25)

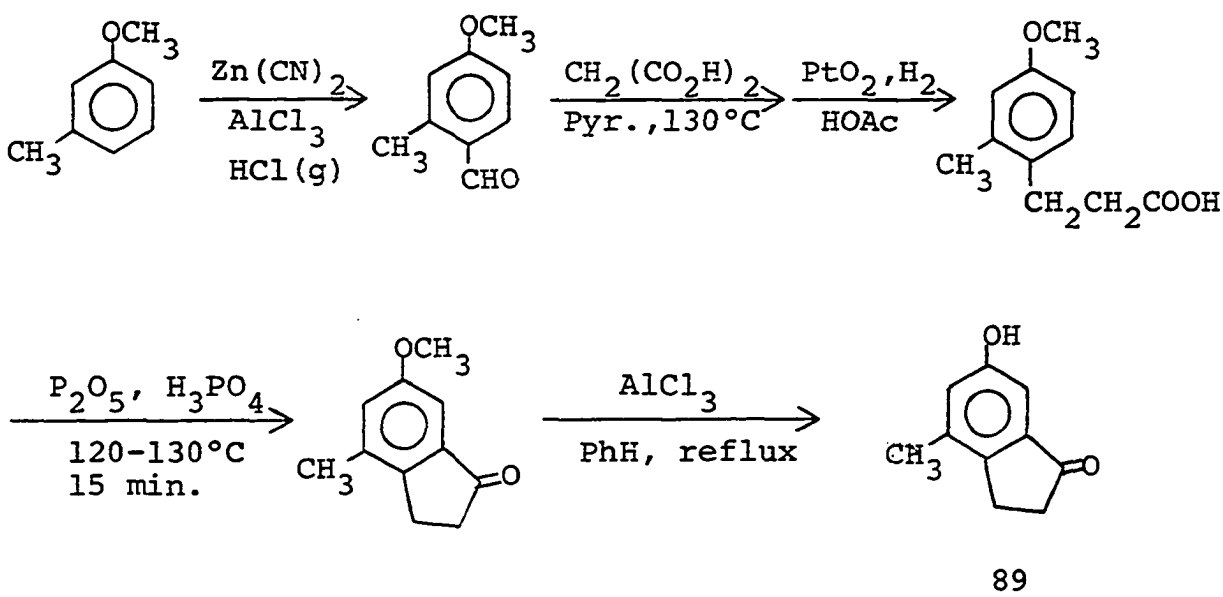
Treatment of 5-indanol with sulfuryl chloride and acetic acid yielded 6-chloro-5-indanol (87).

Synthesis of 6-hydroxy-1-indanone involved the nitration of 1-indanone followed by reduction with stannous chloride to form 6-amino-1-indanone. Diazotization of the amine produced 6-hydroxy-1-indanone (88).

Chlorination of 3-(4-methoxyphenyl)propionic acid with sulfuryl chloride in acetic acid followed by treatment with thionyl chloride produced 3-(3-chloro-4-methoxyphenyl)-propionyl chloride. Cyclization to the indanone was effected with aluminum chloride in methylene chloride at high dilution. The methoxy moiety was converted to hydroxy with aluminum chloride in refluxing benzene.

Synthesis of 4-methyl-6-hydroxy-1-indanone (89) is shown in Scheme XII.

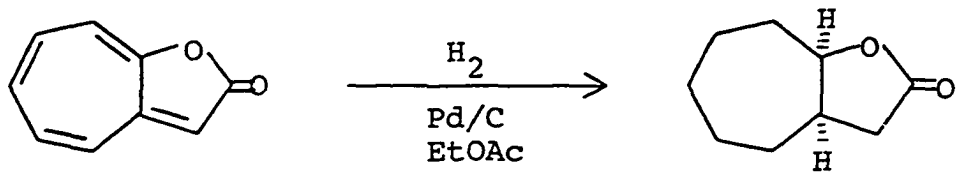
Scheme XII



89

Hydrogenation of Pyrolysis Products

Hydrogenation of 2 with palladium on charcoal in ethyl acetate produced cis-octahydro-2H-cyclohepta[b]furan-2-one (90) (Eq. 26) (Figure 9) which was identified by comparing its nmr spectrum to that reported by Herz and Glick (49).



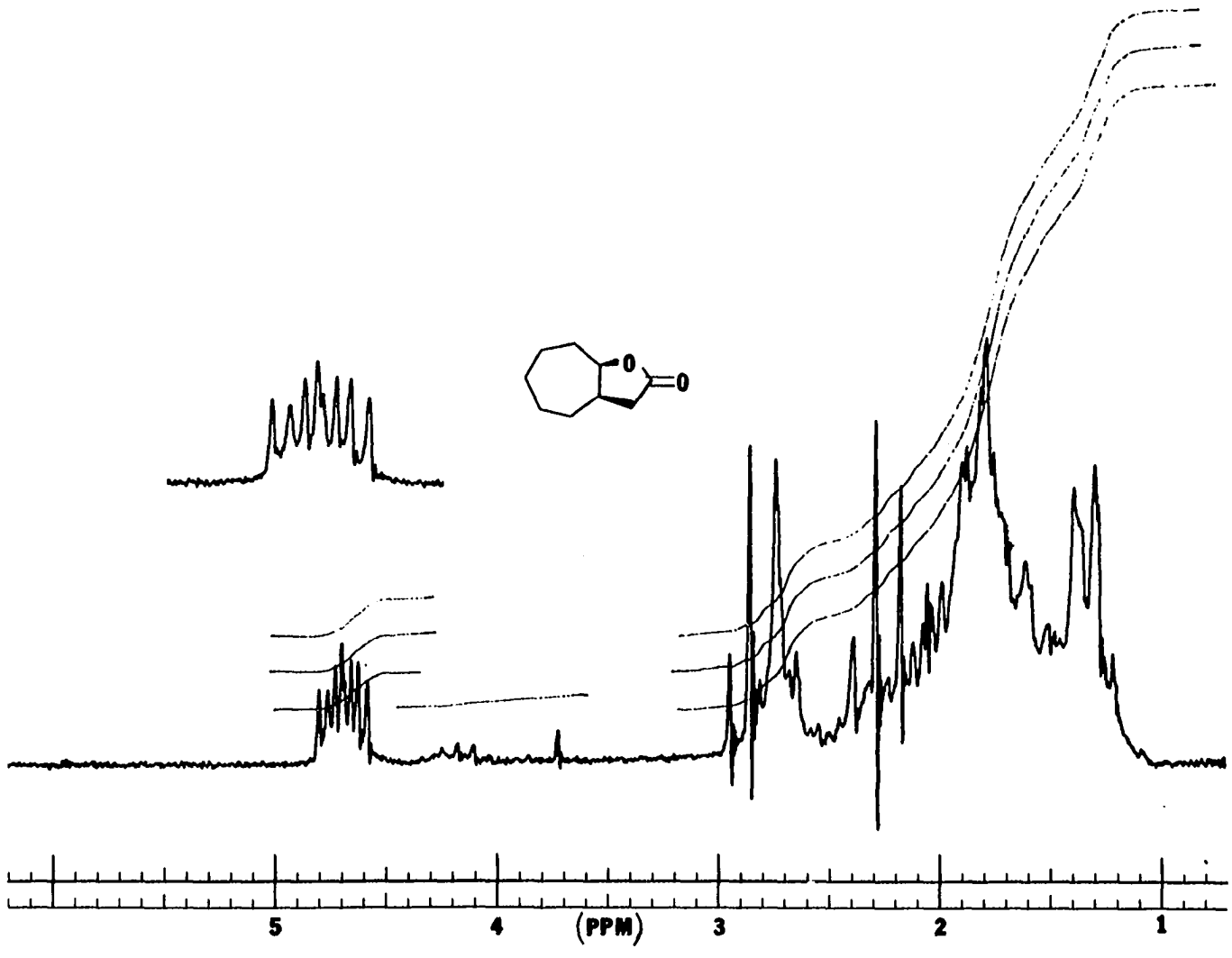
(26)

2 90

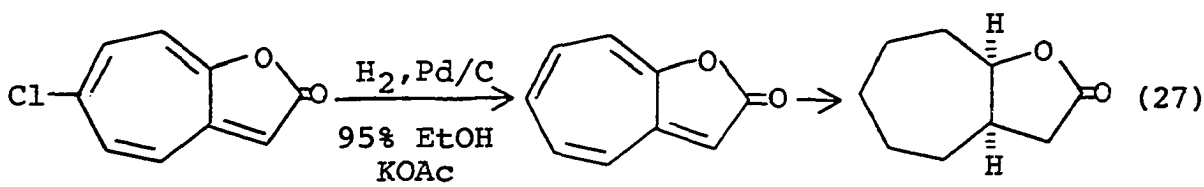
Hydrogenation of 8-methyl-2H-cyclohepta[b]furan-2-one (59) also yielded a complete reduction of the four double bonds as determined from its mass spectrum. It was assigned as a cis-fused product based on its nmr spectrum. However, the stereochemistry of the methyl group was never determined.

Similarly, when a mixture of 6,7-dihydro-azuleno[6,5-b]-furan-2(5H)-one (69) and 7,8-dihydro-azuleno[5,6-b]furan-2(6H)-one (70) was hydrogenated with palladium on charcoal and ethyl acetate, hydrogenation of all four double bonds was observed. Although the stereochemistry at the ring junction between the cyclopentane and cycloheptane rings is not known, the stereochemistry at the other ring junction is believed to be cis-fused.

Figure 9. HA-100 nmr spectrum of *cis*-octahydro-2*H*-cyclohepta[*b*]furan-2-one in chloroform-*d*


O
O
5
4
(PPM)
3
2
1

Subjecting 6-chloro-2H-cyclohepta[b]furan-2-one (56) to hydrogenation condition of palladium on charcoal, 95% ethanol, and potassium acetate caused hydrogenolysis of the chlorine. The reduction could be controlled to obtain 90 from 56 by combination of hydrogenation and hydrogenolysis. Furthermore, reaction of 56 was controlled to yield 2 as the major product with a small amount of partially reduced 2 as the minor product (Eq. 27) (Figure 10).



(27)

56 2 90

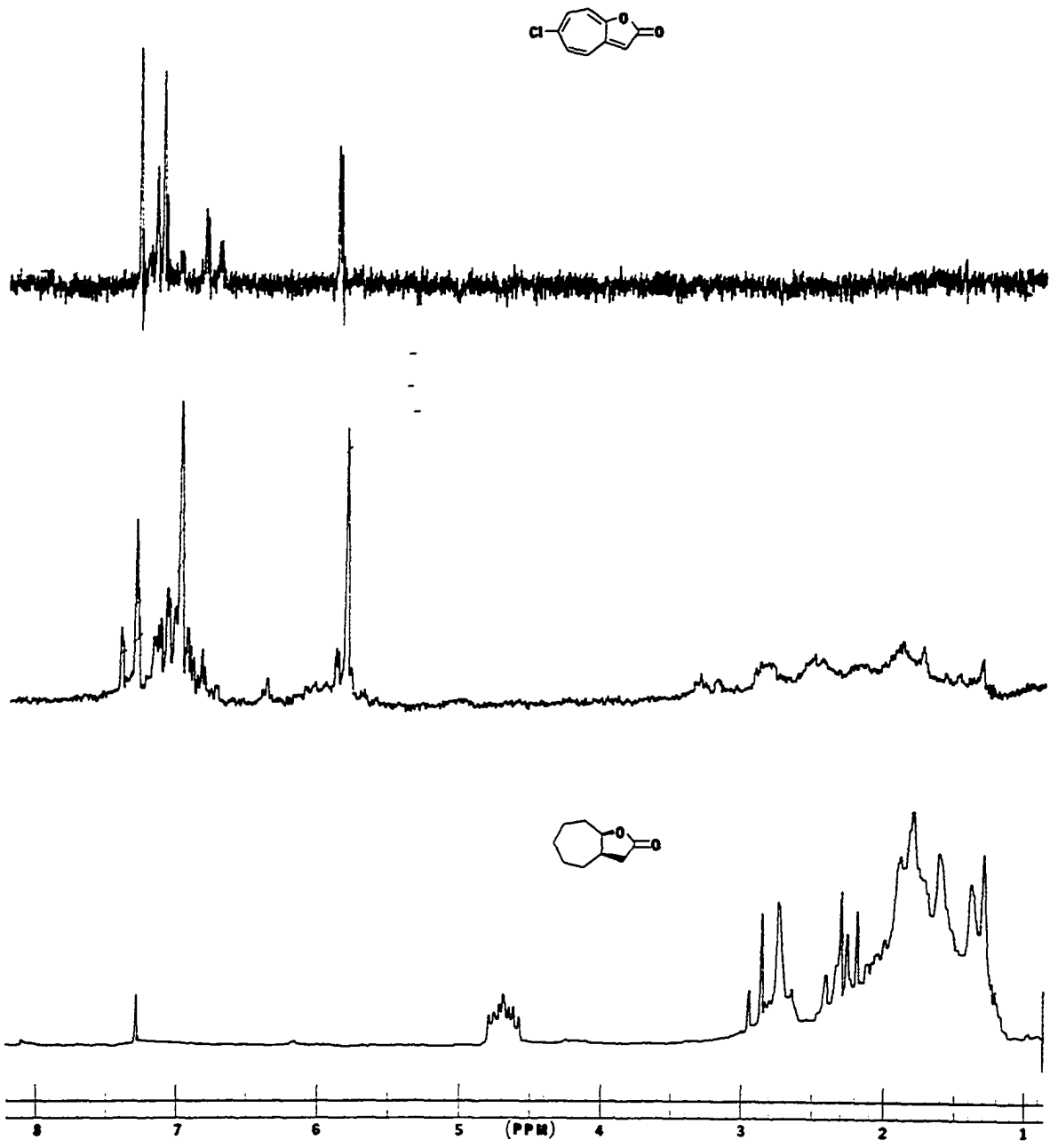
The ease of complete hydrogenation of the double bonds in 2, 56, 59, 69, and 70 was not observed for compounds 81, 83, and 84. Attempts were made to completely reduce the double bonds in 81, 83, and 84 without obtaining a mixture of products. However, the product mixture obtained in each of the three compounds was too complicated to identify. Mass spectral data suggested a mixture of completely saturated and mono-olefinic products.

Figure 10. HA-100 nmr spectra in chloroform-d

Top: Spectrum of 6-chloro-2H-cyclohepta[b]-furan-2-one (56)

Middle: Spectrum of a mixture of 56, 2H-cyclohepta[b]furan-2-one (2), and partially hydrogenated 2

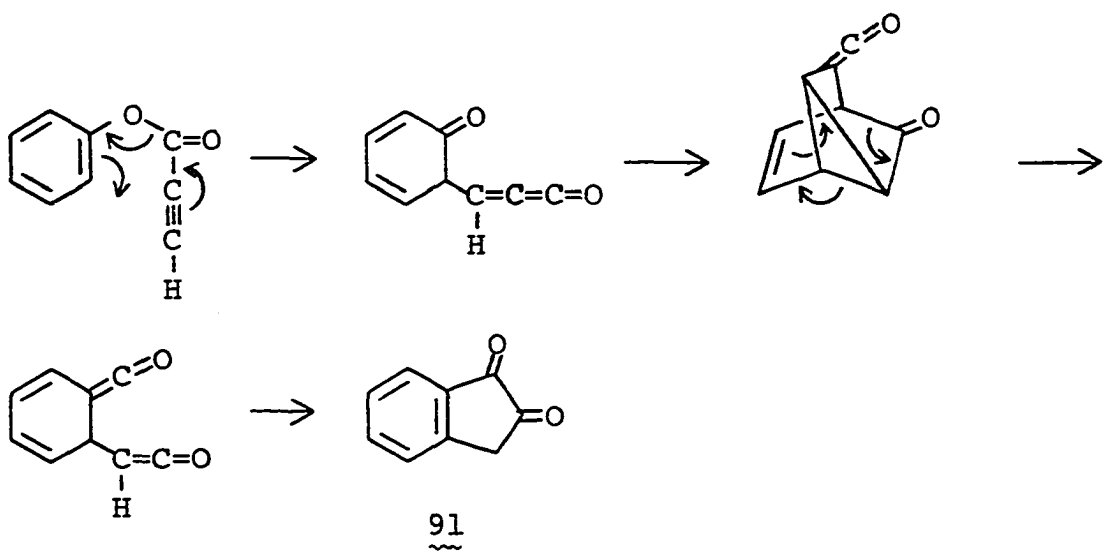
Bottom: Spectrum of cis-octahydro-2H-cyclohepta-[b]furan-2-one


Cl
O
O
O
O
8
7
6
5
(PPM)
4
3
2
1

DISCUSSION

It has been reported that flash vacuum pyrolysis of phenyl propargyl ether gave 2-indanone; furthermore, ortho- and para-substituted phenyl propargyl ethers gave the corresponding substituted 2-indanones. If the thermal rearrangement of phenyl propiolate went according to the mechanism proposed for the phenyl propargyl ether rearrangement, then 1,2-indanedione (91) should be obtained (Scheme XIII). However, only 2H-cyclohepta[b]furan-2-one (2) was obtained in the pyrolysis.

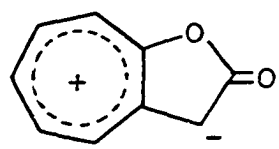
Scheme XIII



91

The product 2 was identified by comparison of its melting point and color to that reported in the literature (15) and on the basis of its spectral data. Furthermore, from the observed proton chemical shifts of the ring

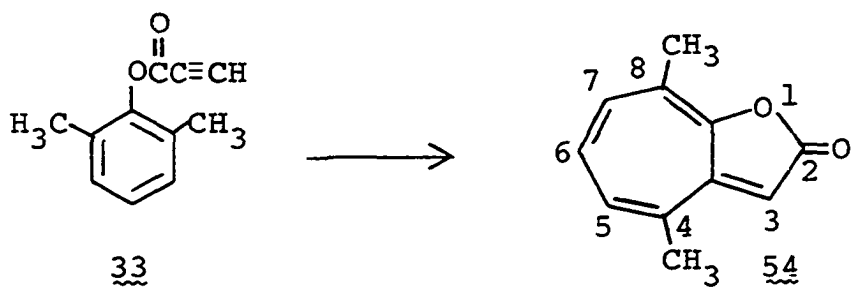
hydrogens of 2, the double bonds in the seven-membered ring appeared to be somewhat delocalized (Figure 2, Page 30). This suggested that 92 is an important resonance structure of 2. The aromaticity of the compound accounts for the downfield shift of the ring hydrogen signals.



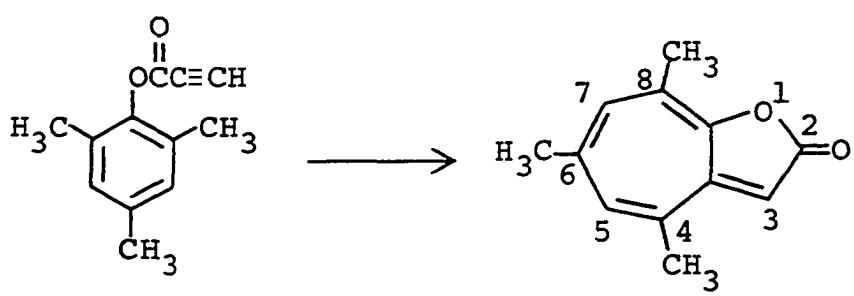
92

Mechanistic Work

Next, 2,6-dimethylphenyl (33) and 2,4,6-trimethylphenyl (34) propiolates were pyrolyzed to provide some insights into the rearrangement (Eqs. 7 and 8). The products obtained



33 54 (7)



34 55 (8)

4,8-dimethyl- (54) and 4,6,8-trimethyl- (55) 2H-cyclohepta-[b]furan-2-ones were identified based on their spectral data. IR spectra of both 54 and 55 show ν(C=O) at 1765 cm^{-1}; whereas, the ν(C-O) is at 1275 cm^{-1} for 54 and 1239 cm^{-1} for 55, which are consistent with the two structures assigned. In addition, comparison of the UV-VIS spectra of 2 and 54 further supports that the structure of 54 does contain the parent system of a seven-membered ring fused to a γ-lactone. The assignment of the proton nmr signals at δ5.57(s, 1H) of 54 and δ5.22(s, 1H) of 55 to the protons on the carbons alpha to the carbonyl groups restricted the location of the methyl groups to the seven-membered ring. The exact positions of the methyl groups were elucidated from ^{13}C nmr data.

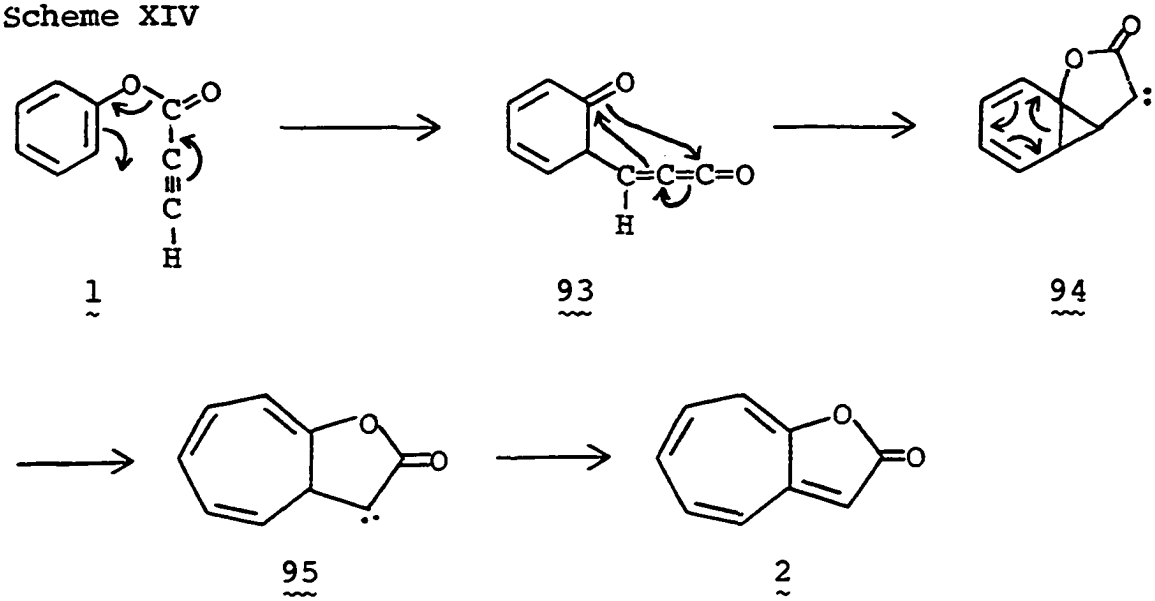
The ^{13}C broad band decoupled nmr spectrum of 55 showed the three methyl signals at 19.72 ppm, 24.27 ppm, and 27.39 ppm relative to tetramethylsilane (TMS). Gated decoupled spectrum of 55 showed that the signals at 19.72 ppm and 24.27 ppm are split into quartets of doublets with J_{C-H} of 129.43 hz and 127.95 hz, respectively. The third signal is split into a quartet of triplets with J_{C-H} of 127.95 hz. These data fit the assignment of the three methyl groups to the positions of 4, 6, and 8 with the quartet of triplets signal assigned to the methyl group at position 6. The assignment of the remaining two methyl groups could not be

made. There are no other arrangements of the three methyl groups that would give rise to the observed pattern. The broad band decoupled spectrum of 54 gave rise to two signals corresponding to the two methyl groups at 19.46 ppm (J_{C-H}= 132.36 Hz) and 23.99 ppm (J_{C-H}=127.95 Hz). Although there are other arrangements of the two methyl groups that could give rise to the observed signals, the information obtained from ^{13}C nmr spectrum of 55 gave strong support that the two methyl groups are at positions 4 and 8. These results indicated that the phenyl ring positions 2-6 remained intact during the rearrangement.

Scheme XIV shows the mechanism proposed for the rearrangement. The initial Claisen rearrangement leads to the allenyl ketene intermediate (93) which then via a concerted six-electron process rearranges to the carbene species (94). Six-electron electrocyclic ring-opening of 94 leads to the formation of 95. Finally, a migration step concludes the rearrangement.

None of the species proposed in the mechanism has been trapped. Apparently the product in its vapor phase was formed in the furnace, and it was condensed immediately when it reached the cooler outside temperature. Trapping these species would require the trapping process be accomplished inside the hot zone. Trapping experiments in

Scheme XIV



1 93 94

95 2

this case would seem unlikely to succeed. At first, it would be difficult to find a trapping agent that would not undergo some sort of rearrangement or decomposition itself. Secondly, FVP is essentially a unimolecular process. And thirdly, if the trapping did succeed inside the hot zone, there existed a high probability that the resulting adduct would fragment or rearrange before it emerges from the furnace.

Generality of the Pyrolysis Reaction

The generality of the pyrolysis reaction is quite evident as suggested by the pyrolysis products listed in Tables IV, V, and VII.

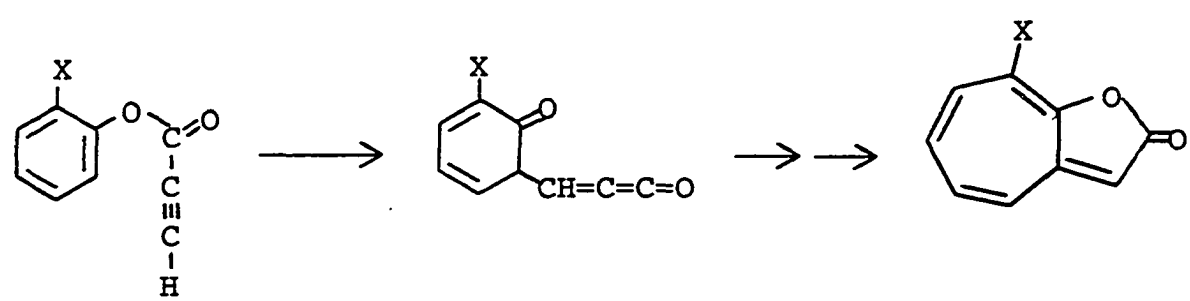
The proposed mechanism suggests that the initial Claisen rearrangement could occur either way. Because of the symmetry in the para-substituted phenyl propiolates, only

one product was formed regardless of the direction of initial Claisen rearrangement. With the chloride, bromine, and formyl substituents, no problems were encountered. However, possibly because of the electron-donating ability of the oxygenated substituents and/or the readily-formed phenoxy-type radicals, no desired lactone system was formed from p-methoxyphenyl, p-acetoxyphenyl and p-hydroxyphenyl propiolates.

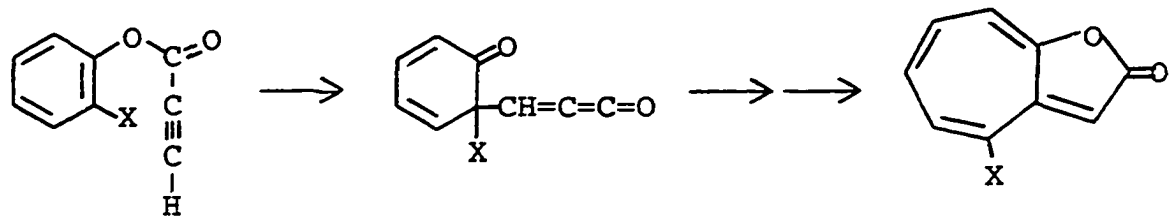
Characterization of the Pyrolysis Products

Again as suggested by the proposed mechanism, two isomers were formed from each ortho-substituted unsymmetrical propiolate. The initial Claisen rearrangement could occur either of two ways. With a substituent on the ortho carbon, the rearrangement away from the substituted carbon was postulated to be favored due to less steric hindrance. The isomer with the substituent at position 8 would then be the major product,

Scheme XV



Scheme XVI

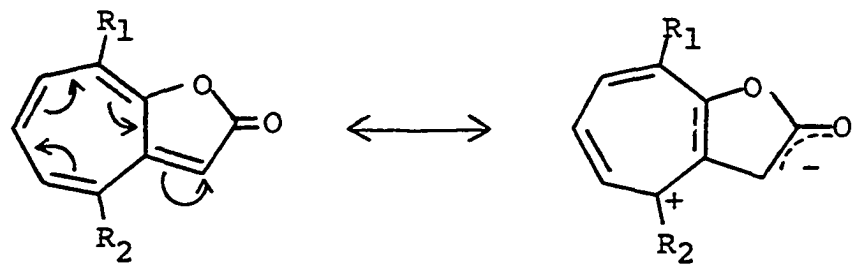


and the isomer with the substituent at position 4 would be the minor product. This hypothesis was first tested on o-methylphenyl propiolate (35).

The pyrolysis of 35 yielded two isomers as indicated by the two nmr signals at δ5.70 and δ5.68 corresponding to the hydrogens alpha to the carbonyl groups (Figure 3, Page 32). Conclusive assignments of the isomers were not possible from the spectra alone due to the similarities of the spectra. The only obvious spectral difference lies in the aromatic region of the nmr spectra. NMR spectrum of the major isomer shows one of its four ring hydrogens signals is further downfield than the signals from the other three hydrogens, which have similar chemical shifts; however, all four hydrogens from the minor isomer have similar chemical shifts which are comparable to the chemical shifts of the three hydrogens from the major isomer. This indicated that either the hydrogen at position 4 or at position 8 is the downfield hydrogen. Conclusive assignments of the isomers were made after each isomer was hydrolyzed and decarboxylated to its

corresponding tropone (Eqs. 10 and 11, Page 45). The major isomer was degraded to 2,7-dimethyltropone indicating that the major isomer is 8-methyl-2H-cyclohepta[b]furan-2-one. This also indicated that the lowfield signal belongs to the hydrogen at position 4.

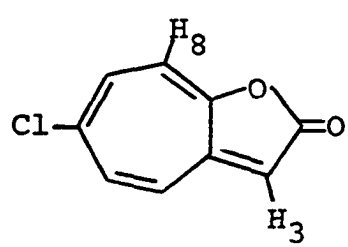
The existence of this low field hydrogen suggests the importance of the resonance structure 96.



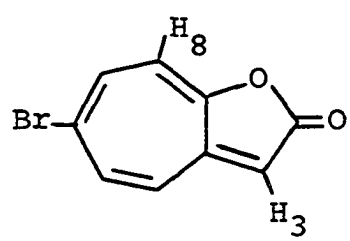
R_1=CH_3, R_2=H
R_1=H, R_2=CH_3

96

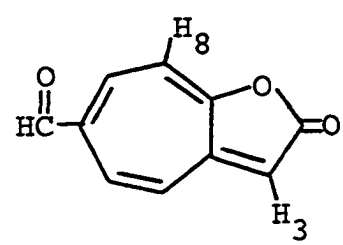
Coplanar "w" coupling (48) played an important role in structure elucidation of some of these lactone compounds. Proton nmr spectra of 6-chloro- (56), 6-bromo- (57), and 6-formyl- (58) 2H-cyclohepta[b]furan-2-ones revealed the presence of coplanar "w" coupling between hydrogens 3 and 8.



56

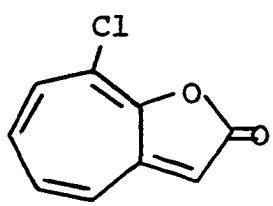


57

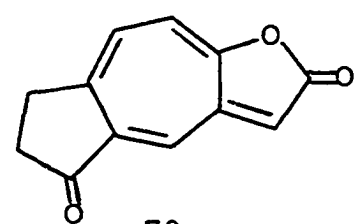


58

Irradiating the hydrogen at position 3 in 56, 57, and 58 caused the doublet of doublets of the hydrogen at position 8 to collapse to a doublet (Figure 6, Page 40 and Figure 7, Page 42). The possibility that the observed coplanar "w" coupling came from the coupling between the hydrogens at positions 3 and 5 was excluded by the following data. Compounds such as 8-chloro-2H-cyclohepta[b]furan-2-one (62) which has a hydrogen at position 5 exhibits no "w" coupling, and compounds such as 6,7-dihydro-azuleno[6,5-b]furan-2,5-dione (79) which has no hydrogen at position 5 shows signs of coplanar "w" coupling.



62



79

Although "w" coupling is not present in all the compounds with hydrogen at position 8, the presence of "w" coupling is always accompanied by the presence of hydrogen at position 8.

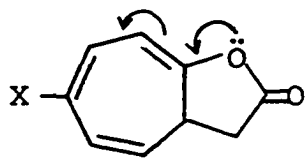
Use of "w" coupling in the structural assignments of 8-methyl- (59) and 4-methyl- (60) 2H-cyclohepta[b]furan-2-ones gave results in complete agreement with the assignments from hydrolysis-decarboxylation findings. The hydrogen at position 3 of the major isomer is a sharp singlet while the

corresponding signal from the minor isomer shows long-range coupling. Therefore, the major isomer has the methyl group at position 8, and the minor isomer has the methyl group at position 4.

The low chemical shift of the hydrogen at position 4 is observed only for compounds with alkyl substituents. With chloro, bromo, and formyl substituents at position 6 in the lactone products, the four seven-membered ring hydrogens gave rise to two sets of AB patterns. The signals from the hydrogens at positions 4 and 8 formed the upper halves of the AB patterns. The signals of the two hydrogens adjacent to the substituent became the lower halves of the AB patterns.

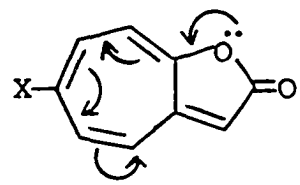
The unusually high chemical shift of the hydrogen at position 8 and also the shift upfield for the hydrogen at position 4 may be due to the importance of the resonance structures involving electron donation by the oxygen. This coupled with the inductive effect of the substituent caused sufficient differences in the chemical shifts of the hydrogens for the two AB patterns to be discernible. Furthermore, the two adjacent hydrogen signals for 6-formyl-2H-cyclohepta[b]furan-2-one are observed at lower chemical shifts than the corresponding hydrogen signals from 6-chloro- and 6-bromo-2H-cyclohepta[b]furan-2-ones. This is probably due to the additional deshielding of the hydrogens

by the formyl carbonyl moiety. The AB patterns became easier to identify when the hydrogen at position 8 was subjected to double irradiation (Figure 6, Page 40 and Figure 7, Page 42).



X=Br, Cl, CHO

97

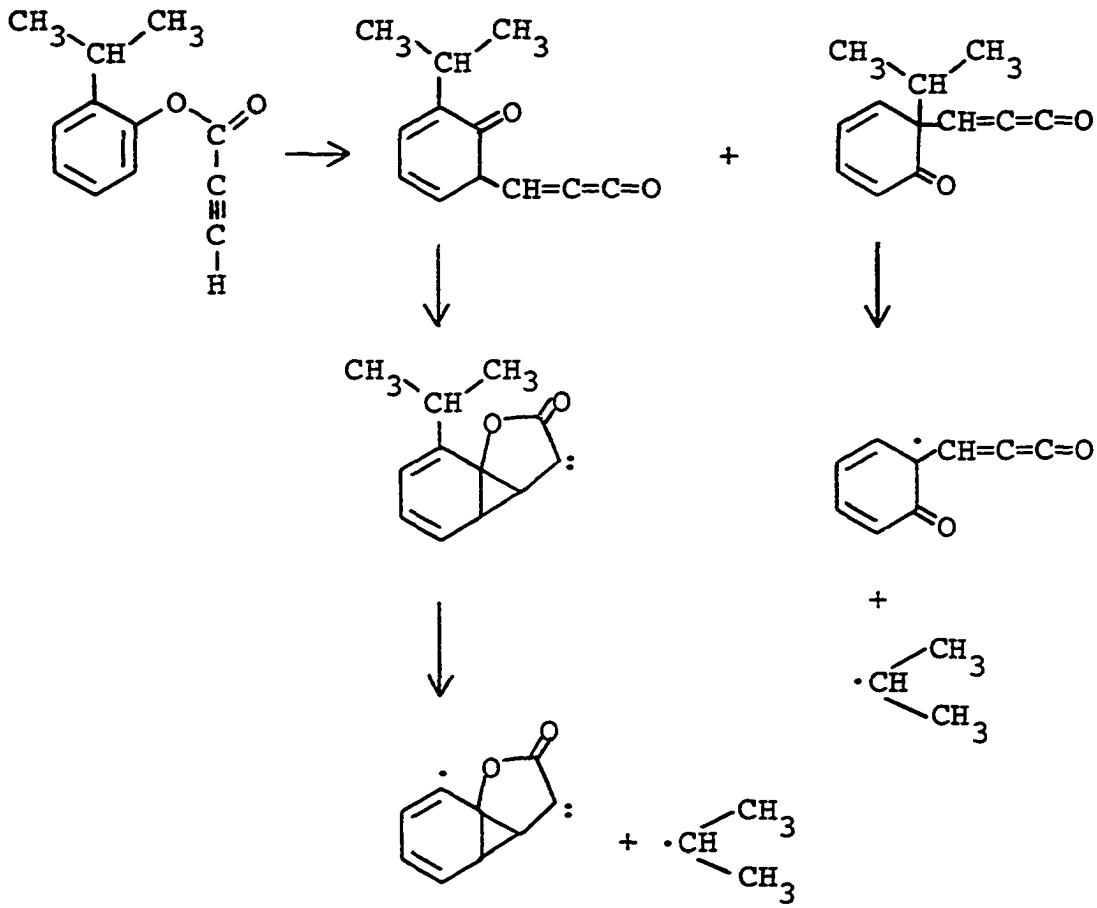


98

The isomeric ratio observed for 59 and 60 was attributed to a steric effect on the initial Claisen rearrangement. An electronic effect was found to be minimal when o-chlorophenyl propiolate (36) yielded similar results.

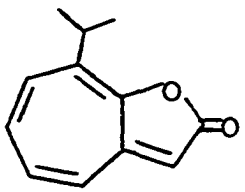
However, the ability of the ortho substituent to form a stable radical does seem to affect the behavior of the pyrolysis. In the o-isopropylphenyl propiolate pyrolysis some brown unidentified product was formed. The unwanted product could have arisen from the fragments readily formed from the allenyl ketene species and the carbene species (Scheme XVII). The formation of the radicals from the allenyl ketene species is a likely process since the resulting two radicals are reasonably stable. But, the formation of the radicals from the carbene species is questionable. However, the brown product that was formed

Scheme XVII

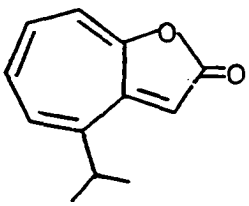


could not have come solely from the fragmentation of the allenyl ketene species since this would require that the carbene species rearranges to produce 65 and undergoes no fragmentation. If this were the case, then the ratio of the isomeric products (65:66) should have been greater than the ratio of the isomeric product (59:60). This is based on the assumption that isopropyl group should have provided a

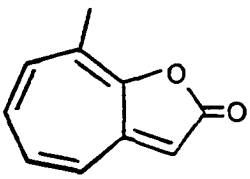
stronger steric effect on the initial Claisen rearrangement. The observed 2.4:1 ratio of 65 to 66 indicated that fragmentation also occurs from the carbene species.



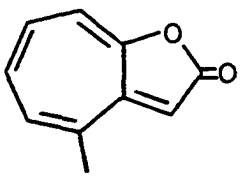
65



66



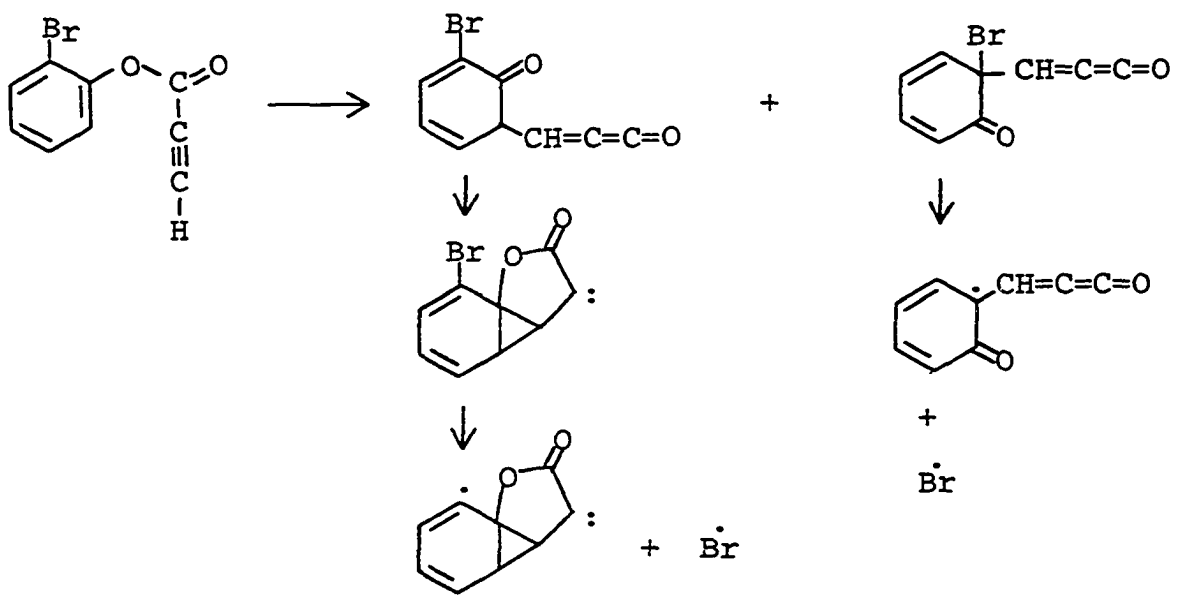
59



60

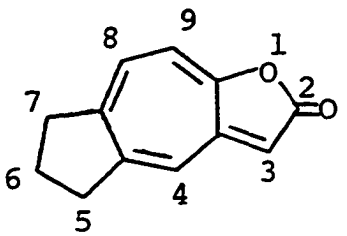
The FVP of o-bromophenyl propiolate produced inconsistent results; whereas, FVP of p-bromophenyl propiolate was well-behaved. Again the formation of radicals from the congested carbenes species and the allenyl ketene species may have caused the problem (Scheme XVIII).

Scheme XVIII

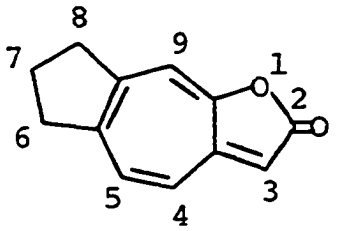


In characterizing 8-chloro-2H-cyclohepta[b]furan-2-one (61) hydrolysis and decarboxylation were again used. The success of the hydrolysis-decarboxylation sequence indicated that FVP of aryl propiolates could be a viable pathway to various substituted tropones (50). However, it was not possible to use a general set of hydrolysis-decarboxylation conditions for all the different compounds. The different conditions required for the degradation of 61 as compared to the conditions required for 55, 59, and 60 suggested conditions must be developed to accommodate the functionalities present.

Structure assignments of 6,7-dihydro-azuleno[6,5-b]-furan-2(5H)-one (69) and 7,8-dihydro-azuleno[5,6-b]furan-2-(6H)-one (70) required the knowledge of the lowfield position of the nmr signal of the hydrogen at position 4 and also, to some extent, the coplanar "w" coupling. Compound 69 was assigned based on the broad singlet at δ6.9 corresponding to the hydrogens at position 8 and 9. The other broad singlet (δ7.28) was assigned to the hydrogen at position 4. Compound 70 was assigned based on the singlet at δ6.95 corresponding to the hydrogen at position 9. The other two hydrogens gave rise to an AB pattern with the downfield signal being assigned to the hydrogen at position 4.

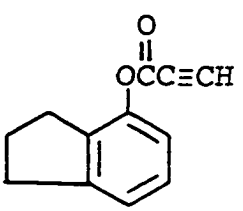


69

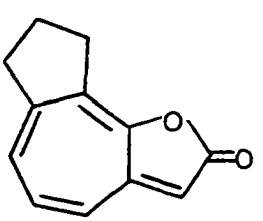


70

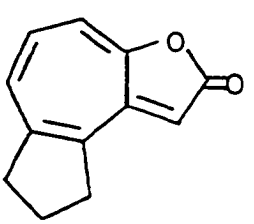
Structure assignments for the pyrolysis products of 4-indanyl propiolate (47) were again based on the hydrogen with the lowfield signal. The nmr spectrum with the multiplet (δ7.40-6.82) of three hydrogens was assigned to 8,9-dihydro-azuleno[4,5-b]furan-2(7H)-one (71). The singlet (δ6.94) of three hydrogens observed in the nmr spectrum was assigned to 5,6-dihydro-azuleno[5,4-b]furan-2(4H)-one (72).



47



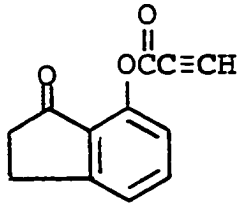
71



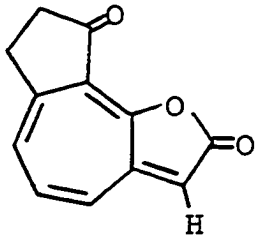
72

With 7-(1-oxoindanyl) propiolate (49) structure assignments of the two isomeric products, 75 and 76, were made easy by the large downfield shift of signal from the hydrogen at position 3 in one of the isomers.

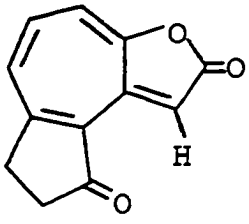
The deshielding cone of the ketonic carbonyl group from 76 encompassed the hydrogen at position 3, and thus, shifted its signal from the normal chemical shift of between 6 and 5 ppm to the aromatic region. The chemical shift of the corresponding hydrogen from 75 was not affected by the ketonic carbonyl (Figure 11).



49



75



76

The isomeric products from 7-(1-oxo-4-methylindanyl) propiolate (50) were similarly identified.

Structure assignments of the two products, 79 and 80, from the FVP of 6-(1-oxoindanyl) propiolate (51) were not straight forward. One of the isomers has one of its ring hydrogen signals shifted extremely downfield (δ7.91). Invoking deshielding by the ketonic carbonyl did not solve the problem of which isomer has this "downfield" proton. It appeared that both isomers have one of its hydrogens in the deshielding cone (Figure 12).

Figure 11. HA-100 nmr spectra of 7,8-dihydro-azuleno[4,5-b]-furan-2,9-dione (75) and 5,6-dihydro-azuleno-[5,4-b]furan-2,4-dione (76) in chloroform-d

Top: Spectrum of a mixture of 75 and 76

Middle: Spectrum of 75

Bottom: Spectrum of 76

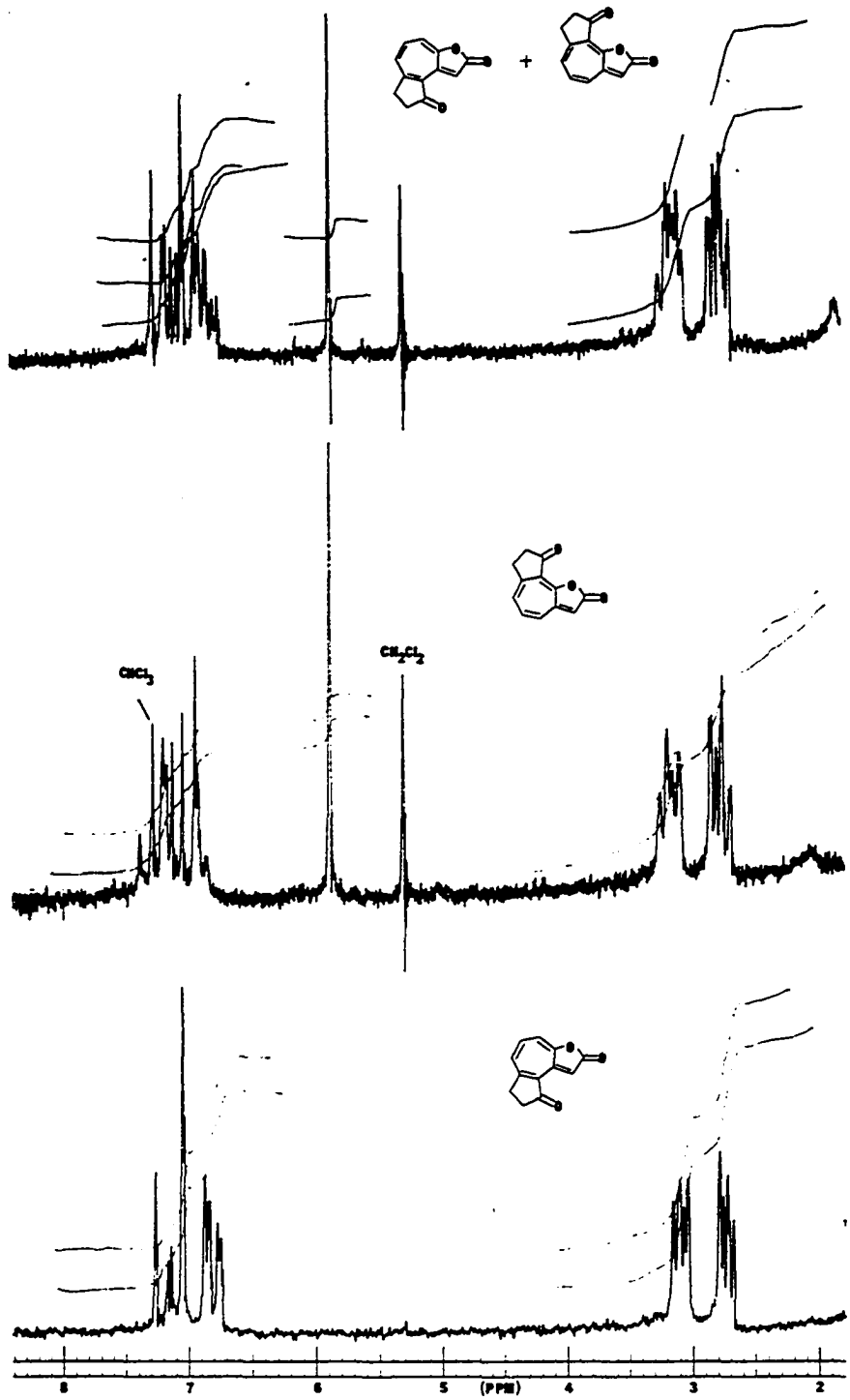
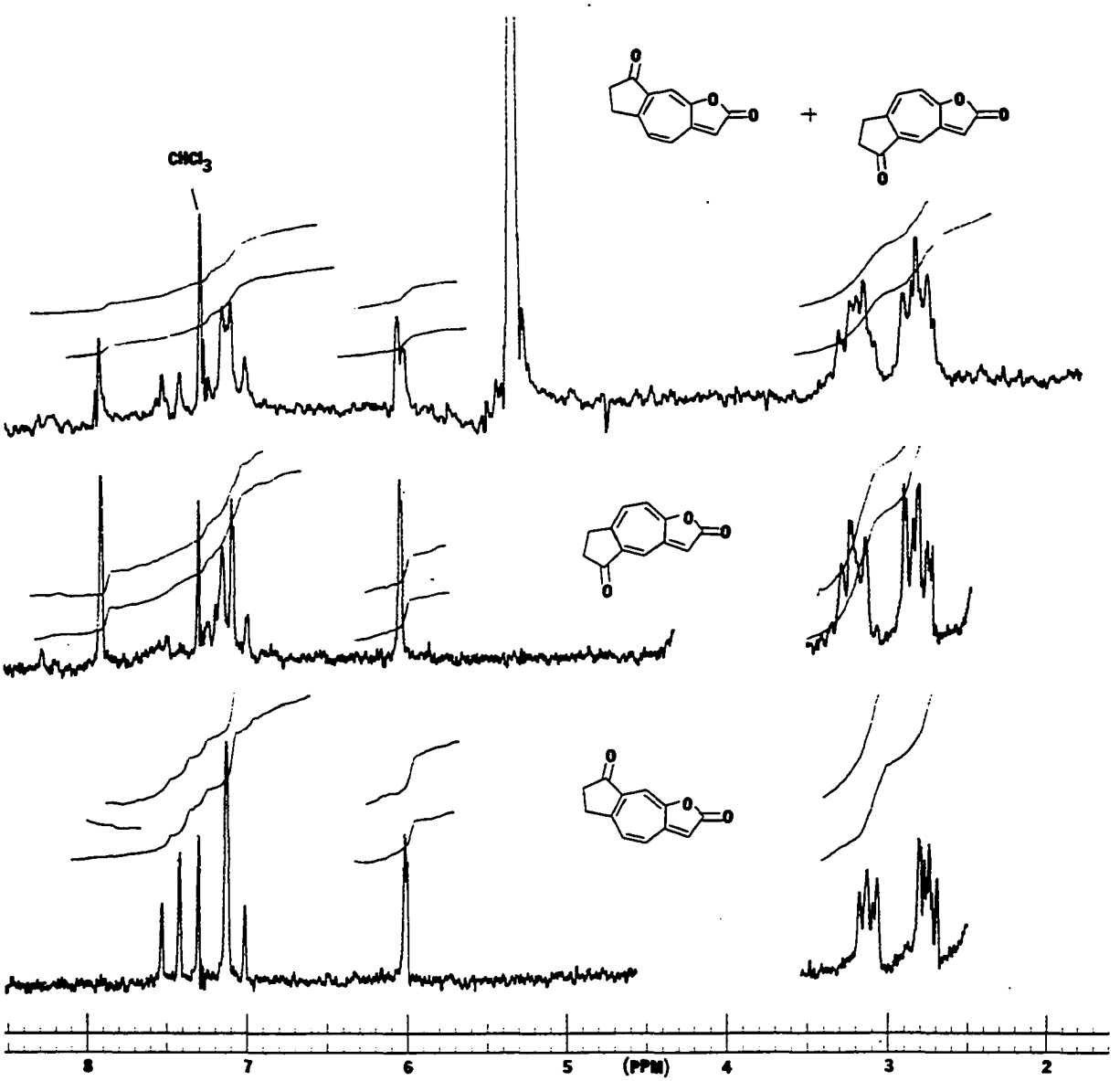

CHCl3
CH2Cl2
8
7
6
5
(PPM)
4
3
2

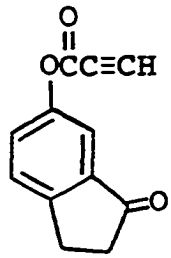
Figure 12. HA-100 nmr spectra of 6,7-dihydro-azuleno[6,5-b]-furan-2,5-dione (79) and 6,7-dihydro-azuleno-[5,6-b]furan-2,8-dione (80) in chloroform-d

Top: Spectrum of a mixture of 79 and 80

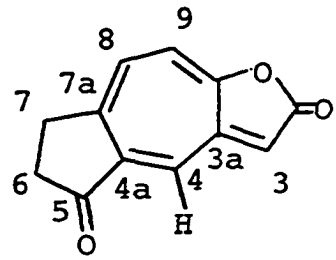
Middle: Spectrum of 79

Bottom: Spectrum of 80

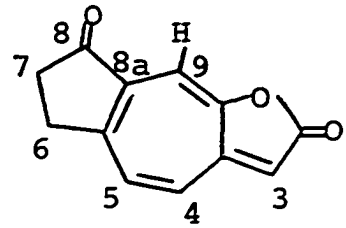

CHCl3
8
7
6
5
(PPM)
4
3
2



51

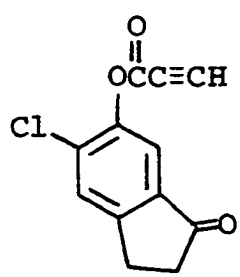


79

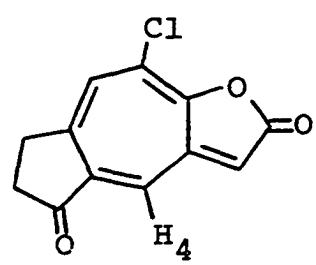


80

In compound 79 the hydrogen at position 4 appeared to be the one shifted downfield; however, in compound 80, hydrogen at position 9 appeared also to be in the deshielding cone. The nmr spectrum of the only product 6,7-dihydro-9-chloro-azuleno[6,5-b]furan-2,5-dione (81) from the pyrolysis of 6-(1-oxo-5-chloroindanyl) propiolate (52) conclusively identified 79 as the compound containing the "lowfield" hydrogen. The nmr spectrum of 81 showed a hydrogen at δ7.85 which would correspond to hydrogen at position 4.



52

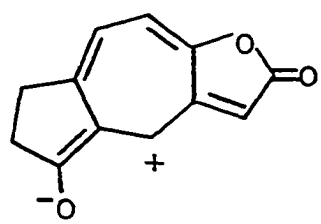


81

The absence of a deshielding effect in 80 is puzzling. One possible explanation may be in the localized nature of the ring double bonds. If this were true, then one could

argue that the hydrogen in question in 80 is further away from the carbonyl group than the corresponding hydrogen in 79. This is based on the difference in the lengths of the carbon-carbon (C_4-C_{4a}) double bond in 79 and carbon-carbon (C_{8a}-C_9) single bond in 80. It could be that the hydrogen in 79 lies in the fringe of the deshielding cone. And that the increased distance in the carbon-carbon single bond is enough to move the hydrogen in 80 outside the deshielding cone.

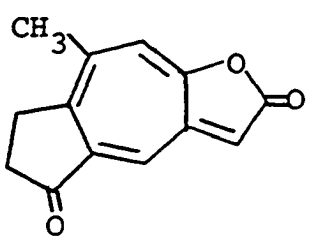
Another possibility or contribution to the shift downfield may lie in the fact that the hydrogen in 79 is bonded to the beta carbon of an α,β-unsaturated ketone system; whereas, the hydrogen in 80 is not (see structure 99).



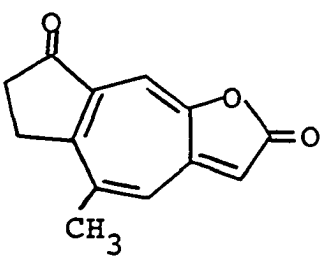
99

The pyrolyses of the indanone series of propiolates summarized in Table VII have some puzzling results. The yields are better when pyrolyses were done with an open tube. The deviation of the isomeric product ratio from 1:1 for the pyrolysis of 6-(1-oxoindanyl)- (51) and 6-(1-oxo-4-methylindanyl)- (53) propiolates was unexpected since there

are no ortho substituents in either 51 or 53. However, the different product ratios observed for 83 to 84 in different pyrolysis conditions may have provided the answer to the puzzling results. When the pyrolysis was carried out with a quartz-packed tube, a ratio of 2:1 was observed for the ratio of 83 to 84. The ratio changed to 1:2 when the pyrolysis was carried out with an open tube.



83



84

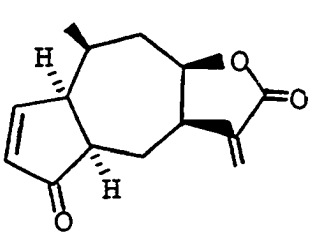
It appears that the activation energies for the formation of the isomeric products are quite different even though there are no ortho substituents. It is believed that compounds 80 and 84 have lower activation energies of formation than their isomeric products 79 and 83, respectively. However, 80 and 84 may not be as thermally stable as 79 and 83. The high pyrolysis temperature and longer residence time used for the pyrolysis of 53 may have decomposed some of the 84 formed before it has a chance to emerge from the hot zone. Without the quartz packing the delicate balance between the energy of activation and residence time favored 84. As for

compounds 79 and 80, the pyrolysis condition favoring the formation of 80 may be at temperatures lower than 750°C.

Feasibility of FVP in Synthesis

The indanyl and indanone series of propiolates were studied mainly to see if FVP of aryl propiolates could be used to get into the pseudoguaianolide and guaianolide carbon skeletons (15, 16, 17, and 18, Page 10) and eventually be incorporated as an intermediate step in the synthesis of some of these natural products. The success of these pyrolyses indicated that both three-ring systems of pseudoguaianolides and guaianolides could be obtained via FVP.

To realize the synthetic goal, Mexicanin-E (100), a nor pseudoguaianolide, was established as the target molecule. Mexicanin-E was chosen because it does not have the quaternary methyl group and it also has less functionalities than most pseudoguaianolides.

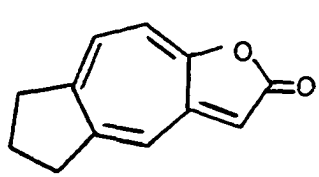


100

As seen from some of the structures of pseudoguaianolides given in the Historical Section, hydrogenation of the

pyrolysis products must occur somewhere in the synthetic sequence. Therefore, hydrogenation studies were done on a number of the pyrolysis products. Later on, hydrogenolysis of chlorinated products was also studied.

Hydrogenation of 2H-cyclohepta[b]furan-2-one (2) with palladium on charcoal in ethyl acetate went quite smoothly. The product obtained, cis-octahydro-2H-cyclohepta[b]furan-2-one (90) encouraged further work in this area (Figure 8, Page 55). Hydrogenation of 8-methyl-2H-cyclohepta[b]furan-2-one yielded a cis-fused ring junction although the stereochemistry of the methyl group is not known. A mixture of 6,7-dihydro-azuleno[6,5-b]furan-2(5H)-one (69) and 7,8-dihydro-azuleno[5,6-b]furan-2(6H)-one (70) was next hydrogenated and the product mixture obtained suggested complete reduction of all the carbon-carbon double bonds. The ^{1}H nmr spectrum suggested cis-fusion at the lactone ring junction. The stereochemistry at the other ring junction is unknown.



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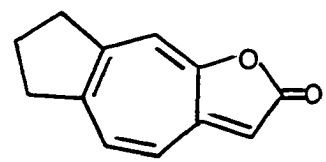


70

The ease with which the above compounds could be hydrogenated, the problems of isomeric product formation with only one isomer having the desired carbon skeleton, and the

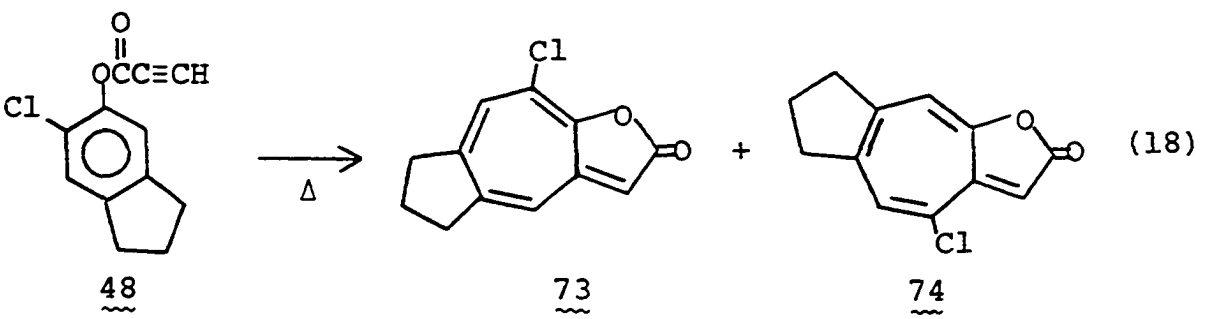
decomposition of products in the separation process instigated the investigation into the synthesis of some chlorinated propiolates which could undergo concurrent catalytical hydrogenation and hydrogenolysis of the carbon-chlorine bond.

o-Chlorophenyl propiolate (36) was initially pyrolyzed to determine whether the isomeric product ratio obtained from ortho-substituted phenyl propiolate was basically steric in nature as demonstrated by the product ratio of 4:1 observed for the pyrolysis of o-methylphenyl propiolate. The product ratio of 5:1 observed for the pyrolysis of 36 suggested minimal electronic effects.

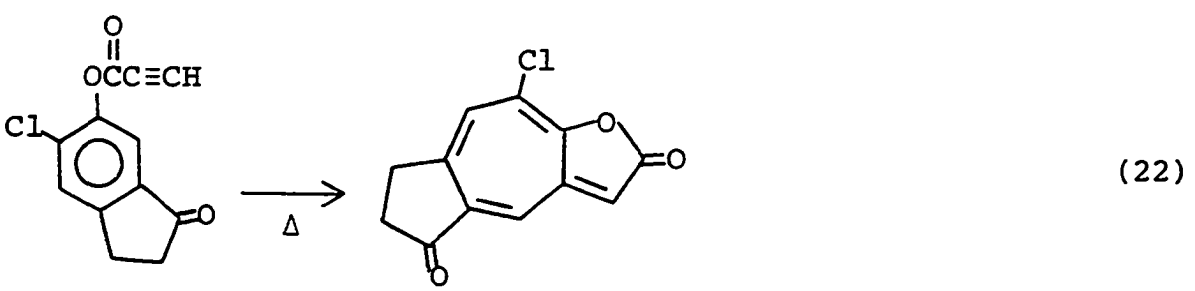
Later on the potential of using chlorine to influence the product ratio was explored. Alkyl groups were capable of controlling the selectivity of the pyrolysis; however, because of the inert nature of alkyl groups, they could not be removed. Chlorine offered both the directing potential and easy removability.

The directing potential was first demonstrated with the pyrolysis of o-chlorophenyl propiolate (36). Pyrolysis of 5-(6-chlorindanyl) (48) and 6-(1-oxo-5-chloroindanyl) (52) propiolates provided additional convincing evidence in support of the directing potential of chlorine. Pyrolysis of 48 yielded a 17:2 ratio of 6,7-dihydro-9-chloro-azuleno-[6,5-b]furan-2(5H)-one (73) to 4-chloro-7,8-dihydro-azuleno-

[5,6-b]furan-2(6H)-one (74) (Eq. 18). Pyrolysis of 52 yielded 51% of 6,7-dihydro-9-chloro-azuleno[6,5-b]furan-2,5-dione (81) and no 4-chloro-6,7-dihydro-azuleno[5,6-b]-furan-2,8-dione (82) (Eq. 22). The enhanced directing

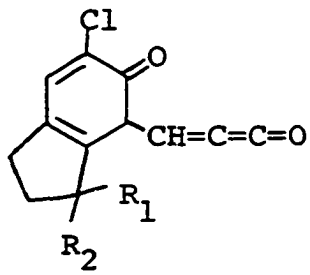


48 73 74 (18)



52 81 (22)

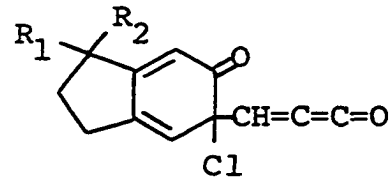
effect of the chlorine in 48 and 52 were attributed to the presence of the cyclopentane and cyclopentanone ring systems. Although the exact nature of how these rings affected the outcome is not obvious, one explanation might be related to the stability of the intermediate species 101 and 102 formed. Besides the steric hindrance involved in getting 102, species 101 may be more stable due to the presence of the tetra-substituted double bond.



101

R_1=H, R_2=H

R_1=R_2=O



102

The selectivity observed for the pyrolysis products from 48 and 52 has another advantage which became very important in the light of the separation problems encountered with the products from the indanone series of propiolates. For 52 separation was not necessary. For 48 fractional recrystallization was used to obtain the major isomer. Thus, the use of silica gel was avoided.

In order for fractional recrystallization to be effective, the ratio of the products must be highly favorable for one of the components. If fractional recrystallization could be used, time-consuming column chromatography can be avoided, and the decomposition problems associated with silica gel based separations can be eliminated.

Separation was not possible with alumina because of its polarity. Florisil was not used because no separation was obtained. GLPC separation was not acceptable because all the compounds are thermally labile.

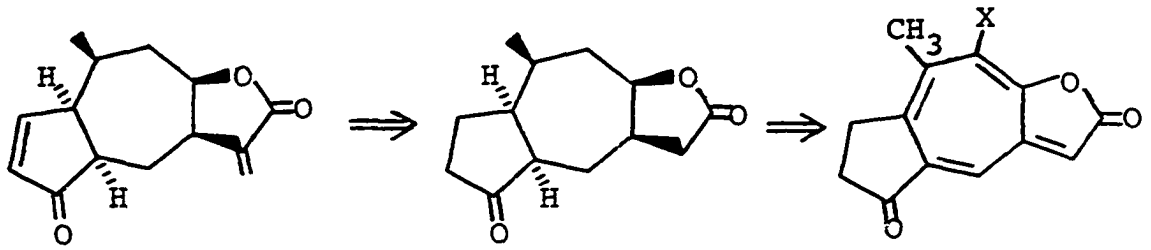
Hydrogenolysis of chlorine has been easily effected using hydrogenation conditions. Treating 6-chloro-2H-cyclohepta[b]furan-2-one (56) with palladium on charcoal in 95% ethanol and potassium acetate, two main products were obtained depending on the reaction time (Figure 10, Page 64). If the hydrogenation was allowed to go to completion, 90 was obtained (Eq. 27, Page 63). However, if the hydrogenation was terminated after a short time, a mixture of 2 and some trace amount of partially reduced 2 was obtained. It was not possible to obtain just pure 2 from the hydrogenolysis.

Attempted Synthesis of Mexicanin-E

The proposed synthesis of Mexicanin-E involves the synthesis and pyrolysis of 6-(1-oxo-4-methyl-5-chloroindanyl) propiolate (103) to yield 8-methyl-9-chloro-azuleno[6,5-b]-furan-2,5-dione (104). This is followed by the hydrogenolysis of the chlorine and hydrogenation of the double bonds of compound 104 to yield 105. The final stage of the proposed synthesis would be to add the exo-methylene moiety alpha to the lactone carbonyl group (Scheme XIX).

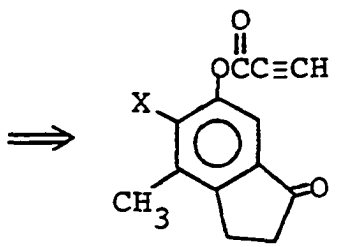
Transforming 105 into 100 could be done by a series of reactions already established by other investigators in this field (see Historical Section).

Scheme XIX



100 105 83 X=H

104 X=Cl



53 X=H

103 X=Cl

Synthesis of 103 was proposed to take advantage of the directing power of chlorine. It was hoped that the pyrolysis of 103 would produce only 104 and thus, would eliminate the problem of decomposition which usually accompanies separation of isomeric products.

However, the synthesis of chlorinated propiolate 103 was unsuccessful in the only attempt tried. Problems were encountered in placing the chlorine at the correct ortho position.

Since the synthesis depended upon the success of the hydrogenation reaction, a step that may not succeed, decision was made to leave the chlorine out and to synthesize and pyrolyze 5-(1-oxo-4-methylindanyl) propiolate (53).

The pyrolysis of 53 yielded 6,7-dihydro-8-methyl-azuleno[6,5-b]furan-2,5-dione (83) and 5-methyl-6,7-dihydro-azuleno[5,6-b]furan-2,8-dione (84) (Eq. 23). However, major difficulties were encountered in the separation of the isomeric mixture. Using silica gel column chromatography only a 11% isolated yield was obtained for 83. The poor isolated yield of 83 was the major obstacle in the subsequent hydrogenation study.

The poor yield could have been tolerated if the pyrolysis of 53 could have been scaled up. However, because of the low volatility of 53, which required about 4 hours to pyrolyze 500 mg of 53, and because of the low volatility and thermal lability of the product, problems were encountered. The low volatility of the products caused the products to condense at region A of the apparatus where they were exposed to the heat from the furnace (Figure 1, Page 27). The thermal lability of the products and the heat from the furnace made some decomposition of the products unavoidable. Scaling up the pyrolysis reaction for 53 beyond 500 mg per

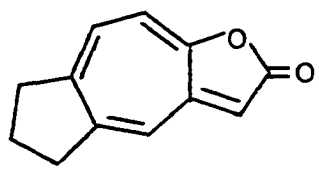
run was not feasible due to the longer time required for pyrolysis which meant more thermal decomposition of the products.

The decomposition problems associated with the separation of the isomeric pyrolysis products exist with all the products containing ketonic moieties. The necessity of applying a concentrated solution of the isomeric products to the acidic silica gel supports made the decomposition problem unavoidable. Although decomposition by silica gel is quite facile, the ketonic products are stable in acidic environments if they are in relatively dilute concentrations. At a concentration of 2 mg per ml of glacial acetic acid compounds 79, 80, 81, and 83 showed no decomposition over a 24 hr period. However, compound 84 was more sensitive to the acidic condition. It showed some decomposition within the 24 hr period. Unfortunately the decomposition problem is still a major obstacle in the study of these pyrolysis products.

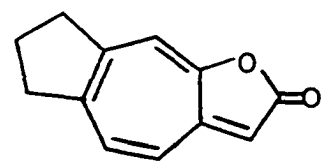
Subsequent hydrogenation of 83 and 84 using palladium on charcoal in ethyl acetate, ethanol, or glacial acetic acid always yielded mixtures of products. Hydrogenations of 81 in ethyl acetate also produced mixtures of products. No attempts were made to identify the products. Mass spectral data of the product mixtures from these hydrogenations

indicated the presence of compounds with all four carbon-carbon double bonds hydrogenated, mono-olefinic compounds, and compounds with two carbon-carbon double bonds remaining. Although no exhaustive hydrogenation study was made, these results suggested that the hydrogenation step may warrant more investigation to see whether it could be controlled somewhat.

The hydrogenation results suggested that the ketonic group is the culprit in these hydrogenations since catalytic hydrogenations of pyrolysis products without ketonic moieties presented no problems. All the carbon-carbon double bonds in isomeric compounds 69 and 70 were hydrogenated without any



69



70

difficulties. However, it is difficult to suggest a mechanism to explain the problems caused by the ketonic moiety without knowing the identities of some of the hydrogenation products.

If indeed, the ketonic groups was causing all the problems, then the possibility of masking the carbonyl group as a ketal or reducing it to a hydroxy group at the

propiolate stage may solve the problems. Then the problems encountered in the hydrogenation and the decomposition problems associated with the separation of the isomeric pyrolysis products may be eliminated.

The feasibility of using FVP of aryl propiolates to find a synthetic pathway to pseudoguaianolides and guaianolides depends on the success of the hydrogenation step. Presently, preliminary studies indicate the hydrogenation step may be a formidable problem. More extensive study of the hydrogenation step and the separation problem are required to provide the answer to whether FVP of aryl propiolate could be used in a synthetic pathway to pseudoguaianolides and guaianolides.

EXPERIMENTAL

Equipment and Special Methods

The pyrolysis apparatus (51,52) and generalized procedure for the flash vacuum pyrolysis (53) have been described previously. In all cases pyrolysis was carried out until all the starting material appeared to have reacted.

The pyrolysis apparatus modified for nitrogen-flow is shown in Figure 8.

IR spectra were obtained using Beckman IR-12A and IR-4250 spectrophotometers. Proton nmr spectra were recorded with Varian Associates HA-100 and A-60 spectrometers and a Hitachi Perkin-Elmer R-20B spectrometer. When only a small amount of sample was available for proton nmr analysis or when ^{13}C nmr spectra were needed, a Bruker HX 90 spectrometer and Nicolet 1089 computer operating in the Fourier transform mode were employed. Mass spectral analysis was performed on an Associated Electronics Industries MS-902 double focusing spectrometer. UV-VIS spectra were obtained with a Cary-14 spectrophotometer. Gas chromatographic analyses were performed with a Varian Aerograph Series 1700 gas chromatograph. Catalytic hydrogenations were done with a Parr hydrogenator and a sloping-manifold atmospheric hydrogenator.

Melting points were obtained with either a Thomas Hoover capillary melting point apparatus or, in the case

of a small quantity of material, with a Kofler Hotstage apparatus. All melting points were uncorrected.

Commercial Compounds

The chemicals obtained from commercial sources are listed in Table VIII.

Synthesis of Aryl Propiolates

All the aryl propiolates were prepared using the general procedure described by Miller (47).

Propiolyl chloride

Propiolyl chloride was prepared using one of the procedures described by Balfour et al. (54). A 5.60g (0.08 mol) portion of propiolic acid was added dropwise over 20 min period to 16.66g (0.08 mol) of phosphorous pentachloride in a 50 ml round bottom flask. The flask was cooled in an ice bath during addition. After completion of addition, the pale brown solution was stirred at room temperature for 2 hr. The solution was then distilled to yield 3.57g (50.4%) of propiolyl chloride (bp 57-58°C).

Phenyl propiolate (1)

Propiolyl chloride (7.14g, 0.08 mol) in 25 ml of benzene was added dropwise to a cooled mixture consisting of 7.55g (0.08 mol) of phenol, 3.21g (0.08 mol) of sodium hydroxide, 25 ml of benzene, and 100 ml of water. After the completion of addition, the mixture was stirred at room temperature for 12 hr. Then the reaction mixture was

Table VIII. Source of commerical compounds

Compound	Source
Acetone	Fisher Scientific Co. (Fisher)
Acetone-d_6	Norell Chemical Co., Inc.
Alumina	J. T. Baker Chemical Co. (Baker)
Aluminum chloride	Fisher
Benzene	Fisher
o-Bromophenol	Matheson Coleman and Bell (MCB)
p-Bromophenol	The Matheson Co., Inc.
Carbon tetrachloride	Fisher
Chloroform	Fisher
Chloroform-d	Aldrich Chemical Co., Inc. (Aldrich)
o-Chlorophenol	Aldrich
p-Chlorophenol	MCB
3-Chloropropionate	Aldrich
p-Cresol	Eastman Organic Chemicals
Cyclohexane	Baker
Deuterium oxide	Columbia Organic Chemicals, Co., Inc.
2,4-Dichlorophenol	Aldrich
2,6-Dimethylphenol	Aldrich
Dimethyl sulfoxide-d_6	Norell Chemical Co., Inc.
Ethyl acetate	Fisher
Ethyl ether	Mallinckrodt
Glacial acetic acid	Fisher
n-Hexane	MCB
Hexanes	Fisher
Hydrochloric acid	Fisher
Hydrogen chloride	Matheson Gas Products
Hydroquinone	Mallinckrodt, Inc.
p-Hydroxybenzaldehyde	Baker
4-Indanol	Pfaltz & Bauer, Inc.
5-Indanol	Aldrich

Table VIII. (Continued)

Compound	Source
o-Isopropylphenol	Aldrich
Magnesium sulfate	Fisher
Malonic acid	Baker
m-Methylanisole	Aldrich
Methylene chloride	Fisher
o-Methylphenol	Aldrich
p-Methoxyphenol	MCB
Palladium on charcoal	MCB
Phenol	Baker
Phosphoric acid	Fisher
Phosphorous pentachloride	MCB
Phosphorous pentoxide	MCB
Platinum oxide	Sargent-Welch Scientific Co.
Pyridine	Baker
Silica gel (60-200 and 40-140 mesh)	Baker
Silica gel (60 PF-254)	Brinkmann Instruments, Inc.
Sodium hydroxide	Fisher
Sodium sulfate	Fisher
Sulfuryl chloride	Baker
Thionyl chloride	Fisher
Toluene	Baker
p-Toluenesulfonic acid	Baker
2,4,6-Trimethylphenol	Aldrich
Zinc cyanide	Fisher

extracted three times with 50 ml of ether. The combined ethereal solution was washed with 50 ml of 10% sodium hydroxide, 50 ml of 10% hydrochloric acid, and 50 ml of saturated sodium chloride. Then it was dried ($MgSO_4$) and filtered. The ether was removed by vacuum rotary evaporation. The phenyl propiolate (47) was distilled at reduced pressure. Yield, 8.00g (68.5%); bp 77°C/3.9 Torr; nmr (CCl_4) δ7.48-6.95 (m, 5, ArH) and 2.95 (s, 1, -C≡CH); ir(CCl_4) 3310, 2125, 1742, 1490, and 1192 cm^{-1}.

2,6-Dimethylphenyl propiolate (33)

A 3.57g (0.04 mol) portion of propiolyl chloride in 10 ml of benzene was added dropwise to an ice-bath cooled mixture containing 4.98g (0.04 mol) of 2,6-dimethylphenol, 1.60g (0.04 mol) of sodium hydroxide, 10 ml of benzene, and 40 ml of water. After the completion of addition, the mixture was stirred at room temperature for 11 1/2 hr and then extracted three times (50 ml, 25 ml, 25 ml) with ether. The ethereal solution was washed with 30 ml of 10% sodium hydroxide, 30 ml of 10% hydrochloric acid, 30 ml of saturated sodium chloride solution, and then dried ($MgSO_4$). The ether was removed on a rotary evaporator to yield a white crystalline solid. It was recrystallized three times from hexanes. Yield, 2.03g (29.1%); mp 41-42°C; MS, m/e (70 eV), 174, 159, 145, 131, 122, 107, and 91; exact mass calcd for $C_{11}H_{10}O_2$: 174.0681; found: 174.0684 ± 0.0008;

nmr (proton, $CDCl_3$) δ7.02 (s, 3, ArH), 3.00 (s, 1, -C≡CH), and 2.17 (s, 6, $-CH_3$); ir (CCl_4) 3310, 2130, 1743, 1205, and 1157 cm^{-1}.

2,4,6-Trimethylphenyl propiolate (34)

A 2.67g (0.03 mol) portion of propiolyl chloride in 10 ml of benzene was added dropwise to an ice-bath cooled mixture containing 4.10g (0.03 mol) of 2,4,6-trimethylphenol, 1.20g (0.03 mol) of sodium hydroxide, 10 ml of benzene, and 40 ml of water. After the addition was completed, the mixture was stirred at room temperature for 28 hr and then extracted three times (75 ml, 50 ml, and 50 ml) with ether. The combined ethereal solution was washed with 50 ml of 10% sodium hydroxide, 50 ml of 10% hydrochloric acid, 50 ml of saturated sodium chloride solution, and then dried ($MgSO_4$). The ether was removed on a rotary evaporator to yield a yellow oil from which a white solid was precipitated. The white solid was recrystallized from n-heptane. Yield, 2.53g (33.7%); mp 57-58°C; MS, m/e (70 eV), 188, 136, and 91; exact mass calcd for $C_{12}H_{12}O_2$: 188.0837; found: 188.0846 ± 0.0010; nmr (proton, $CDCl_3$) δ6.83 (s, 2, ArH), 2.98 (s, 1, -C≡CH), 2.25 (s, 3, $-CH_3$), and 2.13 (s, 6, $-CH_3$); ir (CCl_4) 3310, 2130, 1740, 1200, and 1130 cm^{-1}.

p-Chlorophenyl propiolate (40)

A 5.23g (0.059 mol) portion of propiolyl chloride in 10 ml of benzene was added dropwise to a cooled mixture containing 2.36g (0.059 mol) of sodium hydroxide, 7.58g (0.059 mol) of p-chlorophenol, 10 ml of benzene, and 40 ml of water. The resulting mixture was stirred at room temperature for 10 hr and then extracted three times (50 ml, 25 ml, and 25 ml) with ether. The combined ethereal solution was washed with 25 ml of 10% sodium hydroxide, 25 ml of 10% hydrochloric acid, 25 ml (twice) of saturated sodium chlcride solution, and then dried ($MgSO_4$). The ether was removed on a rotary evaporator to yield a white solid. The white solid was recrystallized from hexanes. Yield, 9.99g (94%); mp 72-73°C; MS, m/e (18 eV) 182(33), 180(100), 154(10), 152(34), 145(11), 130(13), 128(41), 126(21), and 124(68); exact mass calcd for $C_9H_5ClO_2$: 179.99781; found: 179.99803; nmr ($CDCl_3$) δ7.45-6.90 (AA'BB' pattern, ArH) and 3.00 (s, 1, -C≡CH); ir ($CHCl_3$) 3300, 2120, 1735, 1480, 1165, and 1085 cm^{-1}.

p-Bromophenyl propiolate (41)

A 3.78g (0.043 mol) portion of propiolyl chloride in 10 ml of benzene was added dropwise to a mixture containing 7.39g (0.043 mol) p-bromophenol, 1.72g (0.043 mol) of sodium hydroxide, 10 ml of benzene, and 50 ml of water. The resulting mixture was stirred at room temperature for

18 hr and then extracted three times with 25 ml of ether. The combined ethereal solution was washed with 25 ml of 10% sodium hydroxide, 25 ml of 10% hydrochloric acid, 25 ml of saturated sodium chloride solution, and then dried ($MgSO_4$). The ether was removed on a rotary evaporator to yield a white solid. The solid was recrystallized from hexanes and then sublimed (56° C/0.05 Torr). Yield, 5.68g (60%); mp 57-58°C; MS, m/e (70 eV) 226(32), 224(36), 174(06), 172(100), 130(11), 94(14), and 53(68); exact mass calcd for $C_9H_5BrO_2$: 223.94729; found: 223.94688; nmr ($CDCl_3$) δ7.23 (AA'BB' pattern, ArH) and 3.05 (s, 1, -C≡CH); ir ($CHCl_3$) 3300, 2120, 1735, 1475, 1165, 1060, 1005, and 905 cm^{-1}.

p-Formylphenyl propiolate (42)

A 5.11g (0.058 mol) portion of propiolyl chloride in 10 ml of benzene was added dropwise to a mixture containing 7.08g (0.058 mol) of p-hydroxybenzaldehyde, 2.32g (0.058 mol) of sodium hydroxide, 10 ml of benzene, and 40 ml of water. The resulting mixture was stirred at room temperature for 11 1/2 hr and then extracted with ether (75 ml, 25 ml, and 25 ml). The combined ethereal solution was washed twice, successively with 25 ml of 10% sodium hydroxide, 25 ml of 10% hydrochloric acid, and 25 ml of saturated sodium chloride solution. After drying ($MgSO_4$) the ether was removed to yield a pink solid. The pink solid was recrystallized from chloroform-hexanes to yield

a white solid. Yield, 3.83g (38%); mp 96-97°C; MS, m/e (70 eV) 174(92), 173(33), 145(83), 144(100), 121(25), 120(25), 117(42), and 89(58); exact mass calcd for $C_{10}H_6O_3$: 174.03170; found: 174.03244; nmr ($CDCl_3$) δ10.35 (s, 1, -CHO), 8.08-7.32 (AA'BB' pattern, ArH), and 3.18 (s, 1, -C≡CH); ir ($CHCl_3$) 3300, 2120, 1735, 1700, 1600, 1165, and 1150 cm^{-1}.

p-Hydroxyphenyl propiolate (43)

The procedure of Chattaway (55) as modified by Olcott (56) was used. A 8.27g (0.078 mol) portion of sodium carbonate was dissolved in 25 ml of water. Then 25g of crushed ice was added. Next, 5.72g (0.052 mol) of hydroquinone was added. The mixture was stirred rapidly for 10 min before 4.60g (0.052 mol) of propiolyl chloride was added. The resulting white mixture was stirred for 1 1/2 hr at room temperature, then the solid was filtered and washed with water. The filtrate was acidified with 10% hydrochloric acid and extracted with three 50-ml portions of ether. The combined ethereal solution was washed twice with saturated sodium chloride solution (25 ml) and then dried ($MgSO_4$). The solvent was removed on a rotary evaporator to yield a slightly brown solid. The product was recrystallized from chloroform-ether to yield a tan solid. Yield, 0.49g (6%); mp 169-171°C; MS, m/e (70 eV) 162(0), 110(100), 82(25), 81(43), 55(28), and 53(31); no molecular ion peak observed;

nmr (d_6-acetone) δ8.20 (bs, 1H), 6.72 (s, 4H), and 3.68 (s, 1H); ir ($CHCl_3$) 3600-2400, 3300, 2120, 1715, 1600, and 1160 cm^{-1}.

p-Acetoxyphenyl propiolate (44)

A 2.11g (0.024 mol) portion of propiolyl chloride in 10 ml of benzene was added dropwise to a brown solution containing 3.62g (0.024 mol) of hydroquinone monoacetate, 0.952g (0.024 mol) of sodium hydroxide, 10 ml of benzene, and 40 ml of water. The resulting mixture was stirred at room temperature for 12 hr and then extracted three times with ether (25 ml). The combined ethereal solution was washed with 25 ml of 10% sodium hydroxide, 25 ml of 10% hydrochloric acid, 25 ml of saturated sodium chloride solution, and then dried ($MgSO_4$). The ether was removed to yield a white solid. The solid was recrystallized twice from Skelly B-ether. Yield, 1.91g (42%); mp 90-91°C; MS, m/e (70 eV) 204(16), 163(10), 162(100), 134(20), 110(96), 109(12), and 106(31); exact mass calcd for $C_{11}H_8O_4$: 204.043362; found: 204.041427; nmr ($CDCl_3$) δ7.22 (m, 4, ArH), 3.07 (s, 1, -C≡CH), and 2.30 (s, 3, $-OCOCH_3$); ir ($CHCl_3$) 3300, 2130, 1755 and 1735 (doublet), 1495, 1370, and 1160 cm^{-1}.

p-Methoxyphenyl propiolate (45)

A 2.96g (0.033 mol) portion of propiolyl chloride in 10 ml of benzene was added dropwise to a mixture containing

4.16g (0.033 mol) of p-methoxyphenol, 1.34g (0.033 mol) of sodium hydroxide, 10 ml of benzene, and 40 ml of water. The resulting mixture was stirred at room temperature for 2 hr and then extracted three times with ether (25 ml). The combined ethereal solution was washed twice, successively with 25 ml of 10% sodium hydroxide, 25 ml of 10% hydrochloric acid, and 25 ml of saturated sodium chloride solution. After drying ($MgSO_4$) the ether was removed to leave an orange oil. p-Methoxyphenyl propiolate was crystallized from the oil; it was then recrystallized from hexanes to yield a white solid. Yield, 3.57g (61%); mp 38-39°C, lit (47) bp 90°C/0.3 Torr; MS, m/e (70 eV) 176(57), 124(100), 123(45), 120(24), 109(34), 95(19), and 53(33); exact mass calcd for $C_{10}H_8O_3$: 176.04735; found: 176.04680; nmr ($CDCl_3$) δ6.87(m, 4, ArH), 3.67 (s, 3, $-OCH_3$), and 3.08, (s, 1, $-C\equiv CH$); ir ($CHCl_3$) 3300, 2130, 1735, 1500, and 1175 cm^{-1}.

o-Methylphenyl propiolate (35)

A 4.46g (0.05 mol) portion of propiolyl chloride in 10 ml of benzene was added dropwise to a cooled mixture containing 2.0g (0.05 mol) of sodium hydroxide, 5.46g (0.05 mol) of o-cresol, 10 ml of benzene, and 50 ml of water. The resulting mixture was stirred at room temperature for 16 hr and then extracted three times (25 ml) with ether. The combined ethereal solution was washed with 25 ml of 10% sodium hydroxide, 25 ml of 10% hydrochloric acid, and twice

with saturated sodium chloride solution (25 ml). After drying ($MgSO_4$) the ether was removed on a rotary evaporator to yield a red oil. The red oil was vacuum distilled to give 4.22g (53%) of o-methylphenyl propiolate, a clear, colorless liquid. BP 64-66°C/1.0-1.1 Torr; MS, m/e (70 eV), 160(95), 108(100), 107(35), 53(75), and 43(40); exact mass calcd for $C_{10}H_8O_2$: 160.05243; found: 160.051; nmr ($CDCl_3$) δ7.08 (m, 4, ArH), 2.92 (s, 1, -C≡CH), and 2.17 (s, 3, $-CH_3$); ir ($CHCl_3$) 3300, 2120, 1730, 1490, 1170, and 1105 cm^{-1}.

o-Chlorophenyl propiolate (36)

A 5.14g (0.058 mol) portion of propiolyl chloride in 10 ml of benzene was added dropwise to a cooled mixture containing 7.46g (0.058 mol) of o-chlorophenol, 2.32g (0.058 mol) of sodium hydroxide, 10 ml of benzene, and 40 ml of water. The resulting mixture was stirred at room temperature for 11 hr and then extracted with ether (three times, 25 ml). The combined ethereal solution was washed with 25 ml of 10% hydrochloric acid, and twice with saturated sodium chloride solution (25 ml). After drying ($MgSO_4$) the ether was removed to yield an oil. The oil was vacuum distilled to yield 8.96g (86%) of o-chlorophenyl propiolate. BP 85°C/1.3 Torr MS, m/e (20 eV) 182(17), 180(50), 154(6), 152(19), 145(100), 130(10), 128(29), 126(12), 124(35), and 90(19); exact mass calcd for $C_9H_5ClO_2$: 179.99781; found: (70 eV): 179.99767;

nmr ($CDCl_3$) δ7.62-7.00 (m, 4, ArH), and 3.13 (s, 1, -C≡CH); ir ($CHCl_3$) 3290, 2110, 1740, 1470, 1445, 1160, 1125, and 1055 cm^{-1}.

o-Bromophenyl propiolate (37)

A 4.49g (0.051 mol) portion of propiolyl chloride in 10 ml of benzene was added dropwise to a cooled mixture containing 8.77g (0.051 mol) of o-bromophenol, 2.03g (0.051 mol) of sodium hydroxide, 10 ml of benzene, and 40 ml of water. The resulting mixture was stirred at room temperature for 27 1/2 hr and then extracted with ether (three times, 25 ml). The combined ethereal solution was washed with 25 ml of 10% sodium hydroxide, 25 ml of 10% hydrochloric acid, and twice with saturated sodium chloride solution (25 ml). After drying ($MgSO_4$) the ether was removed to yield a viscous pink oil. The pink oil was vacuum distilled to give 10.22g (90%) of o-bromophenyl propiolate, a clear, colorless liquid. BP 70-72° C/0.18 Torr; MS, m/e (70 eV) 226(19), 224(19), 174(22), 172(21), 146(33), 145(100), 94(26), 90(38), 89(35), 65(22), 64(19), and 63(30); exact mass calcd for $C_9H_5BrO_2$: 223.94729; found: 223.94644; nmr (CCl_4) δ7.83-7.00 (m, 4, ArH) and 3.06 (s, 1, -C≡CH); ir ($CHCl_3$) 3300, 2120, 1735, 1460, and 1160 cm^{-1}.

o-Isopropylphenyl propiolate (38)

A 6.04g (0.068 mol) portion of propiolyl chloride in 10 ml of benzene was added dropwise to a mixture containing

9.6g (0.068 mol) of o-isopropylphenol, 2.72g (0.068 mol) of sodium hydroxide, 20 ml of benzene, and 40 ml of water. The resulting mixture was stirred at room temperature for 11 hr and then extracted three times with ether (25 ml). The combined ethereal solution was washed with 25 ml of 10% sodium hydroxide, 25 ml of 10% hydrochloric acid, 25 ml of saturated sodium chloride solution, and then dried (Na_2SO_4). The solvent was removed on a rotary evaporator to yield an oil. The oil was distilled (57°C/0.22 Torr) to yield 10.5g (82.1%) of o-isopropylphenyl propiolate. MS, m/e (70 eV) 188(12), 173(10) 145(53), 136(27) 135(51), 121(100), 118(24), 117(12), and 103(18); exact mass calcd for $C_{12}H_{12}O_2$: 188.08373; found: 188.08371; nmr ($CDCl_3$) δ7.38-6.87(m, 4, ArH), 3.33-2.80 (septet, J=7 Hz, 1, -CH-), 3.00(m, 1, -CH-), 3.00(s, 1, -C≡CH), and 1.20(d, 6, CH_3); ir (CCl_4) 3300, 2960, 2120, 1735, 1190, and 1075 cm^{-1}.

2,4-Dichlorophenyl propiolate (39)

A 5.74g (0.065 mol) portion of propiolyl chloride in 10 ml of benzene was added dropwise over 15 min period to a mixture containing 10.60g (0.065 mol) of 2,4-dichlorophenol, 2.6g (0.065 mol) of sodium hydroxide, 10 ml of benzene, and 40 ml of water. The resulting mixture was stirred at room temperature for 18 hr and then extracted three times with ether (25 ml). The combined ethereal solution was washed with 25 ml of 10% sodium hydroxide, 25 ml of 10% hydro-

chloric acid, twice with 25 ml of saturated sodium chloride solution, and then dried ($MgSO_4$). The ether was removed to yield a white solid. The solid was sublimed (58° C/0.2 Torr) to give 9.4g (68%) of 2,4-dichlorophenyl propiolate, a white solid. MP 59-60°C, lit (47) mp 61-62°C; MS, m/e (70 eV) 216(9), 214(15), 181(34), 179(100), 164(25), 162(46), 160(33), 158(51), 135(37), 133(57), and 123(27); exact mass calcd for $C_9H_4Cl_2O_2$: 213.95884; found: 213.96056; nmr ($CDCl_3$) δ7.53-7.05 (m, 3, ArH) and 3.07 (s, 1, -C≡CH); ir ($CHCl_3$) 3290, 2110, 1740, 1595, 1465, 1165, 1130, and 1090 cm^{-1}:

5-Indanyl propiolate (46)

The 5-indanol was recrystallized from n-hexane before use. A 6.02g (0.068 mol) portion of propiolyl chloride in 25 ml of benzene was added dropwise to a mixture containing 9.12g (0.068 mol) of 5-indanol, 2.72g (0.068 mol) of sodium hydroxide, 25 ml of benzene, and 100 ml of water. The resulting mixture was stirred at room temperature for 11 hr and then extracted three times with ether (25 ml). The combined ethereal solution was washed with 10% sodium hydroxide, 10% hydrochloric acid, and saturated sodium chloride solution. After drying ($MgSO_4$) the solvent was removed to yield a white solid. The solid was recrystallized three times from n-hexane. Yield, 5.64g (44.6%); mp 69-70°C; MS, m/e (70 eV) 186(100), 158(50), 134(75), 129(69), 114(44),

91(12), 77(31), and 53(44); exact mass calcd for $C_{12}H_{10}O_2$: 186.0681; found: 186.0682 ± 0.0009; nmr (CCl_4) δ6.97 (m, 3, ArH), 2.46 (m, 5, -C≡CH, -CH_2-CH_2-CH_2-), and 2.09 (m, 2, -CH_2-CH_2-CH_2-); ir (CCl_4) 3310, 2120, 1740, and 1195 cm^{-1}.

4-Indanyl propiolate (47)

4-Indanol was purified by sublimation before use. A 4.14g (0.0468 mol) portion of propiolyl chloride in 110 ml of benzene was added dropwise to a mixture containing 6.27g (0.0468 mol) of 4-indanol, 1.872g (0.0468 mol) of sodium hydroxide, 10 ml of benzene, and 40 ml of water. The resulting mixture was stirred at room temperature for five hr and extracted three times with ether (25 ml). The combined ethereal solution was washed with 25 ml of 10% sodium hydroxide, 25 ml of 10% hydrochloric acid, 25 ml of saturated sodium chloride solution, and then dried ($MgSO_4$). The solvent was removed to yield a solid. The solid was purified by sublimation (40-42°C/0.05 Torr). Yield, 7.56g (87%); mp 47-49°C; MS, m/e (18 eV) 187(17), 186(100), 185(13), 158(40), 157(33), 134(30), 130(30), 129(40), 117(17), 116(50), and 115(20); exact mass calcd for $C_{12}H_{10}O_2$: 186.068082; found (70 eV): 186.066443; nmr (CCl_4) δ7.30-6.77 (m, 3, ArH), 3.17-2.65 (m, 5, -C≡CH, -CH_2-CH_2-CH_2-), and 2.42-1.77 (m, 2, -CH_2-CH_2-CH_2-); ir (CCl_4) 3300, 2950, 2120, 1735, 1465, 1185, and 1155 cm^{-1}.

5-(6-Chloroindanyl) propiolate (48)

A 2.53g (0.0286 mol) portion of propiolyl chloride in 10 ml of benzene was added dropwise to a mixture containing 6.30g (28.6 mmol) of 6-chloro-5-indanol, 1.14g (28.6 mmol) of sodium hydroxide, 10 ml of benzene, and 40 ml of water. The resulting white mixture was stirred at room temperature for five hr and then extracted three times with ether. The combined ethereal solution was washed with 25 ml of 10% sodium hydroxide, 25 ml of 10% hydrochloric acid, 25 ml of saturated sodium chloride solution, and dried ($MgSO_4$). The solvent was removed on a rotary evaporator to yield a white solid. The solid was recrystallized from hexanes. Yield, 5.22g (70%); mp 90-91°C; MS, m/e (70 eV) 222(9), 220(26), 185(100), 170(12), 168(38), 167(14), 133(38), 132(8), 129(17), and 103(23); exact mass calcd for $C_{12}H_9O_2Cl$: 220.02911; found: 220.02877; nmr ($CDCl_3$) δ7.38 (s, 1, ArH), 7.10 (s, 1, ArH), 3.12 (s, 1, -C≡CH), 3.08-2.67 (m, 4, -$\underline{CH_2}$-CH_2-$\underline{CH_2}$-), and 2.42-1.75 (m, 2, -CH_2-$\underline{CH_2}$-CH_2-); ir ($CHCl_3$) 3300, 2130, 1740, and 1170 cm^{-1}.

7-(1-Oxoindanyl) propiolate (49)

A 0.628g (7.1 mmol) portion of propiolyl chloride in 10 ml of benzene was added dropwise to a mixture containing 1.05g (7.1 mmol) of 7-hydroxy-1-indanone, 0.42g (7.1 mmol) of sodium hydroxide, 10 ml of benzene, and 30 ml of water. The resulting mixture was stirred at room temperature for

16 hr and then extracted three times with ether (25 ml). The combined ethereal solution was washed with 25 ml of 10% sodium hydroxide, 25 ml of 10% hydrochloric acid, 25 ml of saturated sodium chloride solution, and dried ($MgSO_4$). The solvent was removed to yield a white solid. The solid was recrystallized from hexanes. Yield, 1.035g (72.9%); mp 102-104°C; MS, m/e (70 eV) 200(13), 172(94), 171(15), 148(100), 147(33), 146(14), 144(75), 120(39), 119(22), 116(37), and 115(32); exact mass calcd for $C_{12}H_8O_3$: 200.04735; found: 200.04571; nmr ($CDCl_3$) δ7.58-6.90 (m, 3, ArH), 3.28-2.97 (m, 3, -C≡CH, $-CH_2-CH_2-CO$) and 2.83-2.50 (m, 2, $-CH_2CO$); ir ($CHCl_2$) 3300, 2120, 1735, 1710, 1610, and 1165 cm^{-1}.

7-(1-Oxo-4-methylindanyl) propiolate (50)

A 3.17 g (0.036 mol) portion of propiolyl chloride in 10 ml of benzene was added dropwise to a mixture containing 5.80g (0.036 mol) of 4-methyl-7-hydroxy-1-indanone, 2.86g (0.072 mol) of sodium hydroxide, 50 ml of benzene, and 60 ml of water. The resulting mixture was stirred at room temperature for 10 hr and then extracted three times with ether (100 ml). The combined ethereal solution was washed with three 25-ml portions of 10% sodium hydroxide, two 50-ml portions of saturated sodium chloride solution, and then dried ($MgSO_4$). The solvent was removed to yield a solid. The solid was sublimed (70°C/0.55 Torr). Yield, 3.17g

(41.4%); mp 163-165°C; MS, m/e (70 eV) 214(15), 186(82), 162(100), 161(28), 158(75), 134(28), 133(61), 129(30), 120(32), and 115(30); exact mass calcd for $C_{13}H_{10}O_3$: 214.062997; found: 214.06409; nmr ($CDCl_3$) δ7.41 and 6.98 (AB pattern, J=8 Hz, ArH), 3.13 (s, 1, -C≡CH), 3.22-2.92 (m, 2, -CH_2-CH_2-CO), 2.82-2.53 (m, 2, -CH_2-CO), and 2.35 (s, 3, CH_3); ir ($CHCl_3$) 3300, 2120, 1735, 1710, 1600, and 1165 cm^{-1}.

6-(1 Oxoindanyl) propiolate (51)

A 5.73g (0.0647 mol) portion of propiolyl chloride in 20 ml of benzene was added dropwise to a mixture containing 8.33g (0.0563 mol) of 6-hydroxy-1-indanone, 2.25g (0.0563 mol) of sodium hydroxide, 50 ml of benzene, and 100 ml of water. The resulting mixture was stirred at room temperature for 19 hr and then extracted three times with methylene chloride (50 ml). The combined methylene chloride solution was washed with 50 ml of 10% sodium hydroxide, 50 ml of 10% hydrochloric acid, 50 ml of saturated sodium chloride solution, and then dried ($MgSO_4$). The solvent was removed to yield a yellow solid. The yellow solid was sublimed (108°C/0.25 Torr) to yield a white solid.

Yield, 7.20g (63.9%); mp 115-116°C; MS, m/e (70 eV) 200(100), 199(31), 148(25), 144(14), 130(10), and 120(20), exact mass calcd for $C_{12}H_8O_3$: 199.03952; found: 199.03943; nmr ($CDCl_3$) δ7.67-7.30 (m, 3, ArH), 3.22 (s, 1, -C≡CH);

3.32-3.03 (m, 2, $-CH_2-CH_2-CO$), and 2.92-2.63 (m, 2, $-CH_2CO$); ir ($CHCl_3$) 3310, 2120, 1735, 1715, 1475, 1255, and 1165 cm^{-1}.

6-(1-Oxo-5-chloroindanyl) propiolate (52)

A 467 mg (5.28 mmol) portion of propiolyl chloride in 10 ml of benzene was added dropwise to a mixture containing 863 mg (473 mmol) of 5-chloro-6-hydroxy-1-indanone, 211 mg (5.28 mmol) of sodium hydroxide, 40 ml of benzene, and 20 ml of water. The resulting mixture was stirred at room temperature for 26 hr. After 26 hr the layers were separated. The organic layer was then washed with 25 ml of 5% sodium hydroxide, 25 ml of 10% hydrochloric acid, and 25 ml of saturated sodium chloride solution. After drying ($MgSO_4$) the solvent was removed. The solid that was left was recrystallized twice from methylene-hexanes. Yield, 411 mg (37%); mp 125-126°C; MS, m/e (70 eV), 235(11), 234(20), 233(25), 199(100), 182(17), 178(10), 154(18), 115(11), and 89(16); exact mass calcd for $C_{12}H_7ClO_3$: 233.00055; found: 233.00140; nmr ($CDCl_3$) δ7.65 (s, 1, ArH), 7.60 (s, 1, ArH), 3.25 (s, 1, $-C\equiv CH$), 3.30-3.00 (m, 2, $-CH_2-CH_2-CO$), and 2.88-2.63 (m, 2, $-CH_2-CO$); ir ($CHCl_3$) 3300, 2120, 1740, 1715, 1600, 1270, and 1145 cm^{-1}.

6-(1-Oxo-4-methylindanyl) propiolate (53)

A 4.51g (0.051 mol) portion of propiolyl chloride in 20 ml of benzene was added dropwise to a mixture containing 8.2g (0.051 mol) of 4-methyl-6-hydroxy-1-indanone, 2.04g

(0.051 mol) of sodium hydroxide, 50 ml of benzene, and 100 ml of water. The resulting mixture was stirred at room temperature for 13 hr and then extracted twice with ether (25 ml). The combined ethereal solution was washed with 25 ml of 10% sodium hydroxide, 25 ml of 10% hydrochloric acid, 25 ml of saturated sodium chloride solution, and then dried (Na_2SO_4). The solvent was removed under reduced pressure to leave a yellow solid. The yellow solid was sublimed (115° C/1.3 Torr) to yield a white solid. Yield, 6.1g (56%); mp 148-150° C; MS, m/e 214(100), 213(60), 200(22), 163(42), 158(44), 144(42), 134(36), 133(22), 115(37), 107(27), 106(32), and 105(22); exact mass calcd for $C_{13}H_{10}O_3$: 214.062997; found: 214.062404; nmr ($CDCl_3$) δ7.36 (bs, 1, ArH), 7.20 (bs, 1, ArH), 3.08 (s, 1, -C≡CH), 2.08-2.90 (m, 2, $-CH_2-CH_2-CO$), 2.84-2.66 (m, 2, $-CH_2-CO$), and 2.38 (s, 3, CH_3); ir ($CDCl_3$) 3300, 2110, 1735, 1715, 1295, 1200, and 1160 cm^{-1}.

Flash Vacuum Pyrolysis of Aryl Propiolates

All pyrolyses were done with the pyrolysis tube packed with quartz chips and 10^{-4}-10^{-5} Torr pressure, unless otherwise specified. After the completion of pyrolysis the desired products were washed from region A (Figure 1) of the apparatus with methylene chloride, ethyl acetate, acetone, or chloroform. The solvent was then removed on

a rotary evaporator. The product was purified, if necessary, by recrystallization, column chromatography, dry column chromatography, or preparative TLC.

Pyrolysis of phenyl propiolate (1)

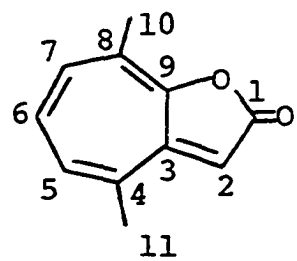
Pyrolysis of phenyl propiolate at 650°C yielded 2H-cyclohepta[b]furan-2-one. The yellow crystals were recrystallized from cyclohexane. Yield, 30-45%; mp 70-71°C (dec), lit (15) mp 69-70°C; MS, m/e (70 eV) 146, 118, and 90; exact mass calcd for $C_9H_6O_2$: 146.0368; found: 146.0364 ± 0.0007; nmr (proton, CCl_4) δ7.48-6.82 (m, 5H) and 5.77 (s, 1H); nmr (carbon, $CDCl_3$)[1] 169.45(s), 158.27(s), 153.14(s), 135.40(d, J_{C-H}=160.3 Hz), 132.48(d, J_{C-H}=181.8 Hz), 130.46 (d, J_{C-H}=160.3 Hz), 127.80(d, J_{C-H}=173.5 Hz), 113.77(d, J_{C-H}=160.3 Hz), and 98.63(d, J_{C-H}=180.9 Hz); ir (CCl_4) 1785, 1760, 1602, 1510, 1265, and 1220 cm^{-1}; UV (95% ethanol) nm (ε), 253(2.14×10^4), 375(1.37×10^4), and 388(1.39×10^4).

Pyrolysis of 2,6-dimethylphenyl propiolate (33)

The pyrolysis of 2,6-dimethylphenyl propiolate at 650°C yielded 4,8-dimethyl-2H-cyclohepta[b]furan-2-one. The yellow crystals were recrystallized from cyclohexane. Yield, 45%; mp 161°C (dec); MS, m/e (70 eV) 174, 146, 118, and 91; exact mass calcd for $C_{11}H_{10}O_2$: 174.0681; found: 174.0681 ±

[1]Data obtained from Susan L. Emeis.

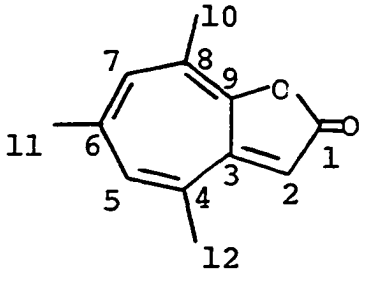
0.0009; nmr (proton, $CDCl_3$) δ7.13-6.62 (m, 3H), 5.57 (s, 1H 1H), 2.43 (s, 3H), and 2.32 (s, 3H); nmr (carbon, $CDCl_3$) δ168.68 (C_1), 153.53 and 152.72 (C_3 and C_9), 138.26, 135.46, 134.27, 128.61, and 125.64 (C_4 to C_8), 96.69 (C_2), 23.99 (q, J_{C-H}=127.95 Hz, of d, J_{C-H}=2.0 Hz) and 19.46 (q, J_{C-H}= 132.37 Hz, of d, J_{C-H}=5.88 Hz) (C_{10} and C_{11}); ir (CCl_4) 1765, 1595, 1505, and 1275 cm^{-1}; UV (95% ethanol) nm (ε), 259(3.75×10^4), 266(3.47×10^4), 382(2.17×10^4), and 391(2.33×10^4).



Pyrolysis of 2,4,6-trimethylphenyl propiolate (34)

Pyrolysis of 2,4,6-trimethylphenyl propiolate at 650°C yielded 4,6,8-trimethyl-2H-cyclohepta[b]furan-2-one. The yellow crystals were recrystallized from cyclohexane. Yield, 44%; mp 185-186°C (dec); MS, m/e (70 eV) 188(100), 159(7), 132(12), 117(14), and 91(7); exact mass calcd for $C_{12}H_{12}O_2$: 188.0837; found: 188.0838 ± 0.0009; nmr (proton, $CDCl_3$) δ6.90(s, 1H), 6.78(s, 1H), 5,58(s, 1H), 2.42 (s, 3H), and 2.33(s, 6H); nmr (carbon, $CDCl_3$) δ168.84 (C_1), 151.36 (C_3 and C_9), 139.08, 137.58, 137.06, 133.94, and 125.17

(C_4-C_8), 95.42 (C_2), 27.39(q, J_{C-H}=128.0 Hz, of t, J_{C-H}= 6 Hz, C_{11}), 24.27(q, J_{C-H}=128.0 Hz, of d, J_{C-H}=7.4 Hz) and 19.72(q, J_{C-H}=129.4 Hz, of d, J_{C-H}=5.9 Hz) (C_{10} and C_{12}); ir (CCl_4) 1765, 1508, and 1239 cm^{-1}.



Pyrolysis of p-chlorophenyl propiolate (40)

Pyrolysis of p-chlorophenyl propiolate at 650°C yielded 6-chloro-2H-cyclohepta[b]furan-2-one. The yellow crystals were recrystallized from chloroform-cyclohexane. Yield, 55%; mp 175-176°C (dec); MS, m/e (70 eV) 182(31), 180(75), 126(25), 124(56), 91(38), and 89(100); exact mass calcd for $C_9H_5ClO_2$: 179.99781; found: 179.99658; nmr ($CDCl_3$) δ7.37-7.08 (m, 3H), 6.75 (d, J=10 Hz, of d, J=1.5 Hz, 1H), and 5.85 (d, J=1.5 Hz, 1H); double irradiation at δ5.85, δ6.75 (d, J=10 Hz, 1H); ir ($CHCl_3$) 1755, 1605, and 1490 cm^{-1}.

Pyrolysis of p-bromophenyl propiolate (41)

Pyrolysis of p-bromophenyl propiolate at 650°C yielded 6-bromo-2H-cyclohepta[b]furan-2-one. The orange crystals were purified by sublimation (102°C/0.95 Torr). Yield, 59%; mp 162-165°C (dec), MS, m/e (70 eV) 227(13), 226(100),

225(13), 224(100), 198(9), 196(9), 170(9), 168(9), 89(94), and 63(31); exact mass calcd for $C_9H_5BrO_2$: 223.94729; found: 223.94688; nmr ($CDCl_3$) δ7.50-6.97 (m, 3H), 6.64 (d, J=10 Hz, of d, J=1.5 Hz, 1H) and 5.83 (d, J=1.5 Hz, 1H); double irradiation at δ5.83, δ6.64 (d, J=10 Hz, 1H); ir ($CHCl_3$) 1755, 1600, 5130, 1490, and 1350 cm^{-1}.

Pyrolysis of p-formylphenyl propiolate (42)

Pyrolysis of p-formylphenyl propiolate at 650°C yielded 6-formyl-2H-cyclohepta[b]furan-2-one. The orange crystals were recrystallized from chloroform-cyclohexane. Yield, 31%; mp 227-230° (dec); MS, m/e (70 eV) 175(13), 174(100), 173(18), 141(26), 140(41), 119(21), 91(21), and 90(27); exact mass calcd for $C_{10}H_6O_3$: 174.031696; found: 174.03177; nmr ($CDCl_3$) δ9.67(s, 1H), 7.60-7.40(m, 3H), 7.05(d, J=10 Hz, of d, J=1.5 Hz, 1H), and 5.99(d, J=1.5 Hz, 1H); double irradiation at δ5.99, δ7.05 (d, J=10 Hz, 1H); ir ($CHCl_3$) 1770, 1695, 1605, 1150, and 1130 cm^{-1}.

Pyrolysis of p-hydroxyphenyl propiolate (43)

Pyrolysis of p-hydroxyphenyl propiolate at 660°C and 710°C yielded no desired product, only hydroquinone was recovered in the liquid nitrogen trap. The product was identified by comparing its nmr with the nmr of hydroquinone.

Pyrolysis of p-methoxyphenyl propiolate (45)

The pyrolysis of p-methoxyphenyl propiolate at 540°, 600°, 660°, or 700°C yielded a trace amount of yellow material at region A of the apparatus. The major portion of the product was collected in the liquid nitrogen trap. The product was chromatographed (silica gel column, 1:4, V:V, ethyl acetate:hexanes). The component with the largest R_f value was chromatographed an a 5 ft x 1/4 in, 3% SE-30 on 100/200 mesh VarAport 30 column. The column temperature was 125°C. Four peaks were observed. The last component was identified as the starting propiolate. Spectral data of the first peak are given here. No MS; nmr ($CDCl_3$) δ7.48-6.70 (m, 5H), 5.74(A portion of an ABX, d, J=18 Hz, of d, J=2 Hz, 1H), 5.36 (B portion of an ABX, d, J=12 Hz, of d, J=2 Hz, 1H), and 4.95 (s, 1H); ir ($CHCl_3$) 3600, 1630, 1605, 1500, 1485, 1450, 1325, 1290, 1205, 1165, and 835 cm^{-1}. The second and third components were not analyzed.

Pyrolysis of p-acetoxyphenyl propiolate (44)

Pyrolysis of p-acetoxyphenyl propiolate at 650°C yielded a trace amount of yellow material at region A of the apparatus. The major portion of the product was collected in the liquid nitrogen trap. The product was applied to a preparative TLC plate (silica gel, 1:3, V:V,

ethyl acetate:hexanes). Three bands were observed. Top band, a mixture, nmr ($CDCl_3$) δ7.52-6.65 (m, 7H), 5.68 (A portion of an ABX, J=18 Hz, of d, J=1.5 Hz, 1H), 5.30 (B portion of an ABX, d, J=12 Hz, of d, J=1.5 Hz, 1H), 3.70 (s, 1H), and 2.25(s, 1H). The middle band was identified as the starting propiolate. The bottom band was not analyzed.

Pyrolysis of o-methylphenyl propiolate (35)

Pyrolysis of o-methylphenyl propiolate at 650°C yielded a 4:1 ratio of 8-methyl-2H-cyclohepta[b]furan-2-one (59) to 4-methyl-2H-cyclohepta[b]furan-2-one (60). The mixture was partially separated by column chromatography (neutral alumina, 1:3, V:V, ethyl acetate:hexanes). Compound 59, which has a larger R_f, was fractionally crystallized (cyclohexane) from a fraction containing small amount of 60. Compound 60 was obtained in the similar manner.

8-Methyl-2H-cyclohepta[b]-furan-2-one (59)

Yield, 44%; yellow solid; mp 116-117°C (dec); MS, m/e (70 eV) 161(14), 160(100), 132(25), 131(14), 104(39), 103(24), 78(22), and 77(16); exact mass calcd for $C_{10}H_8O_2$: 160.05243; found: 160.05235; nmr ($CDCl_3$) δ7.40-6.70 (m, 4H), 5.70(s, 1H), and 2.43(s, 3H); ir ($CHCl_3$) 1740, 1715 (shoulder), 1600, 1500, and 1265 cm^{-1}.

4-Methyl-2H-cyclohepta[b]furan-2-one (60)

Yield, 11%; yellow solid; mp 116-116.5°C (dec), lit (22) mp 116.5-117.5°C; MS, m/e (70 eV) 161(15), 160(100), 132(12), 131(6), 104(36), 103(17), 78(15), 77(10), and 51(15); exact mass calcd for $C_{10}H_8O_2$: 160.05243; found: 160.05040; nmr ($CDCl_3$) δ7.21-6.67 (m, 4H), 5.68(s, 1H), and 2.39(s, 3H); ir ($CHCl_3$) 1750, 1725 (shoulder), 1595, 1495, and 1260 cm^{-1}.

Pyrolysis of o-chlorophenyl propiolate (36)

The pyrolysis of o-chlorophenyl propiolate at 650°C yielded 42% of a 5:1 ratio of 8-chloro-2H-cyclohepta[b]-furan-2-one (61) to 4-chloro-2H-cyclohepta[b]furan-2-one (62). Lactone 62 was never isolated. It was identified on the basis of its signal at δ6.08. Lactone 61 was fractionally crystallized from cyclohexane and then further purified by sublimation (89°C/1 Torr).

8-Chloro-2H-cyclohepta[b]furan-2-one (61)

Yield, 35%; mp 143-146°C (dec); MS, m/e (20 eV) 182(33), 180(100), 154(4), 152(11), 126(5), 124(14), and 89(10); exact mass calcd for $C_9H_5ClO_2$: 179.99781; found (70 eV); 179.99710; nmr ($CDCl_3$) δ7.5-6.67 (m, 4H), and 5.85 (s, 1H); ir ($CHCl_3$) 1800, 1760, 1625, 1590, 1500, and 1270 cm^{-1}.

Pyrolysis of o-bromophenyl propiolate (37)

The pyrolysis of o-bromophenyl propiolate yielded a mixture of an unidentified brown product, 8-bromo-2H-cyclohepta[b]furan-2-one (63) and 4-bromo-2H-cyclohepta-[b]furan-2-one (64); however, the ratio of 63 to 64 was not reproducible. In six runs 63 to 64 ratios of 4:3, 7:1, 7:1, 1:1, 1:1, and 2:1 were observed and in one run no 63 was detected, only 64. The pyrolysis product mixtures were never purified. The singlet at δ5.83 was assigned to 63; the singlet at δ5.76 was assigned to 64.

Pyrolysis of o-isopropylphenyl propiolate (38)

Pyrolysis of o-isopropylphenyl propiolate yielded a mixture of an unidentified brown product, 8-isopropyl-2H-cyclohepta[b]furan-2-one (65), and 4-isopropyl-2H-cyclo-hepta[b]furan-2-one (66). The mixture was applied to preparative TLC plates and eluted four times (1:4, V:V, ethyl acetate:hexanes). The brown product was removed, but no separation of 65 and 66 was observed. The ratio of 65:66 was 2.4:1. IR (CCl_4) of isomeric mixture, 2960, 1765, 1590, 1500, and 1270 cm^{-1}.

8-Isopropyl-2H-cyclohepta[b]furan-2-one (65)

NMR ($CDCl_3$) ca.δ7.0(m, 4H), 5.75(s, 1H), 3.75 (septet, J=7 Hz, 1H), and 1.23(d, J=7 Hz, 6H).

4-Isopropyl-2H-cyclohepta[b]furan-2-one (66)

NMR ($CDCl_3$) δ~7.0(m, 4H), 5.82(s, 1H), 3.02 (septet, J=7 Hz, 1H), and 1.30(d, J=7 Hz, 6H).

Pyrolysis of 2,4-dichlorophenyl propiolate (39)

Pyrolysis of 2,4-dichlorophenyl propiolate at 650°C yielded a 7:1 ratio of 6,8-dichloro-2H-cyclohepta[b]furan-2-one (67) to 4,6-dichloro-2H-cyclohepta[b]furan-2-one (68). Compound 68 was not isolated. It was identified on the basis of the signal at δ6.10. Compound 67 was purified by fractional crystallization (cyclohexane) and sublimation.

6,8-Dichloro-2H-cyclohepta[b]furan-2-one (67)

Yield, 30%; mp 164-166°C (dec); MS, m/e (70 eV) 217(11), 216(6), 215(60), 214(11), 213(100), 187(17), 185(23), 159(26), 157(40), 124(28), and 122(89); exact mass calcd for $C_9H_4ClO_2$: 213.95884; found: 213.95931; nmr ($CDCl_3$) δ7.28-6.87 (m, 3H), and 5.87 (s, 1H), ir ($CHCl_3$) 1762, 1590, 1495, and 825 cm^{-1}.

Pyrolysis of 5-indanyl propiolate (46)

Pyrolysis of 5-indanyl propiolate at 650°C gave a 20% yield of 6,7-dihydro-azuleno[6,5-b]furan-2(5H)-one (69) and a 20% yield of 7,8-dihydro-azuleno[5,6-b]furan-2(6H)-one (70). Lactones 69 and 70 were separated by thick layer chromatography using multiple elutions (10 times, silica gel, 1:3, V:V, ethyl acetate:hexanes).

6,7-Dihydro-azuleno[6,5-b]furan-2(5H)-one (69)

Smaller R_f; mp 96-98°C (dec); MS, m/e (70 eV) 186(100), 149(25), 129(19), 128(13), and 115(13); exact mass calcd for $C_{12}H_{10}O_2$: 186.0681; found 186.0678; nmr ($CDCl_3$) δ7.28 (br s, 1H), 6.90 (br s, 2H), 5.60 (s, 1H), 2.95(m, 4H), and 2.00(m, 2H); ir ($CHCl_3$) 1750, 1600, and 1520 cm^{-1}.

7,8-Dihydro-azuleno[5,6-b]furan-2(6H)-one (70)

Larger R_f; mp 118-123°C (dec); MS, m/e (70 eV) 186(100), 129(26), 128(19), 115(20), 64(9), and 51(9); exact mass calcd for $C_{12}H_{10}O_2$: 186.0681; found: 186.0677; nmr ($CDCl_3$) δ7.13 and 7.00 (AB pattern, J=11 Hz, 2H), 6.95(m, 1H), 5.65(m, 1H), 3.00(m, 4H), and 2.00(m, 2H); ir ($CHCl_3$) 1750, 1615, and 1500 cm^{-1}.

Pyrolysis of 4-indanyl propiolate (47)

The pyrolysis of 4-indanyl propiolate at 650°C yielded a 6:5 ratio of 8,9-dihydro-azuleno[4,5-b]furan-2(7H)-one (71) to 5,6-dihydro-azuleno[5,4-b]furan-2(4H)-one (72). The isomers were separated by preparative thick layer chromatography with multiple elutions (10 times, silica gel, 1:3, V:V, ethyl acetate:hexanes).

8,9-Dihydro-azuleno[4,5-b]furan-2(7H)-one (71)

Smaller R_f; yield, 15%; mp 126-130°C (dec); MS, m/e (70 eV) 186(100), 158(19), 157(21), 130(13), 129(35), 128(21), 115(54), 64(17), and 63(12); exact mass calcd

for $C_{12}H_{10}O_2$: 186.06808; found: 186.06805; nmr ($CDCl_3$) δ7.40-6.84(m, 3H), 5.66(s, 1H), 3.36-2.92(m, 4H), and 2.28-2.00 (m, 2H); ir ($CHCl_3$) 1740, 1610, 1505, and 1250 cm^{-1}.

5,6-Dihydro-azuleno[5,4-b]furan-2(4H)-one (72)

Larger R_f; yield, 13%; mp 160-163°C (dec); MS, m/e (70 eV) 186(100), 129(9), 128(61), 114(24), and 92(23); exact mass calcd for $C_{12}H_{10}O_2$: 186.06808; found: 186.06880; nmr ($CDCl_3$) δ6.94 (s, 3H), 5.53(s, 1H), 3.30-2.95(m, 4H), and 2.40-2.00(m, 2H); ir ($CHCl_3$) 1740, 1590, 1490, and 1260 cm^{-1}.

Pyrolysis of 5-(6-chloroindanyl) propiolate (48)

The pyrolysis of 5-(6-chloroindanyl) propiolate at 650°C gave a 34% yield of 6,7-dihydro-9-chloro-azuleno-[6,5-b]furan-2(5H)-one (73) and 4% yield of 4-chloro-7,8-dihydro-azuleno[5,6-b]furan-2(6H)-one (74). Compound 74 was never isolated. It was identified on the basis of the signal at δ5.98. Compound 73 was purified by fractional crystallizing from cyclohexane.

6,7-Dihydro-9-chloro-azuleno[6,5-b]furan-2(5H)-one (73)

MP 163-166°C (dec); MS, m/e (70 eV) 222(34), 220(100), 186(10), 129(43), 128(21), 127(15), 84(85), 69(24), 63(11), 56(99), and 55(36); exact mass calcd for $C_{12}H_9ClO_2$: 220.02911; found: 220.02825; nmr ($CDCl_3$) δ7.26(s, 1H),

7.03(s, 1H), 5.65(s, 1H), 2.98(m, 4H), and 2.00 (m, 2H); ir ($CHCl_3$) 1755, 1635, 1600, and 1520 cm^{-1}.

Pyrolysis of 7-(1-oxoindanyl) propiolate (49)

Pyrolysis of 7-(1-oxoindanyl) propiolate (49) at 660°C with an open tube gave a 13.5% yield of 7,8-dihydro-azuleno[4,5-b]furan-2,9-dione (75), a 13.5% yield of 5,6-dihydro-azuleno[5,4-b]furan-2,4-dione (76), and some unidentified compound. Lactones 75 and 76 were isolated from the mixture by column chromatography (silica gel, 1:1, V:V, ether:toluene). Pyrolysis of 49 was also carried out under other conditions. Packed tube, 550-560°C, yield of 75(7.4%), 76(7.4%); packed tube, 600°C, yield of 75(7.9%), 76(7.9%); packed tube, 660°C, yield of 75(6.8%), 76(6.8%); open tube, 660°C, yield of 75(13.5%), 76(13.5%); open tube, 700°C, yield of 75(13.0%), 76(13.0%). In all pyrolyses 1-indanone was recovered in the liquid nitrogen trap. Also, in all pyrolyses the starting material was heated to 80-95°C.

7,8-Dihydro-azuleno[4,5-b]furan-2,9-dione (75)

Smaller R_f; mp 171-175°C (dec); MS, m/e (70 eV) 200(100), 115(10), 91(12), 77(12), 72(11), 70(37), 69(25), and 56(11); exact mass calcd for $C_{12}H_8O_3$: 200.04735; found: 200.04632; nmr ($CDCl_3$) δ7.42-6.83(m, 3H); 5.31(s, 1H), 3.30-3.07(m, 2H), and 2.90-2.68(m, 2H); ir ($CHCl_3$) 1780, 1760, 1730, 1593, 1280, and 1155 cm^{-1}.

5,6-Dihydro-azuleno[5,4-b]furan-2,4-dione (76)

Larger R_f; mp 203-206°C (dec); MS, m/e (70 eV) 200(56), 144(16), 116(25), 115(51), 68(21), 64(16), 62(68), and 61(100); exact mass calcd for $C_{12}H_8O_3$: 200.04735; found: 200.04577; nmr ($CDCl_3$) δ7.20-6.73(m, 4H), 3.20-3.02(m, 2H), and 2.86-2.67(m, 2H); ir ($CHCl_3$) 1765 (shoulder), 1755, 1705, 1610, 1350, 1265, and 1140 cm^{-1}.

Pyrolysis of 7-(1-oxo-4-methylindanyl) propiolate (50)

Pyrolysis of 7-(1-oxo-4-methylindanyl) propiolate (50) at 760°C with an open tube gave a 22% yield of 6-methyl-7,8-dihydro-azuleno[4,5-b]furan-2,9-dione (77), a 22% yield of 5,6-dihydro-7-methyl-azuleno[5,4-b]furan-2,4-dione (78), and a 10.9% yield of 50. Lactones 77 and 78 were isolated by dry column chromatography (silica gel, 35:100, V:V, ether:toluene). Dialysis tubing was used for the dry column. The column was packed in the same manner as an ordinary column. Elution was stopped when the solvent front reached the bottom or separation was visually determined to have been effected. Pyrolyses carried out at 640-650°C and 700°C with an open tube gave a large amount of 50 in addition to 77 and 78.

Nitrogen-flow pyrolysis of 7-(1-oxo-4-methylindanyl) propiolate (50)

Propiolate 50 was pyrolyzed in a quartz-packed nitrogen-flow system. The nitrogen was passed through a 6 ft coiled copper tubing (O.D.=1/4") immersed in an oil bath which was maintained between 148-160°C. The nitrogen then flowed through the sample compartment which was maintained at ca. 80°C. Furnace temperatures of 520°, 570°, 620°, and 720°C with nitrogen flow rate of ca. 29-31 sec/10 ml and pressures of 2.0-3.0 Torr were tried. The composition of the product mixture in the nitrogen trap varied from just one compound, 4-methyl-1-indanone, to four components, 77, 78, 50, and 4-methyl-1-indanone. The composition of the product mixture condensed at the pyrolysis tube consisted of 50, 77 and 78 in various ratios. The yields of 77 and 78 obtained were not better than in the static system.

6-Methyl-7,8-dihydro-azuleno[4,5-b]furan-2,9-dione (77)

R_f=0.093 (silica gel, 35:100, V:V, ether:toluene); mp 195-198°C (dec); MS, m/e (70 eV) 214(71), 158(19), 152(14), 151(39), 129(13), 128(83), 127(41), 115(15), 92(46), and 91(100), exact mass calcd for $C_{13}H_{10}O_3$: 214.062998; found: 214.06229; nmr ($CDCl_3$) δ7.16 and 7.00

(AB pattern, J=11 Hz, 2H), 5.85(s, 1H), 3.00(m, 2H), 2.76(m, 2H), and 2.35(s, 3H); ir ($CHCl_3$) 2920, 1775, 1750, 1590, 1490, 1280, and 1170 cm^{-1}.

5,6-Dihydro-7-methyl-azuleno[5,4-b]furan-2,4-dione (78)

R_f=0.24 (silica gel, 35:100, V:V, ether:toluene); mp 205-210°C (dec); MS, m/e (70 eV) 214(41), 186(55), 171(12), 147(25), 129(100), 113(14), 112(28), and 111(20); exact mass calcd for $C_{13}H_{10}O_3$: 214.062998; found: 214.06335; nmr ($CDCl_3$) δ7.40-6.70(m, 3H), 3.10(m, 2H), 2.70(m, 2H), and 2.38(s, 3H); ir ($CHCl_3$) 2920, 1755, 1705, 1605, 1255, and 905 cm^{-1}.

Pyrolysis of 6-(1-oxoindanyl) propiolate (51)

Pyrolysis of 6-(1-oxoindanyl) propiolate (51) at 750°C with an open tube gave a 48% yield of 6,7-dihydro-azuleno[6,5-b]furan-2,5-dione (79), a 14% yield of 6,7-dihydro-azuleno[5,6-b]furan-2,8-dione (80), and an unknown compound. Lactones 79 and 80 were isolated by column chromatography (silica gel, 15:100, V:V, hexanes:ethyl acetate).

6,7-Dihydro-azuleno[6,5-b]furan-2,5-dione (79)

R_f=0.44 (silica gel, 15:100, V:V, hexanes:ethyl acetate). Isolated yield, 36.2%; mp 203-204°C (dec); MS, m/e (70 eV) 200(19), 186(6), 185(5), 184(5), 170(7), and 116(100); exact mass calcd for $C_{12}H_8O_3$: 200.04735; found:

200.04732; nmr ($CDCl_3$) δ7.91(s, 1H), 7.19 and 7.05 (AB pattern, J=8 Hz, 2H), 6.04(d, J=2 Hz, 1H), 3.20-3.06 (m, 2H), and 2.96-2.71(m, 2H); ir ($CDCl_3$) 1755, 1735, 1540, 1510, 1190, and 1245 cm^{-1}.

6,7-Dihydro-azuleno[5,6-b]furan-2,8-dione (80)

R_f=0.31 (silica gel, 15:100, V:V, hexanes:ethyl acetate). Isolated yield, 10%; mp 190-193°C (dec); MS, m/e (70 eV) 200(100), 172(15), 162(13), 144(22), 117(15), 116(27), 115(52), 105(11), and 91(14); exact mass calcd for $C_{12}H_8O_3$: 200.04735; found: 200.04740; nmr ($CDCl_3$) δ7.46 and 7.08 (AB pattern, J=11 Hz, 2H), 7.12(s, 1H), 6.00(d, J=2 Hz, 1H), 3.30-3.04(m, 2H), and 2.96-2.68 (m, 2H); ir ($CDCl_3$) 1770 and 1755 (doublet), 1710, 1540, 1345, and 1265 cm^{-1}.

Pyrolysis of 6-(1-oxo-5-chloroindanyl) propiolate (52)

Pyrolysis of 6-(1-oxo-5-chloroindanyl) propiolate (52) at 720°C with an open tube gave a 51% yield of 6,7-dihydro-9-chloro-azuleno[6,5-b]furan-2,5-dione (81) and some 52. Lactone 81 was isolated by column chromatography (silica gel, 1:1, V:V, ethyl acetate:hexanes).

6,7-Dihydro-9-chloro-azuleno[6,5-b]furan-2,5-dione (81)

MP 188-198°C (dec); MS, m/e (70 eV) 236(31), 234(100), 219(37), 214(17), 193(12), 135(14), 131(21), 119(20), 115(18), and 105(13); exact mass calcd for $C_{12}H_7ClO_3$:

234.00838; found: 234.00978; nmr ($CDCl_3$) δ7.85(s, 1H), 7.23(s, 1H), 6.05(s, 1H), 3.40-3.02(m, 2H), and 2.90-2.60 (m, 2H); ir ($CDCl_3$) 1765, 1735, 1535, 1505, 1250, and 1150 cm^{-1}.

Pyrolysis of 6-(1-oxo-4-methylindanyl) propiolate (53)

Pyrolysis of 6-(1-oxo-4-methylindanyl) propiolate (53) at 750°C with a packed tube gave a 28% yield of 6,7-dihydro-8-methyl-azuleno[6,5-b]furan-2,5-dione (83) and a 14% yield of 5-methyl-6,7-dihydro-azuleno[5,6-b]-furan-2,8-dione (84). Pyrolysis of 53 at 720°C with an open tube gave a 16% yield of 83 and a 32% yield of 84. In both pyrolyses some unknown compound was also formed. Lactones 83 and 84 were isolated by column chromatography (silica gel, 3:7, V:V, hexanes:ethyl acetate).

6,7-Dihydro-8-methyl-azuleno[6,5-b]furan-2,5-dione (83)

Larger R_f; mp, started subliming at 195°C and completely disappeared at 205°C; MS, m/e (70 eV) 214(100), 158(16), 129(21), 128(13), and 115(28); exact mass calcd for $C_{13}H_{10}O_3$: 214.062997; found: 214.063037; nmr ($CDCl_3$) δ7.84 (bs, 1H), 7.08 (bs, 1H), 5.95(d, J=2 Hz, 1H), 3.12-2.90(m, 2H), 2.90-2.58(m, 2H), and 2.42(s, 3H); ir ($CDCl_3$) 1755 and 1740 (doublet), 1715, 1495, 1280, and 1225 cm^{-1}.

5-Methyl-6,7-dihydro-azuleno[5,6-b]furan-2,8-dione (84)

Smaller R_f; mp, started subliming at 180°C and turned black at 205°C; MS, m/e (70 eV) 215(6), 214(52), 129(12), 128(10), 115(16), 100(18), 99(15), and 84(100); exact mass calcd for $C_{13}H_{10}O_3$: 214.062997; found: 214.063037; nmr ($CDCl_3$) δ7.42(s, 1H), 7.12(d, J=2 Hz, 1H), 5.85(d, J=2 Hz, 1H), 3.12-2.93(m, 2H), 2.76-2.60(m, 2H), and 2.43(s, 3H); ir ($CHCl_3$) 1770 and 1745 (doublet), 1715, 1615, 1535, and 1280 cm^{-1}.

Synthesis of Phenol Derivatives

Hydroquinone monoacetate

The procedure of Chattaway (55) as modified by Olcott (56) was used. A 79.5g (0.75 mol) portion of sodium carbonate was added to 100 ml of water and stirred until dissolved. Then 250g of crushed ice and 55g (0.5 mol) of hydroquinone were added. After the mixture was well-mixed, 73.7g (0.625 mol) of acetic anhydride was added rapidly. The resulting mixture was stirred for 3 hr and then filtered. The filtrate was acidified and extracted with ether. The ethereal solution was washed with saturated sodium chloride solution and dried (Na_2SO_4). Removal of ether yielded a red residue. The red residue was extracted with pentane using a Soxhlet extractor to yield a white solid. MP 56-61°C; lit (56) 62-63°C; nmr ($CDCl_3$) δ6.95-6.57 (AA'BB' pattern, 4H) and 2.23(s, 3H).

Phenyl 3-chloropropionate

A 63.48g (0.5 mol) portion of β-chloropropionyl chloride in 50 ml of benzene was added dropwise to a cooled mixture containing 47.06g (0.5 mol) of phenol, 20g (0.5 mol) of sodium hydroxide, 200 ml of water, and 50 ml of benzene. The resulting yellowish-orange mixture was stirred at room temperature for 58 hr. The benzene and the aqueous layers were then separated. The aqueous layer was extracted three times with ether (100 ml). The combined organic solution was washed with 100 ml of 10% sodium hydroxide, 100 ml of 10% hydrochloric acid, and twice with 100-ml portions of saturated sodium chloride solution. After drying ($MgSO_4$) the solvent was removed under reduced pressure to yield a yellow liquid. Vacuum distillation of the yellow liquid yielded phenyl 3-chloropropionate, a colorless liquid (84°C/0.5 Torr), lit (57) 148-149°C/24 Torr. Yield 77.4g (84%); nmr (CCl_4) δ7.50-6.93(m, 5H), 3.73(t, J=7 Hz, 2H), and 2.88(t, J=7 Hz, 2H).

7-Hydroxy-1-indanone (85)

The procedure of Wagatuma and co-workers (58) was used in the synthesis of 7-hydroxy-1-indanone. A 276g (2.07 mol) portion of aluminum chloride was added to 76.4g (0.414 mol) of phenyl 3-chloropropionate at 60°C. The resulting amorphous mixture was heated to 90-100°C and

maintained at this temperature range for 1 hr. Then the temperature was gradually increased to 160°C over a 2 hr period and maintained at 160°C for 1 hr. Then the temperature was raised to 180°C quickly and maintained at that temperature for 1 hr. The mixture was cooled, and ice was added carefully to decompose the mixture until no hydrogen chloride was given off. Then 100 ml of concentrated hydrochloric acid was added. The resulting intense purple mixture was steam distilled to yield a white solid which was recrystallized from hexanes-ether. Yield, 24g (39.2%); mp 109-111°C, lit (59) mp 111°C; nmr ($CDCl_3$) δ9.08 (bs, 1H), 7.45(t, J=8 Hz, 1H), 6.92(d, J=8 Hz, 1H), 6.72(d, J=8 Hz, 1H), 3.25-2.93(m, 2H), and 2.83-2.55(m, 2H).

p-Tolyl 3-chloropropionate

A 63.5g (0.5 mol) portion of β-chloropropionyl chloride in 50 ml of benzene was added dropwise over a 1 hr period to a mixture containing 50g (0.56 mol) of practical grade p-cresol, 20g (0.5 mol) sodium hydroxide, 200 ml of water, and 50 ml of benzene. The resulting mixture was stirred at room temperature for 43 hr. Then the benzene and the aqueous layers were separated. The aqueous layer was extracted with three 50-ml portions of ether. The combined organic solution was washed with two 50-ml portions of 10% sodium hydroxide, 50 ml of 10%

hydrochloric acid, 50 ml of saturated chloride solution, and then dried ($MgSO_4$). The solvent was removed on a rotary evaporator. The residual liquid was vacuum distilled to give p-tolyl 3-chloropropionate. BP 64°C/0.7 Torr, lit (60) 145-155°C/12 Torr; nmr (CCl_4) δ6.98 (AA'BB' pattern, 4H), 3.68(t, J=7 Hz, 2H), and 2.28(s, 3H).

4-Methyl-7-hydroxy-1-indanone (86)

The procedure of Wagatuma and co-workers (58) was used. A 122.3g (0.917 mol) of aluminum chloride was added to 36.41g (0.183 mol) of p-tolyl 3-chloropropionate under 60°C. The amorphous mixture was then heated to 90-100°C and maintained at that temperature range for 1 hr. Then it was gradually raised to 160°C over a 2 hr period and maintained at 160°C for 1 hr. Then the temperature was raised to 180°C quickly and maintained at that temperature for 1 hr. The mixture was cooled, and ice was added slowly. After most of the residue had been decomposed, 50 ml of concentrate hydrochloric acid was added. The resulting mixture was steam distilled. The distillate was cooled in an ice bath and then filtered to give the crude product. The product was recrystallized from hexanes-ether to yield a white solid. Yield, 8.7g (29.3%), mp 110-111°C, lit (61) 111-112°C; nmr ($CDCl_3$) δ8.75 (bs, 1H), 7.18 and 6.58 (AB pattern, J=8 Hz, 2H), 3.08-2.77(m, 2H), 2.77-2.47(m, 2H), and 2.20 (s, 3H).

6-Chloro-5-indanol

The procedures of Buck (62) was used. A 5-ml portion of sulfuryl chloride was added dropwise to a 3-necked round bottom flask containing 6.71g (0.05 mol) of 5-indanol 13 ml of glacial acetic acid, and a small crystal of iodine. During the addition of sulfuryl chloride, the temperature of the mixture rose to 45°C. After the addition the dark violet solution was stirred at room temperature for 1 1/2 hr. Then it was poured on ice, made alkaline with 35% sodium hydroxide, and then made slightly acidic with 10% hydrochloric acid. The resulting solution was then extracted three times with chloroform. The combined chloroform solution was washed twice with saturated sodium chloride solution and then dried ($MgSO_4$). A violet liquid was left after the solvent was removed. The liquid was distilled under reduced pressure (63-64°C/0.2 Torr) to yield a colorless liquid. The colorless liquid solidified overnight. Yield, 6.3g (74.5%); mp, lit (62) 37-40°C, nmr (CCl_4) δ7.17(s, 1H), 6.90(s, 1H), 5.32(s, 1H), 3.08-2.58 (m, 4H), and 2.33-1.75(m, 2H); ir ($CHCl_3$) 3540, 3460-3100, 2940, 1605, 1580, 1265, and 1105 cm^{-1}.

6-Hydroxy-1-indanone

Procedure of Ingold and Piggott (63) was used to synthesize 6-hydroxy-1-indanone from 1-indanone. 6-Nitro-1-indanone was synthesized from 1-indanone using potassium

nitrate and concentrated sulfuric acid. The 6-nitro-1-indanone in 95% ethanol was converted to 6-amino-1-indanone using concentrated hydrochloric acid and stannous chloride dihydrate. 6-Hydroxy-1-indanone was then obtained from 6-amino-1-indanone by a diazotization reaction. 6-Hydroxy-1-indanone, nmr (d_6-acetone) δ7.50-6.92(m, 3H), 3.17-2.80 (m, 2H), and 2.75-2.45(m, 2H).

3-(3-Chloro-4-methoxyphenyl)propionic acid

The procedure of Buck (62) was used. A 15-ml (0.185 mol) portion of sulfuryl chloride was added dropwise to a mixture containing 21g (0.116 mol) of 3-(p-methoxyphenyl)-propionic acid, 35 ml of glacial acetic acid, and a crystal of iodine. During the addition the mixture gradually turned to a brown solution and the temperature rose to about 45°C. Then the solution was stirred at ca. 87°C for 13 hr. Then 50 ml of water and 100 ml of ether were added to the solution and the layers were separated. The organic layer was washed with two 50-ml portions of water, 50 ml of saturated sodium chloride solution, and then dried ($MgSO_4$). After removal of the solvent, the crude product was recrystallized three times from ether-hexanes. Yield, 95%; mp 113-117°C; nmr ($CDCl_3$) δ8.50 (bs, 1H), 7.25-6.75(m, 3H), 3.85(s, 3H), and 3.08-2.42(m, 4H).

3-(3-Chloro-4-methoxyphenyl)propionyl chloride

A 1.56-ml (21.9 mmol) portion of thionyl chloride was added to 2.35g (10.97 mmol) of 3-(3-chloro-4-methoxyphenyl)-propionic acid. The resulting mixture was stirred at 65°C for 2 1/2 hr. The excess thionyl chloride was then removed under water aspirator pressure to leave a purple solution. The solution was distilled under vacuum (144-146°C/2.2 Torr). Yield 1.88g (73.5%); nmr ($CDCl_3$) δ7.32-6.78(m, 3H), 3.88(s, 3H), and 3.33-2.78(m, 4H).

5-Chloro-6-methoxy-1-indanone

The procedure of House and Hudson (64) was used. A 1.15g (8.61 mmol) portion of aluminum chloride was added over 15-min period to a solution containing 1.88g (8.08 mmol) of 3-(3-chloro-4-methoxyphenyl-propionyl chloride and 205 ml of methylene chloride. The methylene chloride solution turned yellow upon the addition of aluminum chloride. Then the yellow solution was stirred at room tempearture for four hr. It was then added to 250 ml of ice and 100 ml of water. The layers were separated, and the aqueous layer was extracted with three 100-ml portions of ether. The combined organic solution was washed with 50 ml of 10% sodium hydroxide, 50 ml of saturated sodium chloride solution, and then dried ($MgSO_4$). A slightly green solid was left after the solvent was removed on a rotary

evaporator. The product was sublimed (108°C/0.75 Torr). Yield, 1.45g (91.5%); mp 154-156°C; MS, m/e (70 eV) 198(33), 153(21), 127(5), 125(15), and 89(12); exact mass calcd for $C_{10}H_9ClO_2$: 196.02911; found: 196.02519; nmr ($CDCl_3$) δ7.48 (bs, 1H), 7.22(s, 1H), 3.93(s, 3H), 3.20-2.92(m, 2H), and 2.83-2.55(m, 2H); ir ($CDCl_3$) 1710, 1610, 1475, 1460, 1300, and 1250 cm^{-1}.

5-Chloro-6-hydroxy-1-indanone

The general procedure of Sam (65) was followed. A mixture containing 1.454g (7.40 mmol) of 5-chloro-6-methoxy-1-indanone and 3.20g of (23.97 mmol) of aluminum chloride was refluxed in 60 ml of benzene for 7 hr. After 7 hr the mixture was poured into a beaker containing 100 ml of ice and 60 ml of 10% hydrochloric acid. The resulting mixture was extracted with three 100-ml portions of ether. The combined organic solution was washed with 50 ml of saturated sodium chloride solution and then dried ($MgSO_4$). The crude product was sublimed (132°C/0.6 Torr) to yield a white solid. Yield, 83.9%; mp 194-195°C; MS, m/e (70 eV) 184(37), 183(91), 182(100), 156(23), 155(22), 154(76), and 147(24); exact mass calcd for $C_9H_7ClO_2$: 182.01346; found: 182.01321; nmr ($\underline{d}_6$-acetone) δ7.53 (bs, 1H), 7.20(s, 1H), 3.20-2.87 (m, 2H), and 2.77-2.47(m, 2H); ir ($CHCl_3$) 3540, 1705, 1610, 1462, 1445, 1330, and 1295 cm^{-1}.

2-Methyl-2-methoxybenzaldehyde

The procedure of Adams and Montgomery (66) was used. A mixture containing 30g (0.246 mol) of m-methylanisole, 52g (0.293 mol) of zinc cyanide, and 100 ml of benzene was stirred at 0°C for 15 min. Dry hydrogen chloride was then passed through the mixture for 1 hr and then 45g (0.337 mol) of aluminum chloride was added to the pink mixture. After the addition of aluminum chloride, hydrogen chloride was passed through the mixture for 5 1/2 hr at room temperature and then for 2 hr at 40-50°C. The resulting red mixture was cooled to room temperature and was added to 400 ml of 10% hydrochloric acid and ice mixture. The pink amorphous solid was filtered and heated to reflux for 1/2 hr in 10% hydrochloric acid to decompose the solid. The original acidic filtrate and the acidic solution from the reflux were combined and extracted with ether. The combined ethereal solution was washed with water, saturated sodium chloride solution, and dried (Na_2SO_4). The solvent was removed on a rotary evaporator to yield an orange liquid. The liquid was used in the next step without further purification. Yield, 2-methyl-4-methoxybenzaldehyde (70%), 2-methoxy-4-methylbenzaldehyde (14%). For 2-methyl-4-methoxybenzaldehyde, nmr ($CDCl_3$) δ10.07(s, 1H), 7.70 and 6.77 (AB, J=8 Hz, 2H), 6.70(s, 1H), 3.80(s, 3H), and 2.61 (s, 3H).

2-Methyl-4-methoxycinnamic acid

The procedure of Kulkarni et al. (67) was used. A mixture containing 22.9g (0.153 mol) of crude 2-methyl-4-methoxy-benzaldehyde, 15.9g (0.153 mol) of malonic acid, and 4.84g of pyridine was heated at 120°C for 12 hr in an open flask fitted with a condenser. Evolution of carbon dioxide was observed within five min after heating was started. After 12 hr the brown mixture was taken up in 100 ml of 10% sodium hydroxide and 100 ml of ether. The layers were separated. The ether layer was washed twice with 40 ml of 10% sodium hydroxide. The combined basic solution was acidified with 10% hydrochloric acid until a voluminous white solid appeared. The acidic mixture was then cooled in an ice bath and filtered. The white solid was washed with water and then hexanes. The crude product was recrystallized from 95% ethanol. Yield, 48.7%; mp 179-182°C, lit (67) 176°C; nmr ($CDCl_3$-d_6-DMSO) δ7.92 and 6.25 (AB pattern, J=15 Hz, -CH=CH-), 7.60 (A of AB pattern, J=10 Hz, 1H), 6.80(m, 2H), 3.81(s, 3H), and 2.42(s, 3H).

3-(2-Methyl-4-methoxyphenyl)propionic acid

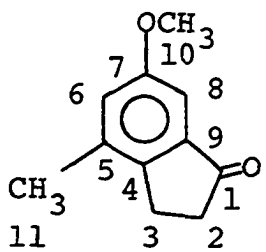
The procedure of Johnson and Shelbery (68) was used. A mixture containing 13.4g (0.070 mol) of 2-methyl-4-methoxycinnamic acid, 0.1g of platinum oxide, and 100 ml of glacial acetic acid was hydrogenated in a Parr hydrogenator. After the hydrogenation was completed, the catalyst

was removed by filtering with suction through Celite. The acetic acid was distilled under reduced pressure to yield a white solid. Yield, 99%; nmr ($CDCl_3$) δ7.17-6.55(m, 3H), 3.75(s, 3H), 3.12-2.42(m, 4H), and 2.28(s, 3H).

4-Methyl-6-methoxy-1-indanone

A modified procedure of Merchant and co-workers (69) was used. A flask containing 250g of phosphorous pentoxide and 225 ml of 85% phosphoric acid was stirred at 125-130°C for 30 min. Then 12.9g (0.0665 mol) of 3-(2-methyl-4-methoxyphenyl)propionic acid was added. The resulting red solution was stirred at 125-130°C for 15 min. Then it was poured into a beaker of ice-water. The resulting yellow solution was cooled to room temperature in an ice bath and then extracted three times with chloroform. The combined chloroform solution was washed with saturated sodium bicarbonate solution until slightly basic. Then it was washed with water, saturated sodium chloride solution, and dried ($MgSO_4$). After removal of solvent a brown liquid was left. After the liquid solidified, the product was purified by sublimation (78°C/0.1 Torr) to yield a white solid. Yield, 8.8g (75.2%); mp 94-96°C; MS, m/e (70 eV) 176(100), 161(21), 148(47), 133(11), and 105(15); exact mass calcd for $C_{11}H_{12}O_2$: 176.08373; found: 176.08339; nmr (proton, $CDCl_3$) δ7.05(s, 2H), 3.80(s, 3H), 3.10-2.85(m, 2H), 2.75-2.55(m, 2H), and 2.30(s, 3H); nmr (carbon, $CDCl_3$) δ206.9

(bs, C_1), 159.3(m, C_7), 147.1(m, C_5), 137.6(s, C_9), 136.6 (m, C_4), 123.7(d, J=157 Hz, of m, C_8), 102.0(d, J=163 Hz, of d, J=5 Hz, C_6), 55.2(q, J=144 Hz, C_{10}), 36.5(t, J=131 Hz, of t, J=4 Hz, C_3), 23.8(t, J=131 Hz, of t, J=4 Hz, C_2), and 17.5(q, J=128 Hz, of d, J=5 Hz, C_{11}); ir ($CDCl_3$) 1700, 1615, 1480, 1310, and 1045 cm^{-1}.



4-Methoxy-4-methyl-1-indanone

White solid; mp 78.5-80°C; MS, m/e (70 eV) 176(100), 148(15), 133(45), 118(20), 117(16), 115(11), 105(36), and 103(13); exact mass calcd for $C_{11}H_{12}O_2$: 176.08373; found: 176.08356; nmr ($CDCl_3$) δ7.15 (bs, 1H), 6.87(s, 1H), 3.88 (s, 3H), 3.10-2.82(m, 2H), 2.75-2.48(m, 2H), and 2.40(s, 3H); ir ($CHCl_3$) 1715, 1625, 1500, 1320, 1285, 1150, and 1105 cm^{-1}.

4-Methyl-6-hydroxy-1-indanone (89)

The general procedure of Sam (65) was followed. A mixture containing 8.8g (0.05 mol) of 4-methyl-6-methoxy-1-indanone, 21.6g (0.162 mol) of aluminum chloride, and 400 ml of benzene was refluxed for 13 hr. The solution was then poured into ice-10% hydrochloric acid mixture. The

resulting yellow heterogenerous mixture was poured into a separatory funnel; the layers were separated. The aqueous layer was extracted twice with ether. The combined benzene and ethereal solution was washed with water and saturated sodium chloride solution, and dried ($MgSO_4$). A yellow solid was left after removal of the solvent. The product was sublimed to yield a white solid. Yield, quantitative; mp 192°C; MS, m/e (70 eV) 162(100), 138(28), 134(62), 133(37), and 110(59); exact mass calcd for $C_{10}H_{10}O_2$: 162.06808; found: 162.06794; nmr ($CDCl_3$-$\underline{d}_6$-acetone) δ7.00 (s, 2H), 3.08-2.86(m, 2H), 2.70-2.58(m, 2H), and 2.30(s, 3H); ir ($CDCl_3$) 3590, 1700, 1470, and 1320 cm^{-1}.

Hydrolysis and Decarboxylation

Hydrolysis and decarboxylation of 2H-cyclohepta[b]furan-2-one (2)

A mixture of 287.8 mg (1.97 mmol) of 2 and 45 ml of 0.5 M sodium hydroxide was stirred at 55°C for 3 hr. After 3 hr the brown solution was acidified with 10% hydrochloric acid and then refluxed at 120°C for 4 hr. The resulting red solution was then extracted with ethyl acetate. The combined ethyl acetate solution was then washed with saturated sodium chloride solution and dried ($MgSO_4$). The solvent was removed on a rotary evaporator to yield 2-methyltropone as the main product and a trace of some other products. 2-Methyltropone was purified by column

chromatography using a 280 x 15 mm silica gel (60-200 mesh) column (1:3, V:V, ethyl acetate:n-hexane). NMR ($CDCl_3$) δ7.08(m, 5H) and 2.28(s, 3H); ir ($CHCl_3$) 1630 and 1570 cm^{-1}; spectral data similar to those reported by Brady and Hieble (70).

2,4-Dinitrophenylhydrazone derivative of 2-methyltropone

The general procedure of Parrick and Rasburn (71) was used. A solution of 0.5g of 2,4-DNP in 5 ml DMF was added to 102 mg (0.85 mmol) of 2-methyltropone. Four drops of concentrated hydrochloric acid were added to catalyze the reaction. The derivative was formed overnight. The derivative was collected, washed with 2N hydrochloric acid, water, and 95% ethanol. Yield 50.2%; black; mp 204°C, lit (72) 206°C.

2,7-Dimethyltropone

A 129 mg portion of 8-methyl-2H-cyclohepta[b]furan-2-one was hydrolyzed in 6 ml of 1% sodium hydroxide and 2 ml of 95% ethanol at 100°C for 24 hr. The resulting brown solution was acidified with 10% hydrochloric acid and extracted three times with chloroform (25 ml). The chloroform solution was washed with two 25-ml portions of saturated sodium chloride solution and dried ($MgSO_4$). The solvent was removed on a rotary evaporator to yield 2-(7-methyltroponyl)acetic acid, a yellow solid. A portion

of the acid was heated neat under nitrogen at 140°C for 30 min to give a brown solid (bottom of reaction flask) and 2,7-dimethyltropone (73), a yellow liquid (upper part of the flask). Molecular distillation (70°C/0.07 Torr) of the yellow liquid gave pure 2,7-dimethyltropone. MS, m/e (70 eV) 134(46), 106(18), 105(13), 91(100), 79(14), 77(11), 68(16), and 67(14); exact mass calcd for $C_9H_{10}O$: 134.07317; found: 134.06964; nmr ($CDCl_3$) δ7.40-6.65 (AA'BB' pattern, 4H) and 2.30(s, 6H); ir ($CHCl_3$) 2980, 1620, 1570, 1365, and 1150 cm^{-1}.

2,3-Dimethyltropone

A 50 mg portion of 4-methyl-2H-cyclohepta[b]furan-2-one was hydrolyzed in 6 ml of 1% sodium hydroxide and 2 ml of 95% ethanol at 100°C for 24 hr. The resulting brown solution was acidified with 10% hydrochloric acid and extracted with three 25-ml portions of chloroform. The combined chloroform solution was washed with two 25-ml portions of saturated sodium chloride solution and dried ($MgSO_4$). The solvent was removed to yield a brown viscous liquid. The brown liquid was sublimed (70°C/0.05 Torr) twice to yield 2,3-dimethyltropone. MP 59-60°C, lit (22) mp 58-59°C; nmr ($CDCl_3$) δ7.08-6.67(m, 4H), 2.31(s, 3H), 2.21(s, 3H); ir ($CHCl_3$) 2980, 1630, 1560, 1470, 1365, and 1110 cm^{-1}.

Hydrolysis of 4,6,8-trimethyl-2H-cyclohepta[b]furan-2-one (55)

A 117 mg (0.622 mol) portion of 55 in 2 ml of 95% ethanol and 6 ml of 1% sodium hydroxide was refluxed at 100°C for 24 hr. The resulting brown solution was acidified with 10% hydrochloric acid and then extracted with three 25-ml portions of chloroform. The combined chloroform solution was washed with two 25-ml portions of saturated sodium chloride solution and then dried ($MgSO_4$). The solvent was removed to yield 119 mg (93%) of 2-(3,5,7-trimethyltroponyl)acetic acid; MP 117-118°C (dec). It was sublimed at 90°C/0.05-0.1 Torr. MP 120-121°C (dec); MS, m/e (20 eV) 206(01), 189(66), 163(68), 134(58), and 119(100); exact mass calcd for $C_{13}H_{14}O_3$: 206.09426; found: 206.0943; nmr ($CDCl_3$) δ13.33 (bs, 1H), 7.17 (bs, 1H), 6.85 (bs, 1H), 3.60(s, 2H), 2.46(s, 3H), and 2.33(s, 6H); ir ($CDCl_3$) 3600-2500, 1740, 1520, 1495, 1425, and 1140 cm^{-1}.

Decarboxylation of 2-(3,5,7-trimethyltroponyl)acetic acid

A 55 mg portion of 2-(3,5,7-trimethyltroponyl)acetic acid was heated neat under nitrogen at 140°C for 30 min to yield a brown solid. The solid was sublimed (30°C/0.2 Torr) to yield 2,3,5,7-tetramethyltropone, a yellow solid. MP 62-63°C; MS, m/e (18 eV) 163(11), 162(100), 135(11), 134(86), 119(6), and 118(61); exact mass calcd for $C_{11}H_{14}O$:

162.10447; found: 162.10285; nmr ($CDCl_3$) δ7.00 (bs, 1H), 6.65 (bs, 1H), and 2.25 (bs, 12H); ir ($CHCl_3$) 1550, 1505, 1365, and 1160 cm^{-1}.

2-Methyl-5-chlorotropone

A mixture containing 48 mg of 6-chloro-2H-cyclohepta-[b]furan-2-one, 6 ml of concentrated hydrochloric acid, and 3 ml of glacial acetic acid was refluxed for 4 hr. After 4 hr the resulting solution was extracted with five 25-ml portions of ether. The combined ethereal solution was then washed with 50 ml of 5% sodium carbonate, 50 ml of water, and then dried ($MgSO_4$). The solvent was removed on a rotary evaporator. The resulting product was then chromatographed on a thick layer silica gel plate (1:9, V:V, ethyl acetate: chloroform). The band with the R_f of 0.50 was scraped off and the product further purified by column chromatography (silica gel, 1:4, V:V, ethyl acetate:cyclohexane) to give 2-methyl-5-chlorotropone, a white solid. MP 58.5-59.5°C; MS, m/e (70 eV) 156(10), 155(3), 154(30), 128(8), 127(6), 126(26), 125(13), 92(10), 91(100), 90(4), and 89(11); exact mass calcd for $C_8H_7C_{10}$: 154.01855; found: 154.014229; nmr ($CDCl_3$) δ7.25-6.85(m, 4H) and 2.20(s, 3H); ir ($CHCl_3$) 2990, 2920, 1625, 1570, 1510, 1375, 1160, and 1015 cm^{-1}.

2-Chloro-7-methyltropone

A mixture containing 160 mg of 8-chloro-2H-cyclohepta-[b]furan-2-one, 24 ml of concentrated hydrochloric acid, and

12 ml of glacial acetic acid was refluxed for 24 hr. After 24 hr the brown solution was extracted continuously with ether for 17 hr. The ethereal solution was then reduced to about 100 ml and then washed with 50 ml of water, 50 ml of 5% sodium carbonate, and 50 ml of water. After drying ($MgSO_4$) the ether was removed to yield a brown liquid. The product was purified by column chromatography (silica gel, 1:9, V:V, ethyl acetate:chloroform) and then sublimed (24°C/0.12 Torr) to yield 2-chloro-7-methyltropone (74), a white solid. MP 30-31°C; MS, m/e (70 eV) 156(12), 155(4), 154(38), 128(5), 127(4), 126(11), 125(9), 92(9), 91(100), 90(11), and 89(13); exact mass calcd for C_8H_7ClO; 154.01855; found: 154.01338; nmr ($CDCl_3$) δ7.86-6.70(m, 4H) and 2.34 (s, 3H); ir ($CHCl_3$) 1615, 1590. 1370, and 1350 cm^{-1}.

3-Acetyl-2H-cyclohepta[b]furan-2-one

A 161 mg (1.10 mmol) portion of 2H-cyclohepta[b]furan-2-one, 0.54g(4.05 mmol) of aluminum chloride, and 30 ml of cyclohexane were added to a 100-ml three-necked round bottom flask equipped with a mechanical stirrer. The resulting yellow mixture was heated in an oil bath at 90°C for 15 min. Then 0.08g (1.02 mmol) of acetyl chloride in 3 ml of cyclohexane was added dropwise to the yellow mixture. After stirring for 10 min the yellow mixture turned to a clear solution. The solution was heated for 4 more hours at 90°C. The resulting solution was poured into a beaker of ice

containing 10% hydrochloric acid. Ethyl acetate and more 10% hydrochloric acid was added to dissolve the solids. The layers were separated and the aqueous layer was washed three times with ethyl acetate. The combined organic solution was washed three times with water, once with saturated sodium chloride solution, and then dried ($MgSO_4$). The solvent was removed to yield a yellow solid. Yield, 138 mg (71%); mp 208-209°C (dec); MS, m/e (70 eV) 189(8), 188(42), 174(17), 173(100), 90(17), and 89(25); exact mass calcd for $C_{11}H_8O_3$: 188.047347; found: 188.047973 ± 0.0011; nmr ($CDCl_3$) δ9.2(d, J=12 Hz, 1H), 7,80-7.32(m, 4H), and 2.65(s, 3H); ir ($CHCl_3$) 1795 (shoulder), 1765, 1750, 1740, 1465, 1270, and 1260 cm^{-1}.

Hydrogenation Reactions

Hydrogenolysis of 6-chloro-2H-cyclohepta[b]furan-2-one (56)

A mixture containing 36 mg (0.199 mmol) of 56, 13 mg of 10% palladium on charcoal, 39 mg of potassium acetate, and 15 ml of 95% ethanol was hydrogenated for 1 hr on a sloping-manifold atmospheric hydrogenator. After 1 hr the catalyst was removed by vacuum filtration through a layer of Celite. Some water was then added to the filtrate, and the resulting solution was extracted with ethyl acetate. The organic solution was washed with saturated sodium chloride solution and dried ($MgSO_4$). The solvent was removed on a rotary evaporator to yield a yellow residue. NMR

spectrum of the residue indicated a mixture of 56, 2H-cyclohepta[b]furan-2-one, and some partially hydrogenated compound. NMR ($CDCl_3$) δ7.40-6.72 (m) 5.88(d, J=2 Hz), 5.80 (s), and 3.32-1.30 (m).

Hydrogenation of 6-chloro-2H-cyclohepta[b]furan-2-one (56)

A mixture containing 34 mg (0.188 mmol) of 56, 9 mg of 10% palladium on charcoal, 38 mg of potassium acetate, and 15 ml of 95% ethanol was hydrogenated for 10 hr. After 10 hr the catalyst was removed by vacuum filtration through a layer of Celite. Some water was then added to the filtrate, and the resulting solution was extracted with ethyl acetate. The organic solution was washed with saturated sodium chloride solution and dried ($MgSO_4$). The solvent was removed on a rotary evaporator to yield a slightly yellow liquid. The liquid was identified as cis-octahydro-2H-cyclohepta[b]furan-2-one (90) by comparing its nmr spectrum to the nmr spectrum of 90 as reported by Herz and Glick (49). NMR ($CDCl_3$) δ4.82-4.56(m, -CH-OC=O) and 2.95-1.10(m, 13H).

All the following hydrogenation reactions were carried out on a sloping-manifold atmospheric hydrogenator. After the reactions were terminated, the catalysts were removed by vacuum filtration through a layer of Celite. The solvent was then removed on a rotary evaporator. In the cases where glacial acetic acid was used as the solvent, ether was added to the filtrate and then the organic solution

was washed with water and 5% sodium bicarbonate until the washings were basic. Then the solution was washed with saturated sodium chloride solution and dried (Na_2SO_4). The solvent was then removed on a rotary evaporator.

Hydrogenation of 2H-cyclohepta[b]furan-2-one (2)

A mixture containing 135 mg (0.925 mmol) of 2, 35 mg of 10% palladium on charcoal, and 15 ml of ethyl acetate was hydrogenated for 29 hr. After work up a clear, slightly yellow liquid was obtained. The liquid was identified as cis-octahydro-2H-cyclohepta[b]furan-2-one (90) by comparing its nmr spectrum to the nmr spectrum of 90 as reported by Herz and Glick (49). NMR ($CDCl_3$) δ4.82-4.56(m, -CH-OC=O) and 2.95-1.10(m, 13H).

Hydrogenation of 8-methyl-2H-cyclohepta[b]furan-2-one (59)

A mixture containing 73 mg (0.456 mmol) of 59, 43 mg of 10% palladium on charcoal, and 15 ml of ethyl acetate was hydrogenated for 27 hr. After work up a clear, colorless liquid was obtained. GLC separation of a 13 1/2 ft x 1/4 in, 20% SE-30 on Chromosorb W 80/100 mesh column with column temp of 205°C gave only one component. MS, m/e (70 eV) 168(40), 109(100), 97(57), 69(43), 68(38), and 56(74); exact mass calcd for $C_{10}H_{16}O_2$: 168.11503; found: 168.11432; nmr ($CDCl_3$) δ4.64(d, J=7 Hz, of m, 1H), 3.00-0.90(m, 12H), and 1.17(d, J=7 Hz, 3H); ir ($CHCl_3$) 2920, 1775, 1455, 1170, 1000, and 990 cm^{-1}.

Hydrogenation of 6,7-dihydro-azuleno[6,5-b]furan-2(5H)-one (69) and 7,8-dihydro-azuleno[5,6-b]furan-2(6H)-one (70) mixture

A mixture containing 104 mg (0.559 mmol) of a 1:1 mixture of 69 and 70, 46 mg of 10% palladium on charcoal, and 15 ml of ethyl acetate was hydrogenated for 29 hr. After work up a slightly yellow liquid was obtained. The liquid was chromatographed on a 13 1/2 ft x 1/4 in, 20% SE-30 on Chromosorb W 80/100 mesh column with column temp of 246°C. Three components were observed. The first component was not identified. The second component was collected, MS, molecular ion, 194; nmr ($CDCl_3$) δ4.54(m, 1H) and 2.83-1.19(m, 17H); ir (CCl_4) 2930, 2860, 1785, and 1155 cm^{-1}. The third component was also collected, MS, molecular ion, 194; nmr ($CDCl_3$) δ4.48(d, J=7 Hz, of m, 1H) and 2.88-1.45(m, 17H); ir (CCl_4) 2950, 2870, 1785, 1165, and 995 cm^{-1}.

Hydrogenation of 6,7-dihydro-9-chloro-azuleno[6,5-b]furan-2,5-dione (81)

A mixture containing 38 mg (0.162 mmol) of 81, 10 mg of 10% palladium on charcoal, and 15 ml of ethyl acetate was hydrogenated for 15 hr. After work up a slightly yellow liquid was obtained. Mass spectral data of the liquid revealed a mixture of components having molecular ion peaks of 208, 206, and 204.

Hydrogenation of 6,7-dihydro-8-methyl-azuleno[6,5-b]furan-2,5-dione (83)

A mixture containing 44 mg (0.206 mmol) of 83, 49 mg of 10% palladium on charcoal, and 25 ml of ethyl acetate was hydrogenated for 24 hr. After work up a slightly yellow liquid was obtained. Mass spectral data of the liquid revealed a mixture of components having molecular ion peaks of 222 and 220. TLC (silica gel, ethyl acetate) revealed at least five components.

A mixture containing 17 mg (0.079 mmol) of 83, 13 mg of 10% palladium on charcoal, and 25 ml of ethanol was hydrogenated for 24 hr. After work up a slightly yellow liquid was obtained. Mass spectral data of the liquid revealed a mixture of components having molecular ion peaks of 222 and 220. TLC (silica gel, ethyl acetate) revealed at least five components.

A mixture containing 90 mg (0.421 mmol) of 83, 24 mg of 10% palladium on charcoal, and 20 ml of glacial acetic acid was hydrogenated for 13 hr. After work up a slightly yellow liquid was obtained. Mass spectral data of the liquid revealed a mixture of components having molecular ion peaks of 222, 220, and 218. TLC (silica gel, 1:4, V:V, hexanes:ethyl acetate) revealed at least five components.

Hydrogenation of 5-methyl-6,7-dihydro-azuleno[5,6-b]furan-2,8-dione (84)

A mixture containing 37 mg (0.173 mmol) of 84, 15 mg of 10% palladium on charcoal, and 20 ml of ethyl acetate was hydrogenated for 24 hr. After work up a slightly yellow liquid was obtained. Mass spectral data of the liquid revealed a mixture of components having molecular ion peaks of 222 and 220. TLC (silica gel, 1:4, V:V, hexanes:ethyl acetate) revealed at least 4 components.

A mixture containing 30 mg (0.140 mmol) of 84, 14 mg of 10% palladium on charcoal, and 20 ml of ethanol was hydrogenated for 24 hr. After work up a slightly yellow liquid was obtained. Mass spectral data of the liquid revealed a mixture of components having molecular ion peaks of 222, 220, and 218. TLC (silica gel, 1:4, V:V, hexanes: ethyl acetate) revealed at least 6 components.

A mixture containing 70 mg (0.327 mmol) of 84, 28 mg of 10% palladium on charcoal, and 20 ml of glacial acetic acid was hydrogenated for 12 hr. After work up a slightly yellow liquid was obtained. Mass spectral data of the liquid revealed a mixture of components having molecular ion peaks of 222, 220, and 218. TLC (silica gel, ethyl acetate) revealed at least 6 components.

SUMMARY

The flash vacuum pyrolysis of aryl propiolates has been examined. Pyrolysis of phenyl propiolate yielded 2H-cyclohepta[b]furan-2-one. Addition of substituents such as methyl, isopropyl, bromo, chloro, or formyl to the benzene ring did not alter the thermal rearrangement. With a symmetrical aryl propiolate only one product was obtained. With an unsymmetrical propiolate two isomers were obtained. The ratio of the two isomers could be controlled somewhat by using substituents in the ortho position of the benzene ring.

Oxygenated substituents such as acetoxy, methoxy, and hydroxy did not give the expected thermal rearrangement.

The pyrolysis reaction was demonstrated to be quite general. Pyrolysis of indanyl propiolates yielded the azulenofuran-2-one system or the azulenofurandione system, the carbon skeletal system of pseudoguaianolides and guaianolides, both of which are hydroazulenic sesquiterpene lactones.

Chlorine substituted at the ortho position has been demonstrated to be a good substituent in directing the initial Claisen rearrangement, and thus has been shown to affect the ratio of the isomeric products. The directing power of the chlorine was found to be more effective in the indanyl series of propiolates than in the phenyl series of propiolates.

Friedel-Crafts acylation at position 3 has been carried out with acetic anhydride and 2H-cyclohepta[b]furan-2-one. Base or acid hydrolysis of some of these lactone compounds, followed by decarboxylation have yielded various substituted tropones. Thus, FVP provides a viable pathway into the troponoid system.

Some limitations of FVP have been characterized by the low yields, the difficulties of the separation of the isomers, and the decomposition associated with the separation of some of the azulenofurandione compounds. Low yields could probably be solved with modifications of the pyrolysis apparatus. The separation step could not be avoided completely. Decomposition of the azulenofurandione compounds could only be solved if silica gel could be avoided in the separation, or if the isomeric ratio of the products formed could be controlled by using chlorine or other directing groups. Then fractional recrystallization could be employed. Another method to avoid decomposition is to mask the carbonyl moiety which is suspected of causing the decomposition problem.

The feasibility of incorporating FVP of aryl propiolates in a synthetic sequence to synthesize pseudoguaianolides and guaianolides depends on the success of the hydrogenation of the lactone compounds. Thus far, results indicate that some

hydrogenations were successful while others were not too promising. Only further investigation will determine the status of this goal.

LITERATURE CITED

1. G. Seybold, Angew. Chem. Int. Ed. Eng. 16, 365 (1977).
2. W. S. Trahanovsky, S. L. Emeis, and A. S. Lee, J. Org. Chem. 41, 4043 (1976).
3. E. Hedaya, Acct. Chem. Res. 367 (1969).
4. P. deMayo, Endeavour 31, 135 (1972).
5. H. J. Hageman and U. E. Wiersum, Chem. Ber. 9, 206 (1973).
6. G. Seybold, Chem. Ber. 110, 239 (1977).
7. W. S. Trahanovsky and P. W. Mullen, J. Am. Chem. Soc. 94, 5911 (1972).
8. J. Zsindley and H. Schmid, Helv. Chim. Acta 51, 1510 (1968).
9. H. J. Hansen and H. Schmid, Chimia 24, 89 (1970).
10. B. H. Al-Sader and D. M. Al-Fekri, J. Org. Chem. 43, 3626 (1978).
11. J. M. Riemann and W. S. Trahanovsky, Tetrahedron Lett. 1867 (1977).
12. J. M. Riemann and W. S. Trahanovsky, Tetrahedron Lett. 1863 (1977).
13. Y. Sasada, Bull. Chem. Soc. Japan 32, 165 (1959).
14. T. Nozoe, S. Seto, and S. Matsumura, Proc. Japan Acad. 28, 483 (1952).
15. S. Seto, Sci. Rep. I Tohoku Univ. 37, 367 (1953).
16. T. Nozoe, H. Seto, T. Mukai, and Y. Kitahara, Japan 8099 (1957); Chem. Abstr. 52, P13801e (1958).
17. T. Nozoe, Bull. Chem. Soc. Japan 41, 2935 (1968).
18. T. Takase, T. Nozoe, and S. Fukuda, Bull. Chem. Soc. Japan 44, 2215 (1971).
19. T. Sato, Nippon Kagaku Zasshi 80, 1342 (1959).

20. T. Sato, Nippon Kagaku Zasshi 80, 1345 (1959).

21. T. Sato, Nippon Kagaku Zasshi 80, 1347 (1959).

22. T. Sato, Nippon Kagaku Zasshi 80, 1349 (1959).

23. T. Nozoe, T. Mukai, and T. Susuzi, Bull. Chem. Soc. Japan 36, 38 (1963).

24. K. Takase, Bull. Chem. Soc. Japan 37, 1460 (1964).

25. N. Junichi, Y. Sato and N. Soma, Sankyo Kenkyusho Nempo 21, 47 (1969).

26. T. Nozoe, K. Takase, M. Kato and T. Nogi, Tetrahedron 27, 6023 (1971).

27. T. Nozoe, T. Mukai, K. Osaka and N. Shishido, Bull. Chem. Soc. Japan 34, 1384 (1961).

28. N. Morita, Y. Kitahara and T. Asao, Tetrahedron Lett. 869 (1972).

29. N. Morita, T. Asao and Y. Kitahara, Chem. Lett. 747 (1974).

30. J. Ciabattoni and H. W. Anderson, Tetrahedron Lett. 3377 (1967).

31. N. Morita, J. Asao and Y. Kitahara, Tetrahedron Lett. 2083 (1974).

32. T. K. Devon and A. I. Scott, Handbook of Naturally Occurring Compounds (Academic Press, New York, 1972), Vol. II.

33. H. Yoshioka, T. J. Mabry and B. N. Timmermann, Sesquiterpene Lactones (University of Tokyo Press, Yokyo, 1973).

34. J. L. Hartwell and B. J. Abbott, Advan. Pharmacol. Chemother. 7, 117 (1969).

35. E. Rodriguez, G. H. N. Towers and J. C. Mitchell, Phytochem. 15, 1573 (1976).

36. R. A. Kretchmer and W. J. Thompson, J. Am. Chem. Soc. 98, 3379 (1976).

37. P. De Clercq and M. Vandewalle, J. Org. Chem. 42, 3447 (1977).

38. P. A. Grieco, Y. Ohfune and G. Majetich, J. Am. Chem. Soc. 99, 7393 (1977).

39. J. A. Marshall and R. H. Ellison, J. Am. Chem. Soc. 98, 4312 (1976).

40. M. F. Semmelhack, A. Y. Yamashita, J. C. Tomesch and K. Hirotsu, J. Am. Chem. Soc. 100, 5565 (1978).

41. P. A. Wender, M. A. Eissenstat and M. P. Filosa, J. Am. Chem. Soc. 101, 2196 (1979).

42. Y. Ohfune, P. A. Grieco, C.-L. J. Wang and G. Majetich, J. Am. Chem. Soc. 100, 5948 (1978).

43. P. A. Grieco, T. Oguri and S. Burke, J. Org. Chem. 42, 4552 (1978).

44. P. Kok, P. De Clercq and M. Vandewalle, Bull. Soc. Chim. Belg. 87, 615 (1978).

45. S. M. Kupchan, M. A. Eakin and A. M. Thomas, J. Med. Chem. 14, 1147 (1971).

46. K. Lee, E. Huang, C. Piantadosi, J. S. Pagano and T. A. Geissman, Cancer Res. 31, 1649 (1971).

47. L. A. Miller, U.S. Patent 3097230 (1963); Chem. Abstr. 59, 13892a (1963).

48. W. L. Mock and J. H. McCausland, J. Org. Chem. 41, 242 (1976).

49. W. Herz and L. A. Glick, J. Org. Chem. 28, 2970 (1963).

50. F. Pietra, Chem. Rev. 293 (1973).

51. W. S. Trahanovsky, C. C. Ong, J. G. Pataky, J. L. Weitl, P. W. Mullen, J. C. Clardy and R. S. Hansen, J. Org. Chem. 36, 3575 (1971).

52. P. W. Mullen, Ph.D. Thesis, Iowa State University, 1971.

53. W. S. Trahanovsky, C. C. Ong and J. A. Lawson, J. Am. Chem. Soc. 90, 2839 (1968).

54. W. J. Balfour, C. C. Greig and S. Visaisouk, J. Org. Chem. 39, 725 (1974).

55. F. D. Chattaway, J. Chem. Soc. 2495 (1931).

56. H. S. Olcott, J. Am. Chem. Soc. 59, 392 (1937).

57. T. O. Soine and F. E. Di Gangi, J. Am. Pharm. Assoc. Sci. Ed. 41, 236 (1952).

58. S. Wagatuma, S. Higuchi, H. Ito, T. Nakano, Y. Naoi, K. Sakai, T. Matsui, Y. Takahashi, A. Nishi and S. Sano, Org. Prep. and Proceed. Int. 5, 65 (1973).

59. N. F. Hayes and R. H. Thomson, J. Chem. Soc. 1585 (1956).

60. O. Dann, G. Volz and O. Huber, Ann. Chem. 587, 16 (1954).

61. J. Sam and J. N. Plampin, J. Am. Chem. Soc. 82, 5205 (1960).

62. J. S. Buck, U.S. 2,990,324 (1961); Chem. Abstr. 56, P432a (1962).

63. C. K. Ingold and H. A. Piggott, J. Chem. Soc. 123, 1469 (1923).

64. H. House and C. B. Hudson, J. Org. Chem. 35, 647 (1970).

65. J. Sam. U.S. 2,820,817 (1958); Chem. Abstr. 52, P10197C (1958).

66. R. Adams and E. Montgomery, J. Am. Chem. Soc. 46, 1518 (1924).

67. S. N. Kulkarni, S. B. Patil, P. V. Panchangam and K. S. Nargund, Indian J. Chem. 5, 471 (1967).

68. W. S. Johnson and W. E. Shelbery, J. Am. Chem. Soc. 67, 1853 (1945).

69. J. R. Merchant, M. S. Kamath and S. Y. Dike, J. Chem. Soc. Perkin I, 2089 (1977).

70. W. T. Brady and J. P. Hieble, Tetrahedron Lett. 3205 (1970).

71. J. Parrick and J. W. Rasburn, Can. J. Chem. 43, 3453 (1971).

72. T. Mukai, Nippon Kagaku Zasshi 79, 1547 (1948).

73. G. L. Closs and L. E. Closs, J. Am. Chem. Soc. 83, 599 (1961).

74. T. Sato, Nippon Kagaku Zasshi, 80, 1167 (1959).

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