INTRAMOLECULAR ACYLATION OF α-SULFINYL CARBANIONS

PREPARATION OF CYCLOPENTENONE AND

CYCLOHEXENONE DERIVATIVES

BY

PRANEE PHINYOCHEEP

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THE DEFENSE OF THESIS

We, the members of the supervisory Graduate Committee

for

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PREPARATION OF CYCLOPENTENONE AND

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We further agree that she has satisfactorily

defended her thesis at the examination given

by

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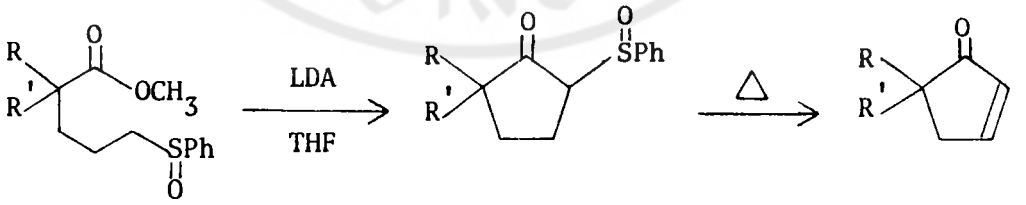
TABLE OF CONTENTS

Abstract

Intramolecular acylation of the α-sulfinyl carbanions of the ester sulfoxides 4 has been shown to give β-ketosulfoxides 6 in moderate to good yields, which compounds subsequently pyrolyse to 5,5-disubstituted cyclopentenones 7. This methodology can be applied, by pyrolysis of the β-ketosulfoxides 11 (prepared from intramolecular acylation of α-sulfinyl carbanions of the amide sulfoxides 10) to the high yield synthesis of 5-monosubstituted cyclopentenones 12, which are useful intermediates in the synthesis of natural products. Moreover, the sulfoxides 18 gave the β-ketosulfoxides 20 by the same reaction, which upon pyrolysis afforded the cyclohexenone derivatives 22. Unfortunately, the phenol annulation reaction starting from the amide sulfoxides 19, and leading to the compounds 23 via intramolecular acylation reaction of the α-sulfinyl carbanions, gave less satisfactory results.



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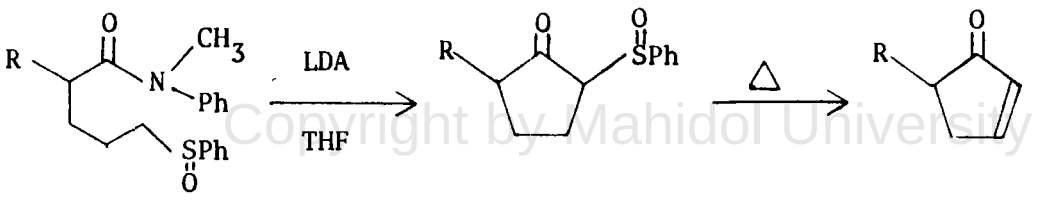

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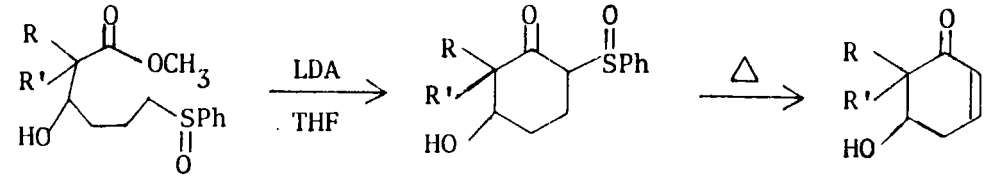

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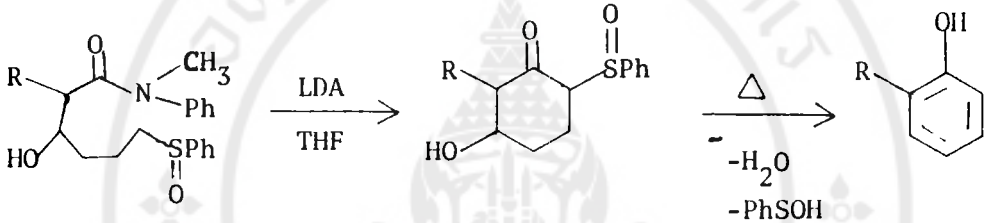
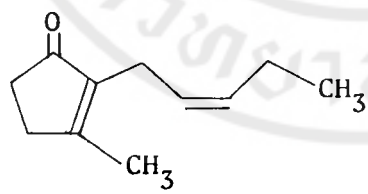


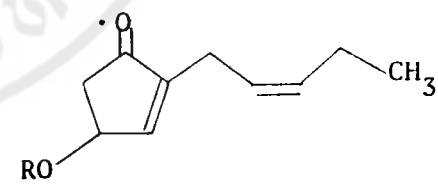
19 21 23

Introduction

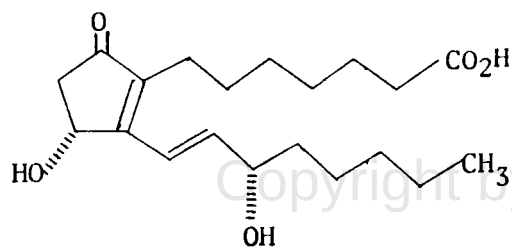
Recently there has been an increasingly large amount of research devoted to developing synthetic routes to substituted cyclopentenones and their 4-hyd oxy derivatives. This has been due in large part to interest in several biologically active natural products which have this moiety as a major structural feature. These include, for example, cis-jasmone[1], an important perfumery constituent, rethrolones[2], the ester components of the insecticidual pyrethrins[3], prostaglandins[4] and methylenomycin B[5]. From an examination of structures of such compounds, it can be seen that a sufficiently general oxocyclopentene synthesis might be suitable, with appropriate modification, for the construction of any of these compounds. Different synthetic pathways, which have been developed, are briefly summarized as follows.



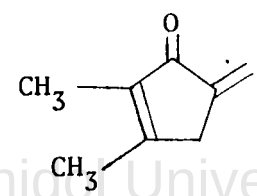
cis-Jasmone



Rethrolones



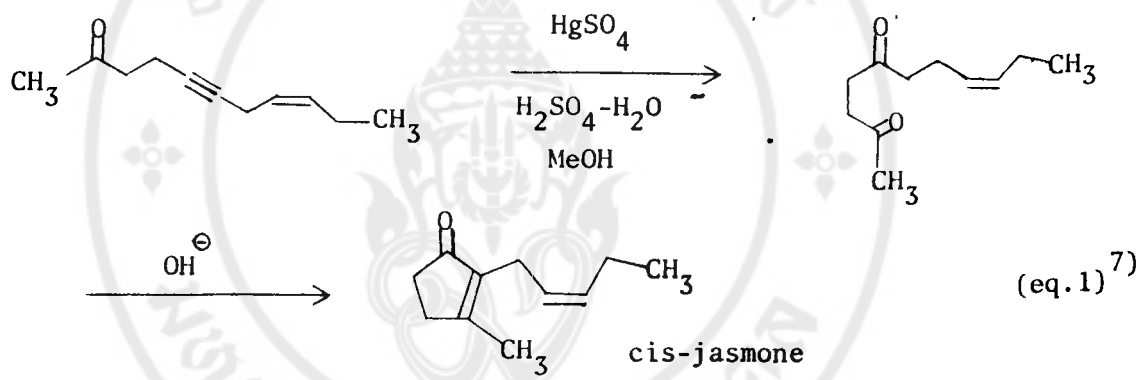
PGE_1



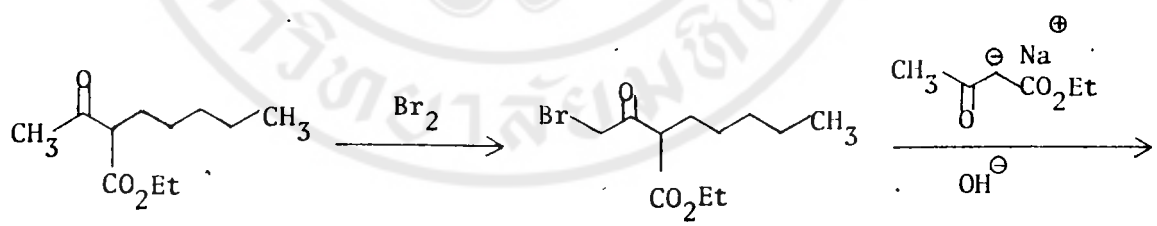
Methylenomycin B

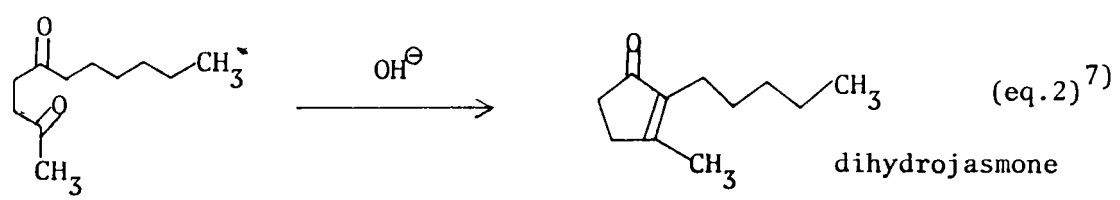
1. Cyclodehydration of 1,4-Diketones[6-13].

The most common method to obtain 2,3-disubstituted cyclopentenone is based on the base-catalyzed intramolecular aldol condensation of 1,4-unsymmetrically substituted 1,4-diketones. Therefore, the synthesis of 1,4-unsymmetrically substituted 1,4-dicarbonyl compounds is still a subject of intensive study. Some examples of this method are shown below (eq.1-4).

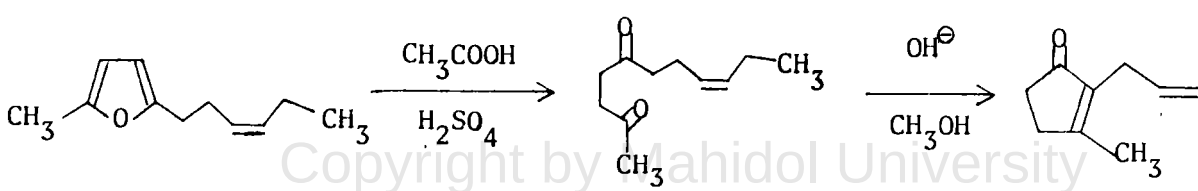


(eq.1)[7]

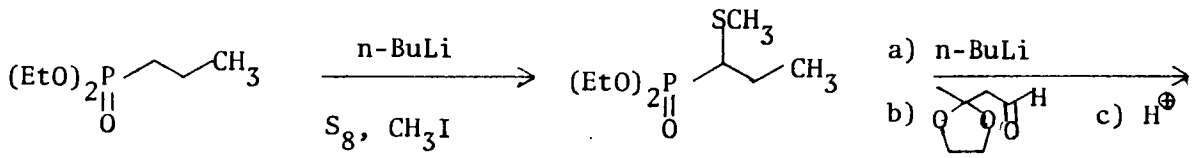


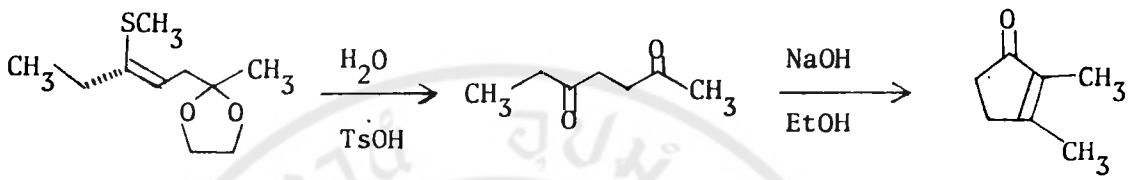


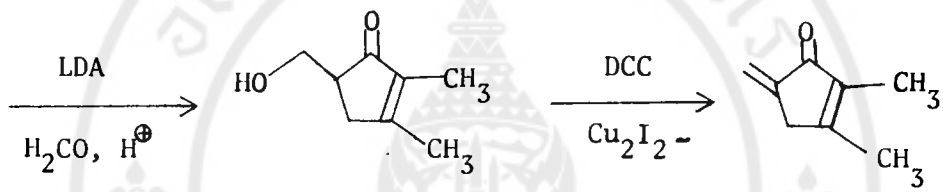
(eq.2)[7]



(eq.3)[7]



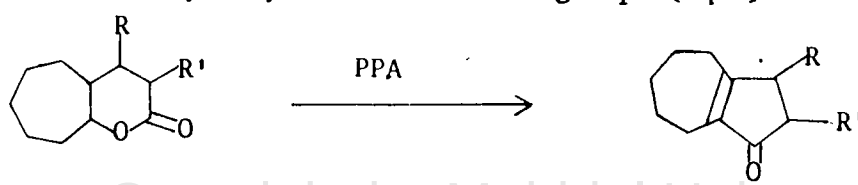




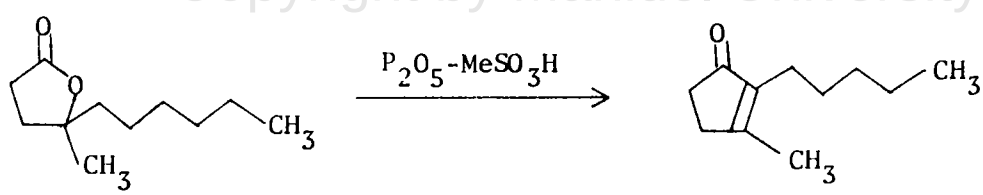
(eq.4)[9]

2. Cyclodehydration of γ-butyrolactones[14-17].

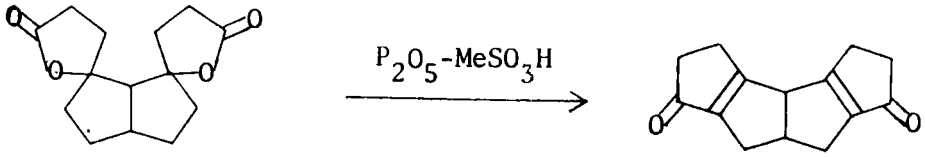
Reactions of certain γ-butyrolactones and δ-lactones with polyphosphoric acid or a phosphorus pentoxide-methanesulfonic acid mixture have been found to yield cyclopentenone derivatives, which presumably arise via intramolecular acylation of the intermediate unsaturated acids (eq.5-8). The mixture of P_2O_5 and CH_3SO_3H has been used to be a very mild cyclodehydrating agent for such a conversion, i.e. some paraconic esters have been converted into cyclopentenone derivatives without hydrolysis of the ester groups (eq.9).



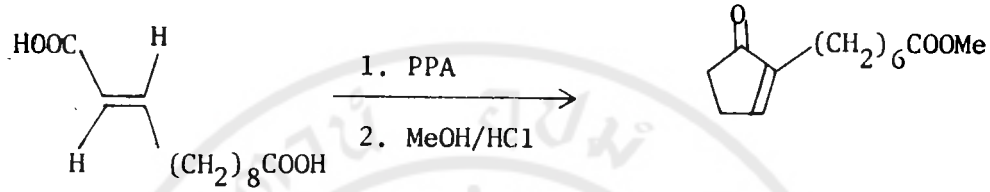
(eq.5)[14]



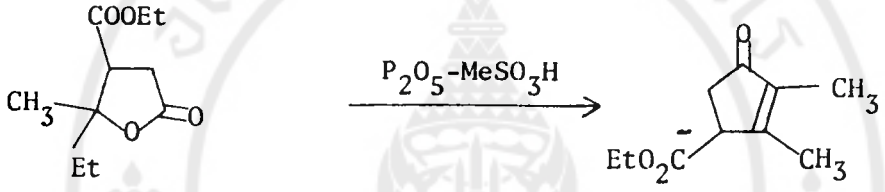
(eq.6)[15]



(eq.7)[15]



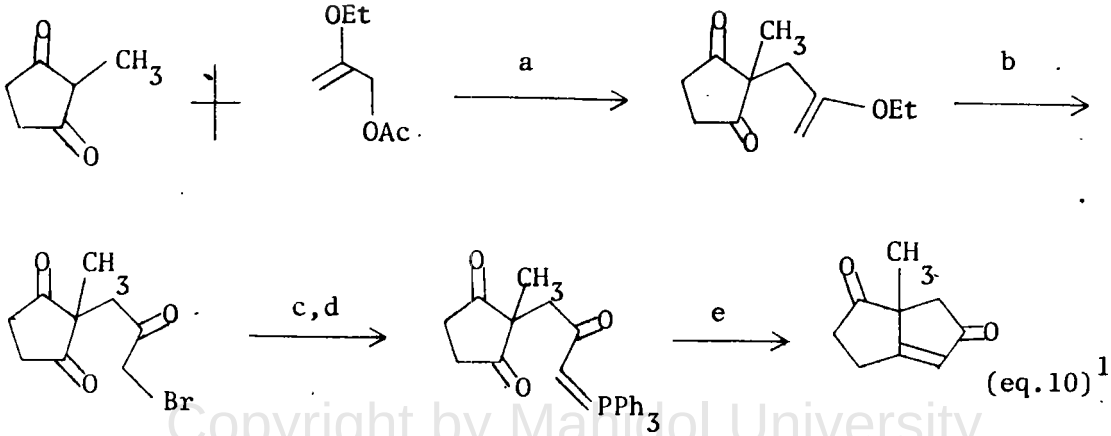
(eq.8)[16]



(eq.9)[17]

3. Intramolecular Wittig- and Wittig-Horner Reaction[18-23].

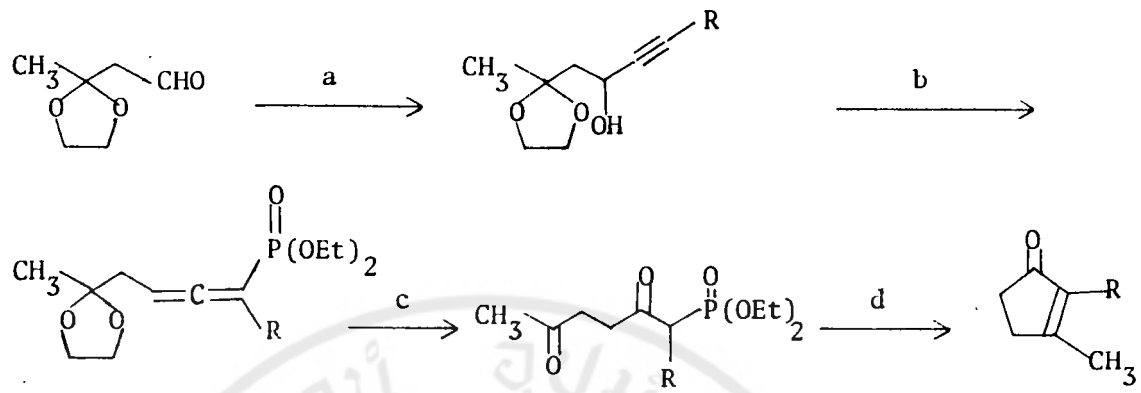
Although the cyclisation of 1,4-diketones is still a generally applicable method for the synthesis of cyclopentenones, the Wittig and Wittig-Horner reactions have also found application for such purpose. Examples are shown as below:



(eq.10)[19]

a) $Pd(Ph_3)_4$ 1-10%, DBU, toluene, 80°C b) NBS, H_2O, Me_2SO, 15-20°C

c) PPh_3, C_6H_6, 80°C d) Aqueous K_2CO_3 e) 40°C



a) 1. $LiC{\equiv}CR$ in THF, -78°C. 2. NH_4Cl

b) $ClP(OEt)_2$, NEt_3, CH_2Cl_2 (14 h, RT)

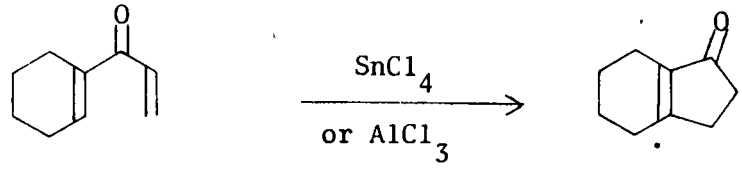
c) 1. 2 h reflux with NaOEt in EtOH 2. 10% HCl

d) NaH in THF (12 h, RT)

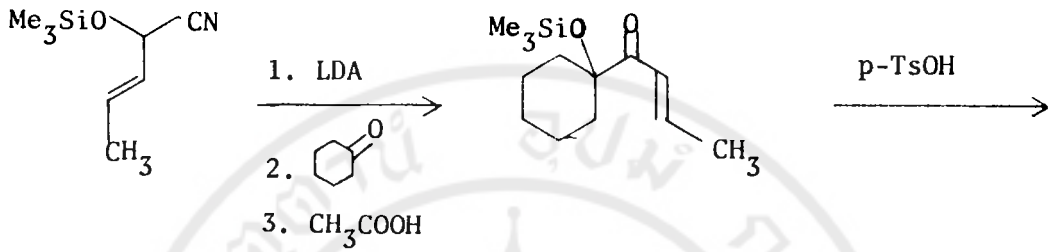
(eq.11)[22]

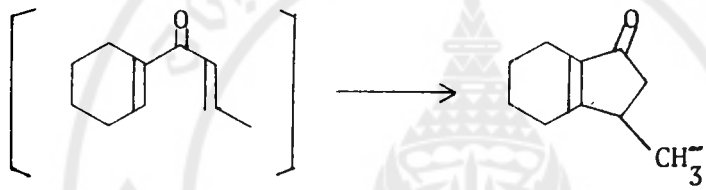
4. Nazarov Cyclisation and related reactions[24-27].

With regard to cyclopentenone annelation the classical Nazarov cyclisation reaction has received much attention and has been extensively modified in the preparation of the divinyl ketone precursors (or their equivalent) and in the cyclisation condition. A major limitation common to all of these methods and, indeed, inherent in the cyclisation itself is the lack of control over the position of the bond which results in the thermodynamically more stable product, i.e., that with the highest degree of substitution (eq.12-14). The introduction of the new double bond in Nazarov cyclisation to the less substituted position, i.e., away from the ring fusion could be directed by the utilization of organosilicon compounds in the reaction (eq.15).

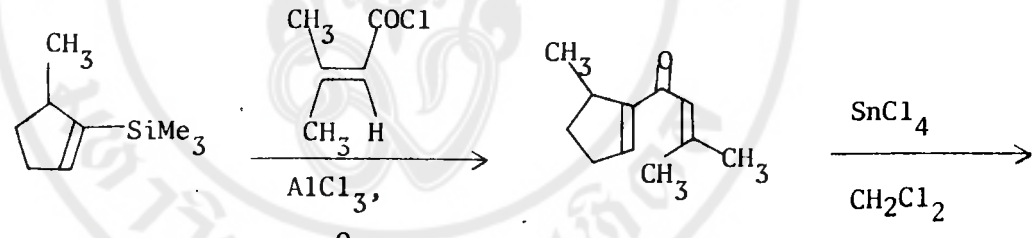


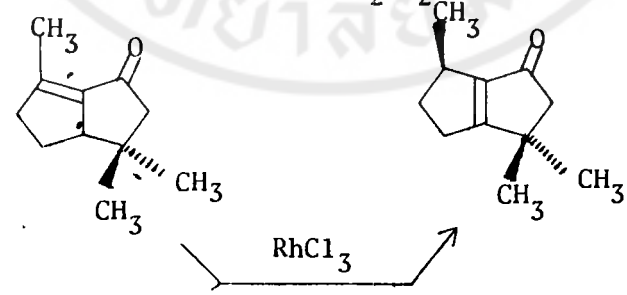
(eq.12)[24]



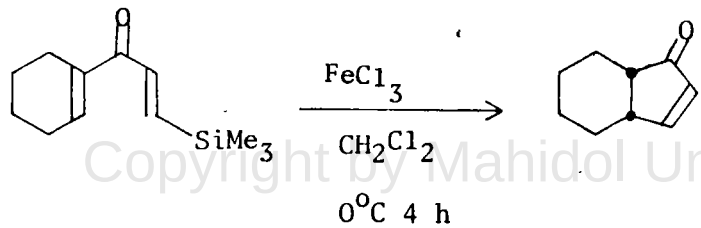


(eq.13)[25]



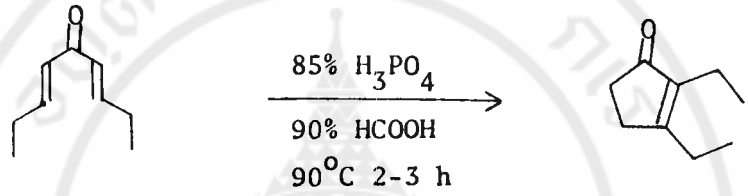


(eq.14)[27a]

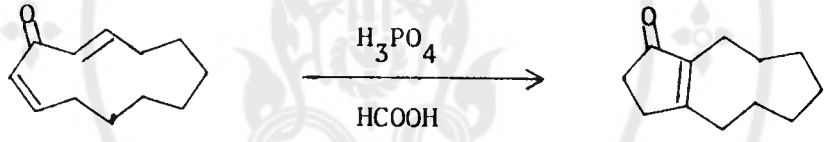


(eq.15)[27b]

Acid-catalyzed reaction of β,β'-disubstituted cross conjugated dienones or the corresponding ethylene acetals gives mainly 2,3-disubstituted-2-cyclopentenones instead of the simple Nazarov cyclisation product, 3,4-disubstituted-2-cyclopentenones. This transformation is explained in terms of electrocyclic ring-closure, addition of hydroxylic solvent(s), tautomerization of the resulting 2-hydroxycyclopentanone intermediate, followed by solvolysis and isomerization.

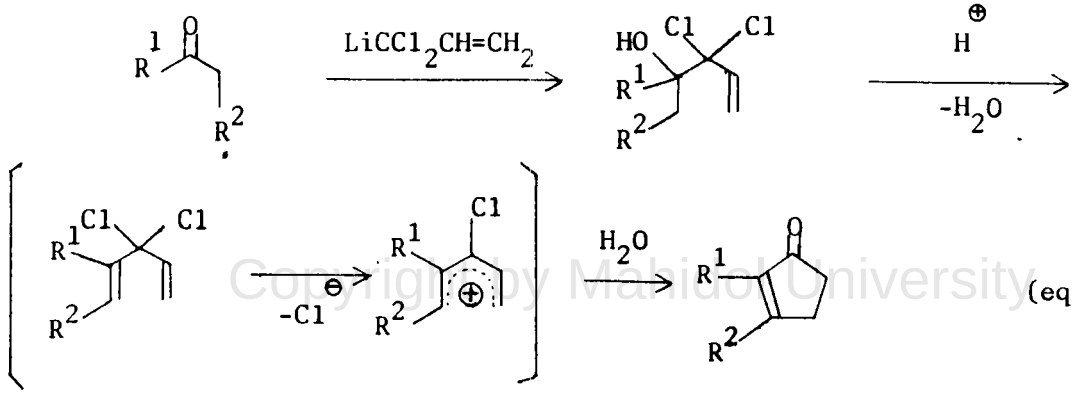


(eq.16)[28]



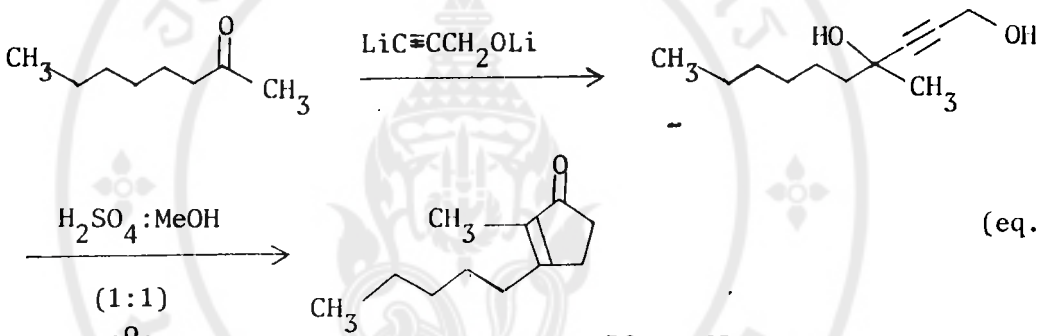
(eq.17)[28]

A closely related method to the Nazarov cyclisation is based on the thermal conrotatory ring-closure of a chloropentadienyl cation followed by hydrolysis as shown in equation 18. A dichlorohomoallyl alcohol, derived from a ketone and 1,1-dichloroallyllithium, is dehydrated by the action of acid to give a dichlorodiene which is further solvolyzed to the cyclopentadienyl cation and then to cyclopentenone.

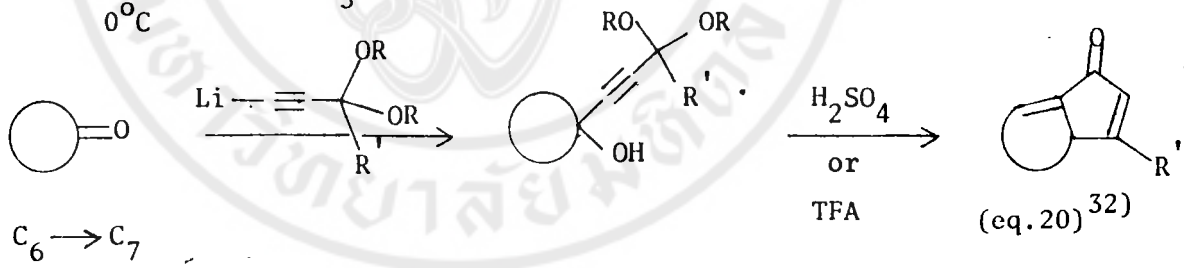


(eq.18)[29]

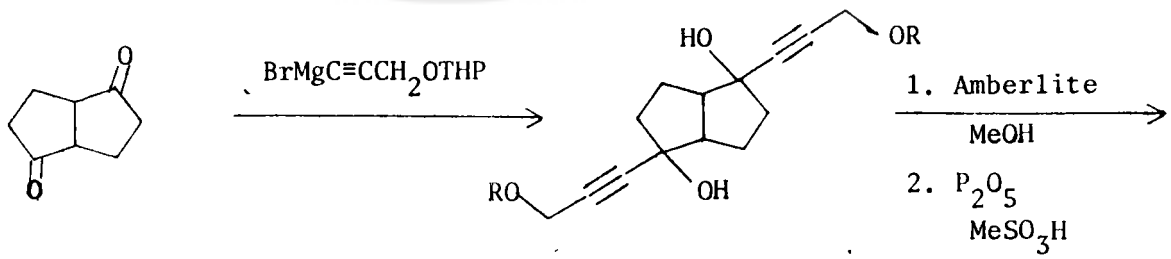
In view of electrocyclic cyclisation of pentadienyl cation intermediates leading to cyclopentenone derivatives, some propagyl alcohol derivatives have been utilized as strating[30-33] material. The reactions have been simply carried out by treatment of propagyl alcohol derivatives with sulfuric acid at $0^{o}C$. A reasonable mechanism may involve dehydration and hydration of acetylene forming a 1,4-pentadien-3-one, which undergoes the Nazarov cyclisation followed by subsequent elimination reactions (eq.19-21).

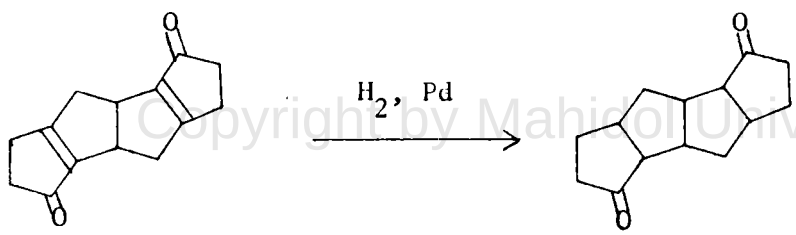


(eq.19)[31]



(eq.20)[32]

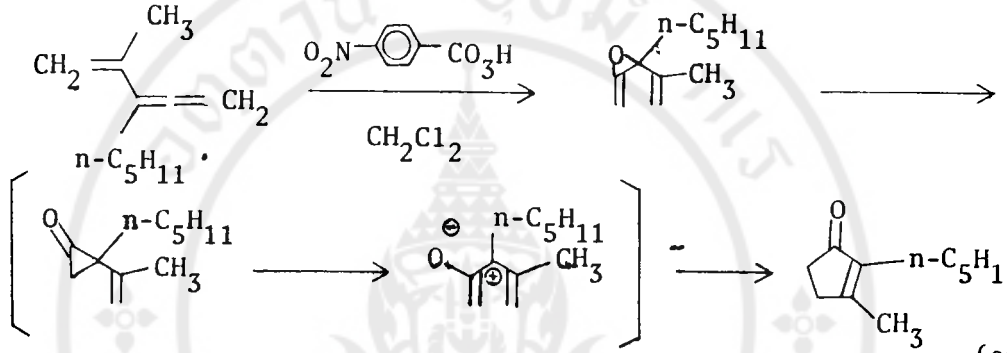




(eq.21)[33]

R = THP

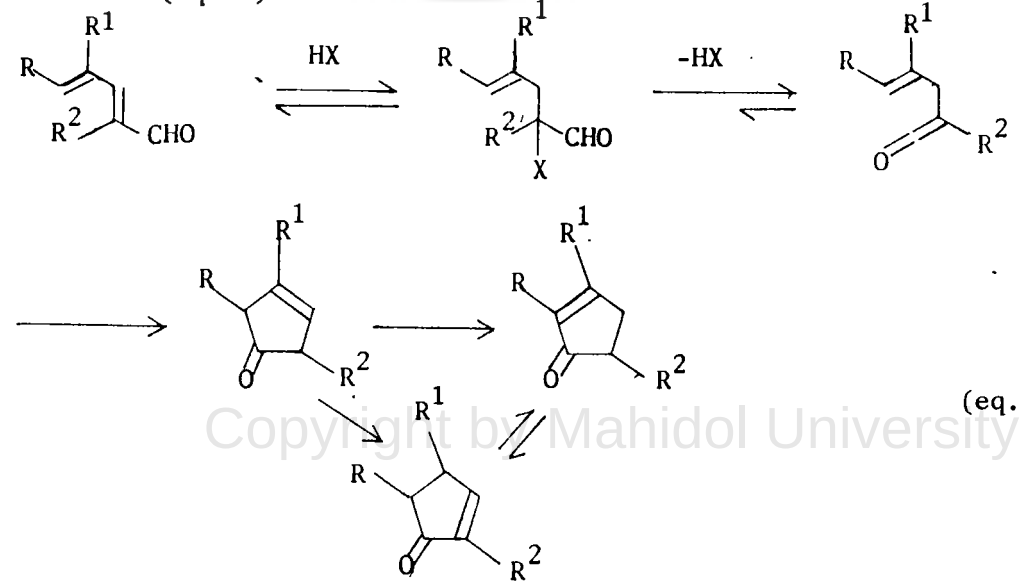
similarly, vinylallene oxides derived from vinylallenes by epoxidation[34,35] seem to be labile: they rearranged readily to cyclopentenones. The formation of cyclopentenones probably occurs via the transposition of an intermediate vinylcyclopropane and a pentadienyl cation. This new method provides a new route to several natural products such as dihydrojasmone (eq.22).



(eq.22)[35]

5. Acid-Catalyzed Cyclisation of 2,4-Dialkyl-2-trans-4-transpentadienals[36].

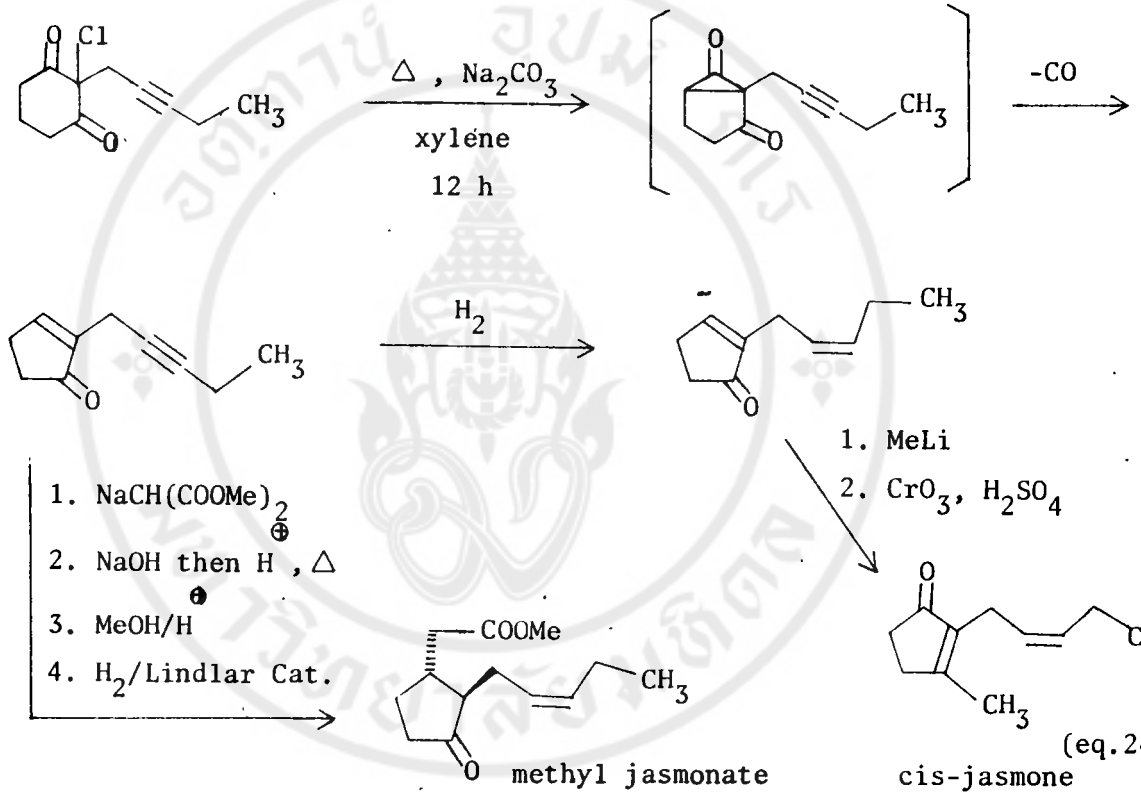
Highly substituted cyclopentenones could be realized most simply by acid catalyzed rearrangement of 2,4-dialkyl-2-trans-4-transpentadienals. The mechanism of this reaction has been proposed as outlined below (eq.23).



(eq.23)[36]

6. Favorski-type Rearrangement[37,38].

The reaction of 2-chloro-2-substituted cyclohexa-1,3-dione with sodium carbonate in boiling xylene afforded 2-substituted cyclopentenone by the Favorski rearrangement. This method has been applied to the synthesis of cis-jasmone and methyl jasmonate (eq.24).

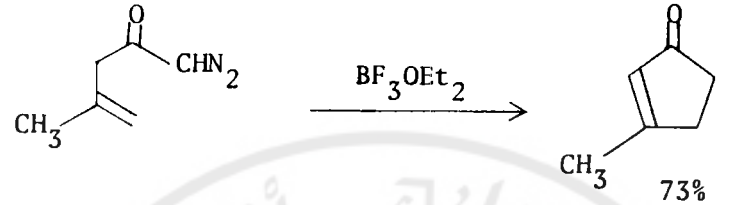


(eq.24)[38]

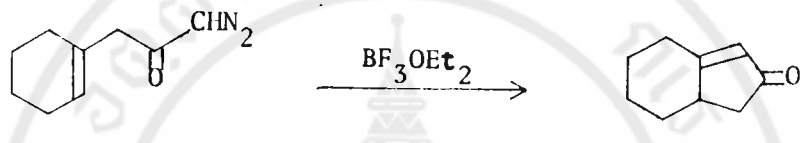
7. Lewis Acid Promoted Decomposition of Unsaturated α-Diazo Ketones[39].

The Lewis acid-catalyzed decomposition of the β,γ unsaturated diazomethylketones (with BF_3OEt_2 in freshly distilled nitromethane or methylene chloride at 0^oC) affords substituted cyclopentenones. The reactions proceed presumably via initial complexation of the Lewis acid with the oxygen of the diazo ketone to afford intermediate A. Subsequent loss of nitrogen and cyclisation leads to a stabilized tertiary carbonium

ion (i.e. B) (eq.25-26).



73% (eq.25)[39]

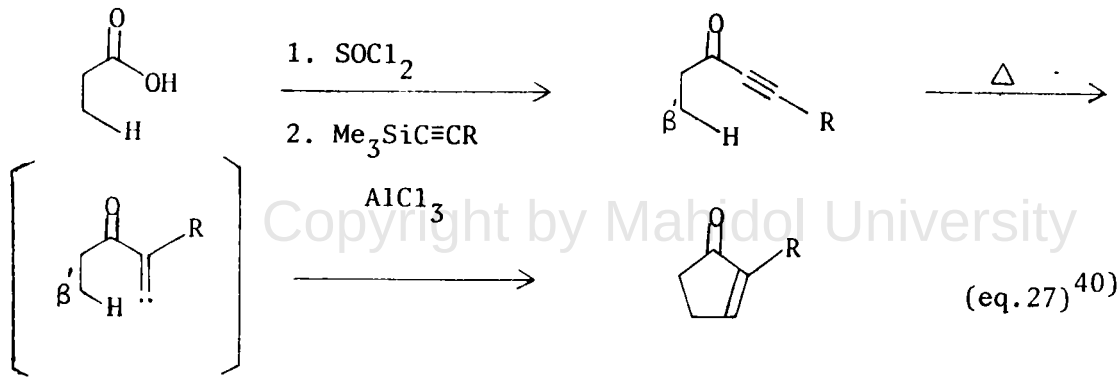


65% (eq.26)[39]

A B

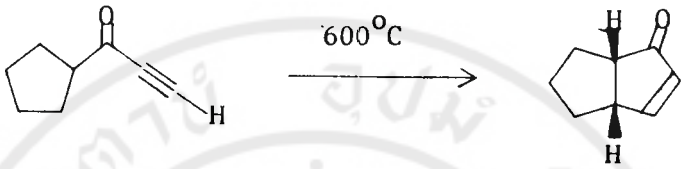
8. Pyrolysis of α-Alkynones[40,41].

The thermal cyclisation of alkynyl alkyl ketone bearing at least one H-atom in a β-position leads specifically to 2-cyclopentenones (eq.27). It is therefore explained by the intermediacy of an alkylidene--carbene which inserts into the C(β)-H bond.

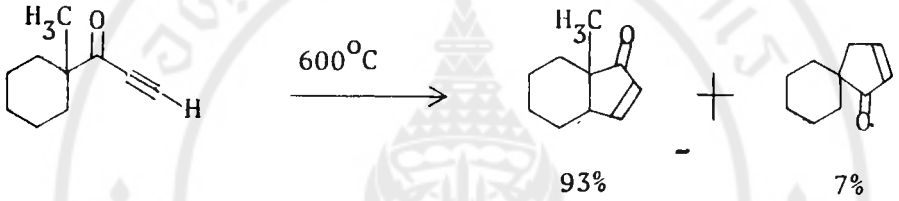


(eq.27)[40]

Several examples have been demonstrated that the α-alkynone cyclisation offers a simple tool for the preparation of certain monocyclic, bicyclic and spiro compounds containing a 2-cyclopentenone moiety (eq.28,29).



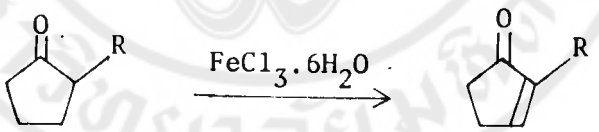
(eq.28)[41]



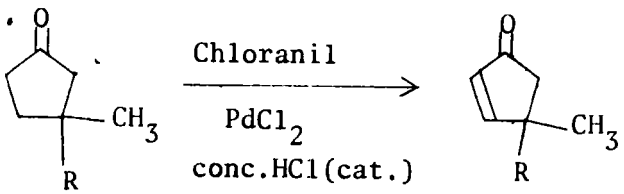
(eq.29)[41]

9. Miscellaneous Methods.

9.1) Direct oxidation of substituted cyclopentanes.



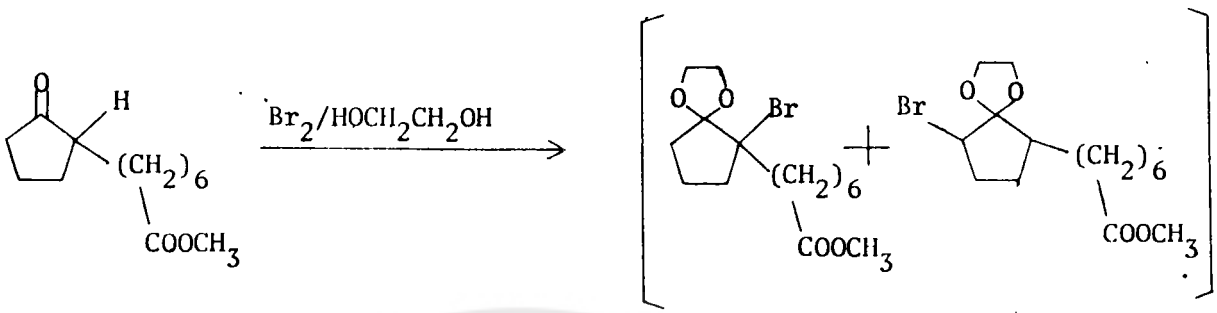
(eq.30)[42]



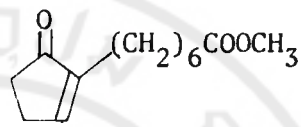
(eq.31)[43]

R = CH_3-, $-CH_2CH(CH_3)_2$, n-C_4H_9-

9.2) Bromoacetalization of methyl substituted ketone followed by dehydrobromination.



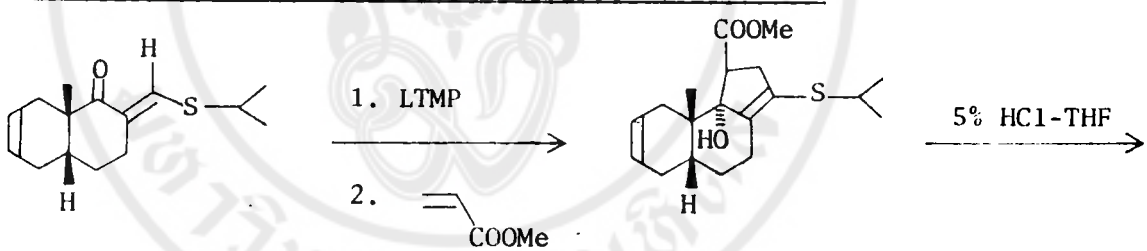
1. $NaOH/CH_3OH$
2. $CH_3OH/TsOH$

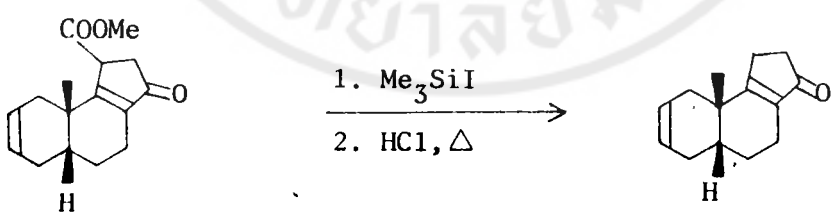


(eq.32)[44]

methyl 7-(5-oxocyclopentenyl)heptanoate

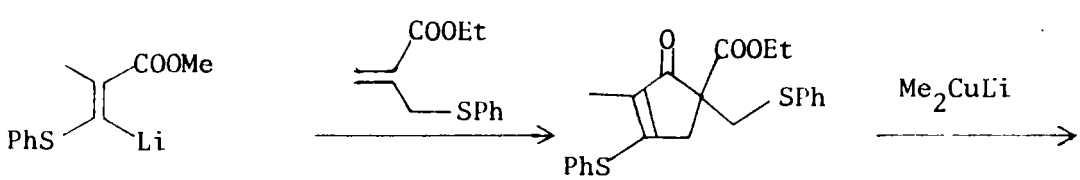
9.3) Michael addition of certain type of Sulfur-stabilized Carbanions to α,β-unsaturated esters followed by cyclisation.

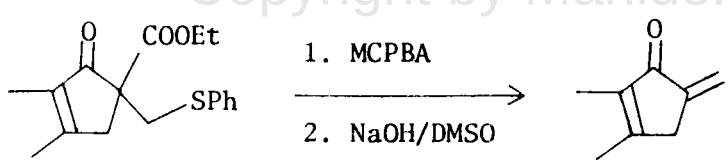




(eq.33)[45]

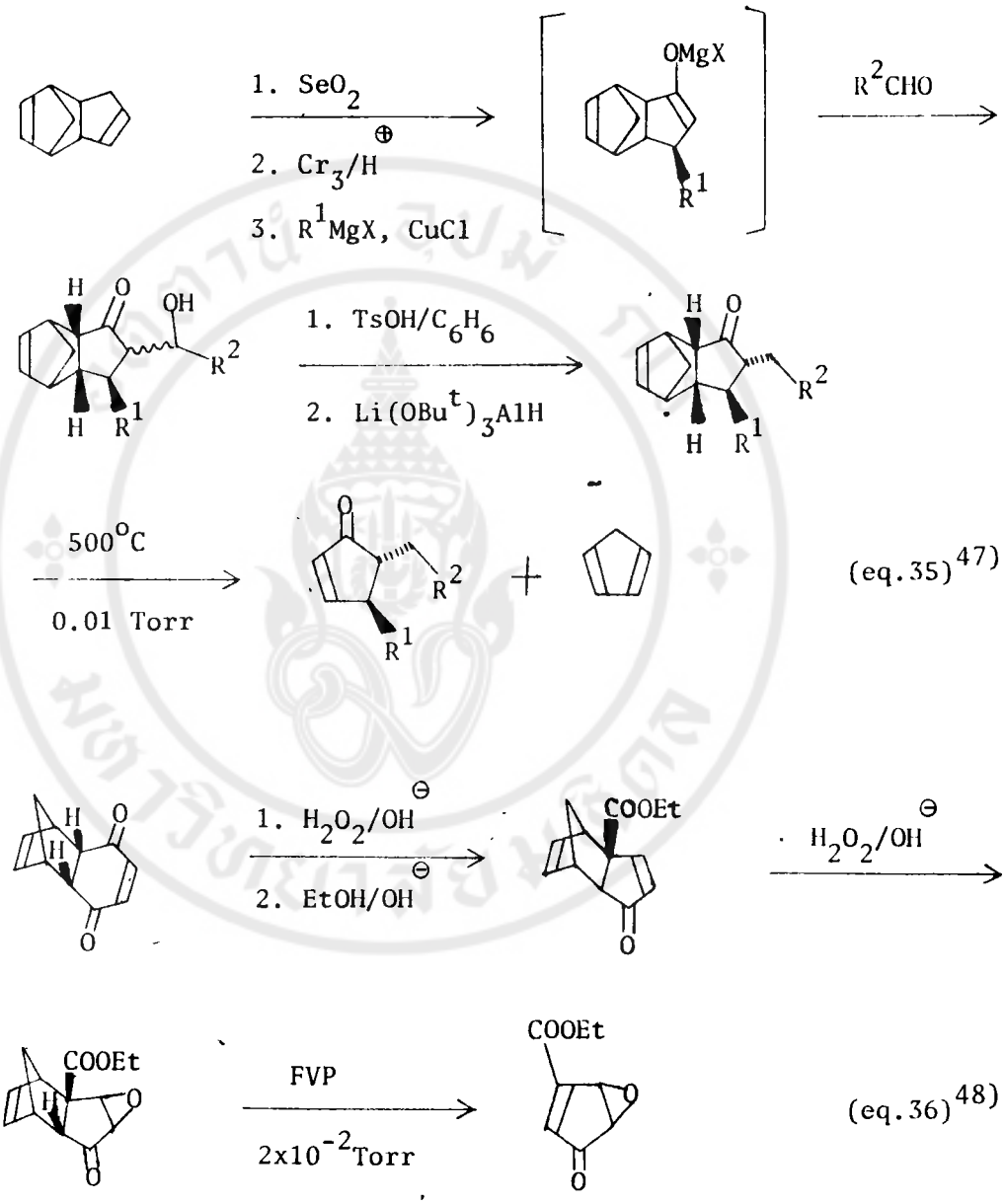
LTMP = lithium 2,2,6,6-tetramethylpiperidide





(eq.34)[46]

9.4) Diels-Alder adducts serve as precursors for the syntheses of cyclopentenones derivatives.



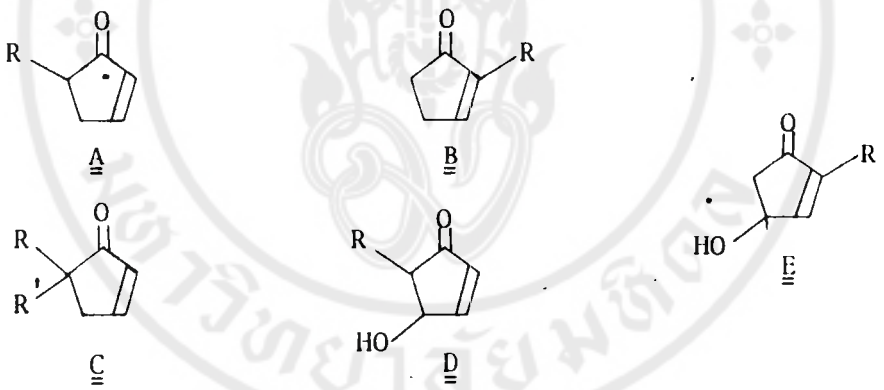
(eq.35)[47]

(eq.36)[48]

FVP = Flash Vacuum Pyrolysis

Results and Discussion

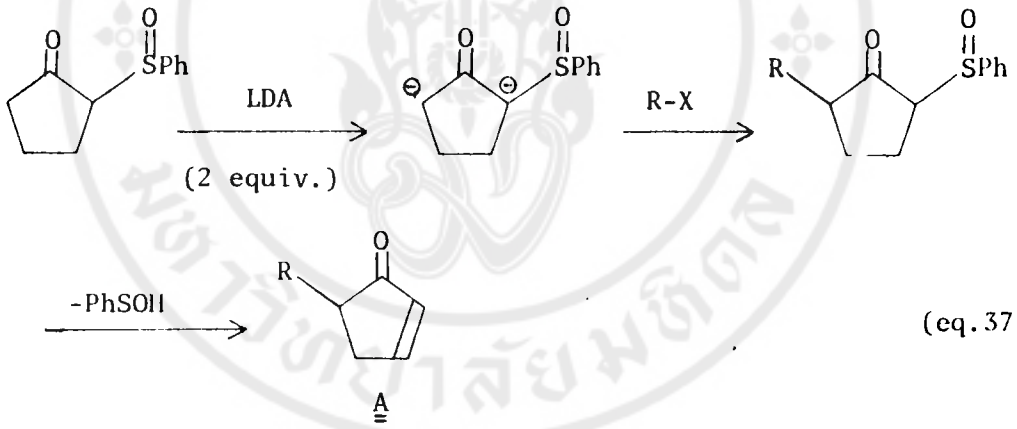
It has been already demonstrated that numerous synthetic methods for the cyclopentenone syntheses have been developed due to their highly important moiety existing in various cyclopentanoid natural products. Despite the existance of numerous synthetic approaches to substituted cyclopentenones, the need for improvement and diversification still remains. Our interest concerning the chemistry of this area prompted us to search for a new method for cyclopentenone annulation reaction; especially, for the syntheses of cyclopentenones of types A, B, C, D and E. The cyclopentenones of types B and E have been proved



to be versatile intermediates for the synthesis of prostaglandins. Δ^2-Cyclopentenones possessing a substituent adjacent to the carbonyl in the C-5 position (A) and/or a hydroxy-substituent at the C-4 position (D) are also potentially important intermediates in organic synthesis; for example, compounds A and D could be isomerised to the thermodynamically more stable isomers B and E using acidic or basic conditions, respectively[49,50]. The cyclopentenone of type A is the most common compound that one could be expected. However, general synthetic methods

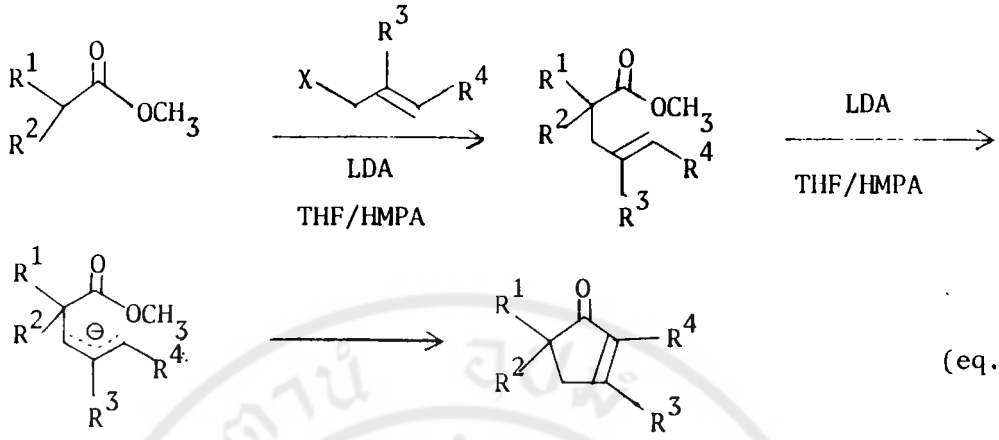
for the preparation of cyclopentenones A and B are still restricted: the cyclisation of 1,4-diketones is still the widest applicable one. It should be expected that kinetic enolate anion derived directly from 2-cyclopentenone would react with alkylating agent to give the cyclopentenone of type A. However this was unsuccessful owing to polymerisation as reported by Smith et al.[51].

Recently, a general method for the synthesis of compounds of type A has been reported by Grieco et al.[52] that the dianion of phenylsulfinyl cyclopentanone underwent exclusively γ-alkylation which upon pyrolysis led to 5-alkyl-2-cyclopentenones (eq.37).



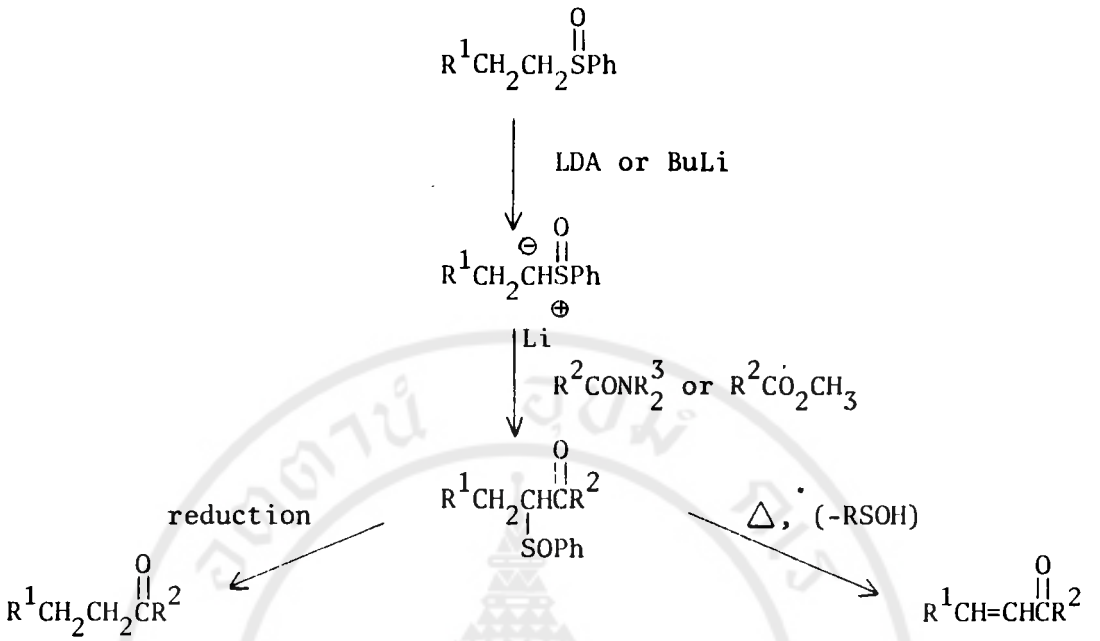
(eq.37)

Thebtaranonth et al. reported[53a] an elegant, direct three-carbon annulation to cyclopentenone derivatives which involved an intramolecular acylation of allylic carbanion as shown in equation 38. This methodology has been applied to the synthesis of methylenomycin B[53b]. However, this annulation reaction is only limited for the synthesis of cyclopentenone of type C (5,5-dialkylsubstituted-2-cyclopentenones).



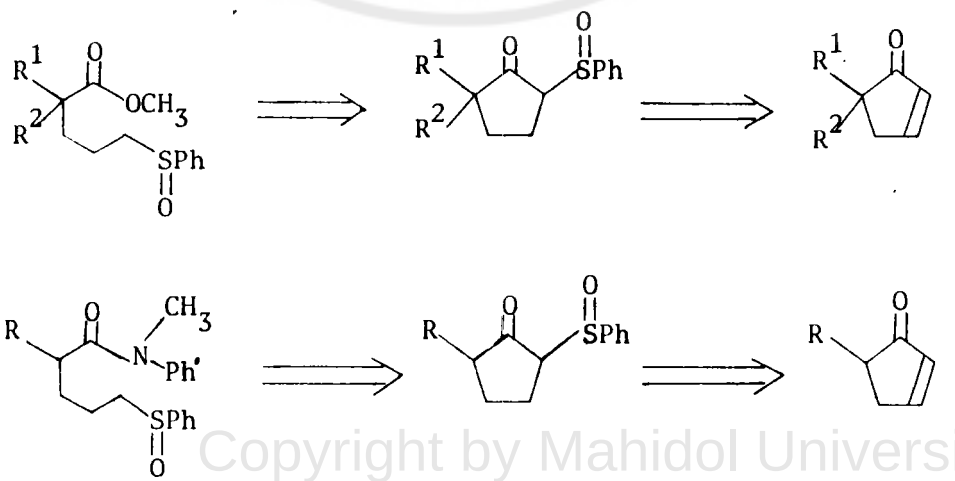
(eq.38)

As briefly shown, the annulation reactions of the cyclopentenones of type A and D are still limited. This led us to investigate a new variation. Our synthetic plan is based on an intramolecular acylation reaction of α-sulfinyl carbanion. Several uses have been reviewed where the RS(O) group activates an adjoining C-H bond for alkylation or condensation with electrophiles. The formation of carbon-carbon bonds utilizing α-sulfinyl carbanions has been a subject of extensive investigation. Both intermolecular and intramolecular alkylations of the anions have been well studied[54]. Normally, α-sulfinyl carbanions undergo readily readily intermolecular acylation reactions with esters or amides leading to β-ketosulfoxides. The RS(O) group is easily removed. In one broad use, the removal is by reduction. In a second use, it is removed by elimination as the sulfenic acid RSOH. Having applied these two methods with β-ketosulfoxides, the corresponding ketones and α,β -unsaturated ketones would be obtained (eq.39). This proved to be one of the efficient strategies for synthesis of ketones and α,β-unsaturated ketones. Even though the intermolecular acylation reactions of α-sulfinyl and α-sulfonyl



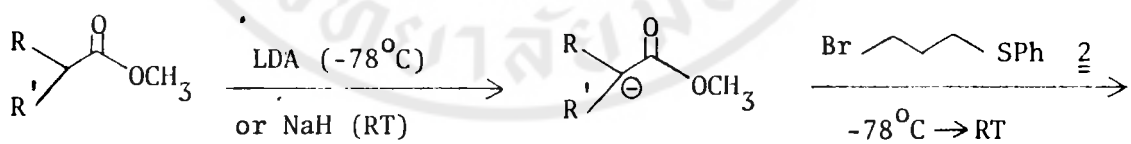
(eq.39)

carbanions have been extensively studied, but there are few reports concerning the intramolecular acylation ones[55-57]. Our interest in the chemistry of cyclopentenones led us to investigate the intramolecular acylation of the α-sulfinyl carbanions as a possible route to the cyclopentenones of types A and B. Our synthetic approach is outlined as below.

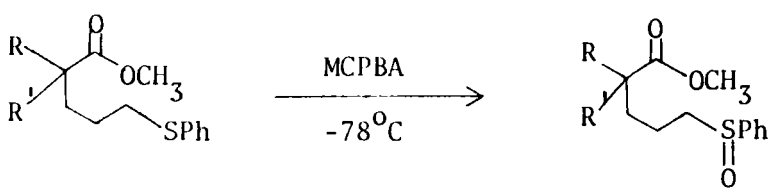


1. Preparation of Methyl 2,2-disubstituted-5-phenylsulfinylpentanoates (4).

Treatment of the ester enolate anions 1, derived from the corresponding esters by the reaction with lithium diisopropylamide (LDA) in THF (1a-d) or NaH in DMF (for 1e-f), with 1-bromo-3-phenylsulfenylpropane 2 (prepared from the reaction of thiolate anion of thiophenol and 1,3-dibromopropane) at -78°C to room temperature overnight in the presence of HMPA provided the sulfides 3 after acidic work up. The crude products 3 were further oxidised to the sulfoxide 4 using 90% m-chloroperbenzoic acid at -78°C[58]. The crude products so obtained were purified by quick-column chromatography (silica gel). The results were summarized in Table 1. In some cases, the corresponding sulfones could also be detected, but only in small amount.



1



3 4

Table 1. Preparation of Methyl 2,2-disubstituted-5-phenylsulfinylpentanoates (4).

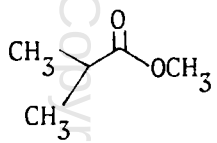
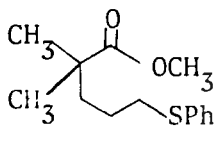
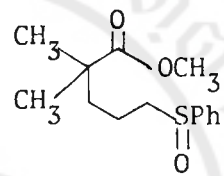
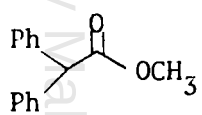
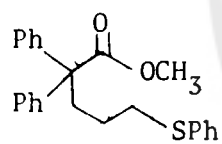
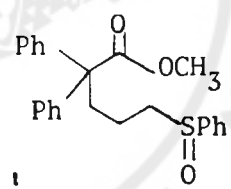
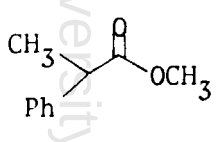
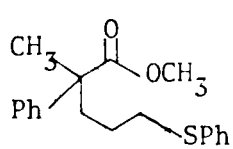
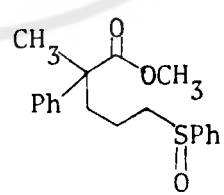
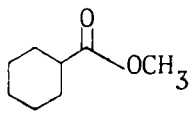
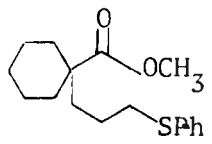
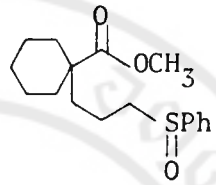
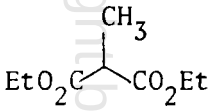
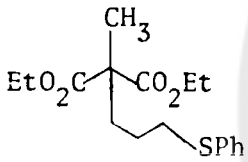
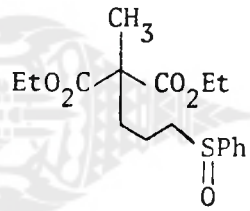
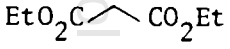
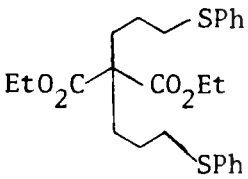
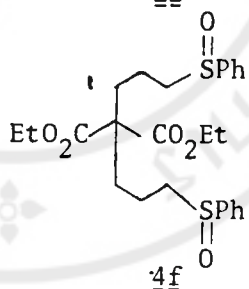
Esters 1	Sulfides 3	Yields (%)[a]	Sulfoxides 4	Yields (%)[b]
 1a	 3a	quantitative	 4a	42.3
 1b	 3b	89.88	 4b	49.43
 1c	 3c	98.26	 4c	51.31

Table 1. (cont.)

Ester 1	Sulfides 3	Yields (%)[a]	Sulfoxides 4	Yields (%)[b]
 1d	 3d	quantitative	 4d	62.87
 1e	 3e	69.04	 4e	63.78
 1f	 3f	87.26	 4f	21.7

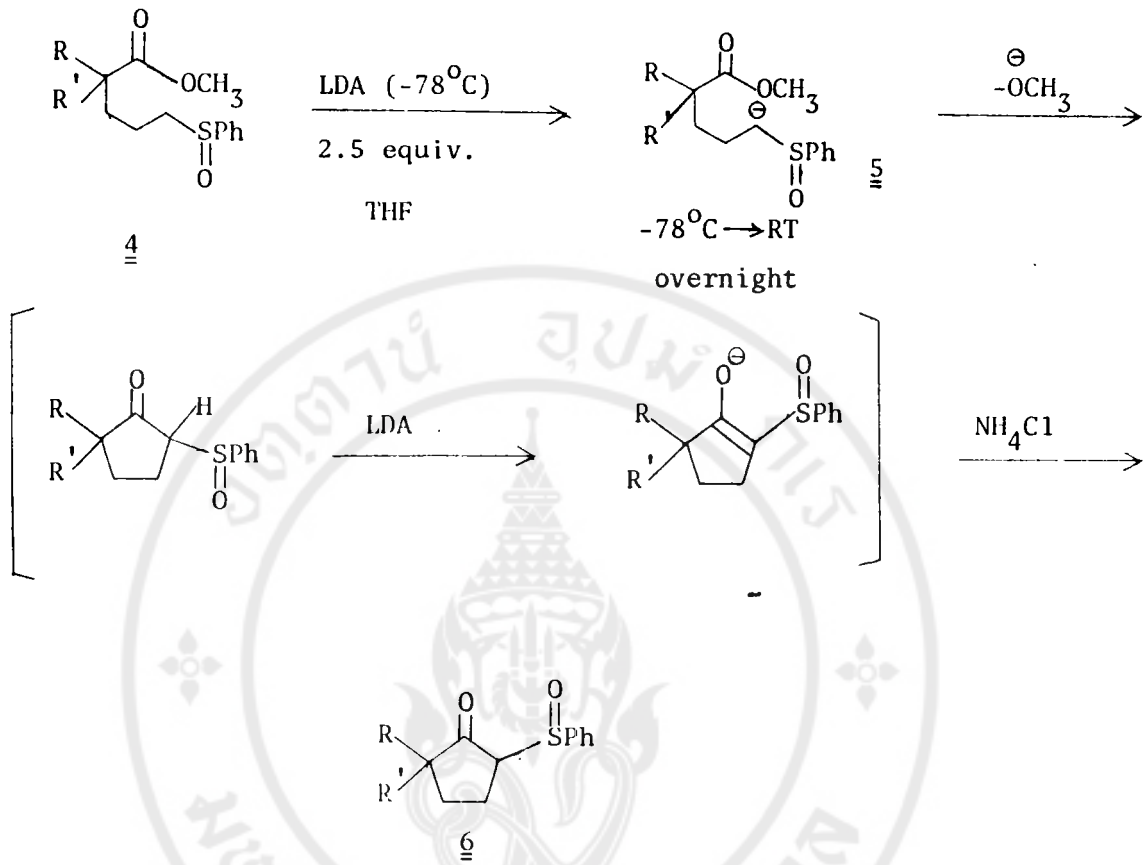
a) % yields of crude product.

b) % isolated yields by quick-column chromatography (silica gel).

2. Intramolecular Acylation of α-Sulfinyl Carbanions.

It has been known that α-sulfinyl carbanions could react with various electrophiles (for examples, alkylating agents, aldehydes and ketones), especially esters and amides via an intermolecular acylation reaction leading to β-ketosulfoxides. However, there are few reports concerning the intramolecular acylation reactions of α-sulfinyl carbanions. Normally, a small entropy of activation is often associated with a cyclic transition state formed in an intramolecular reaction, as fewer degrees of freedom are lost than in a bimolecular reaction. We therefore expected that α-sulfinyl carbanions such as 5 should be readily intramoleculary acylated leading to β-ketosulfoxides 6.

Thus, treatment of the sulfoxide 4a with a THF solution of 2.5 equivalents of lithium diisopropylamide in the presence of HMPA (HMPA: THF=1:10) at -78°C to room temperature overnight afforded the β-ketosulfoxide 6a as the sole crystalline product after acidic work up. In the absence of HMPA the reactions led to the same results, even at 0°C. Under the same cyclisation conditions, several sulfoxides (4b-f) have been examined. It should be noted that at least 2 equivalents of LDA are required for the cyclisation in order to avoid the problem with proton transfer. This is because the initial product of the intramolecular acylation, β-ketosulfoxide, is much more acidic than the starting sulfoxide.



As summarized in Table 2, it has been shown that the intramolecular acylation reactions of α-sulfinyl carbanions could occur easily providing the ketosulfoxides 6 in moderate to good yields. We found, however, that cyclisation reaction of 4b under the standard conditions led to the isolation of the expected ketosulfoxide 6b together with the unreacted starting sulfoxide 4b (≅ 13.67%). It seemed to us that the steric hindrance of disubstituted phenyl groups is responsible for this problem. The low yield of the β-ketosulfoxide 6e (24.8%) might be due to the instability of the initial cyclised product. Unsatisfactory result was obtained, when we tried to perform the reaction with the sulfoxide 4f. The thin-layer chromatography analysis of the crude

Table 2. Preparation of 5,5-Disubstituted-2-phenylsulfinylcyclopentanones (6).

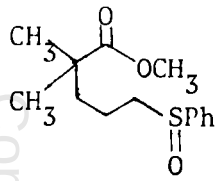
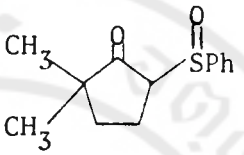
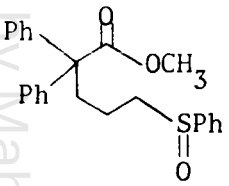
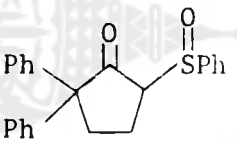
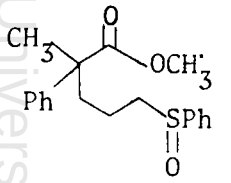
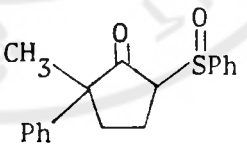
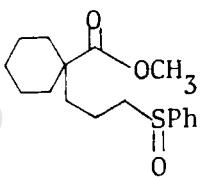
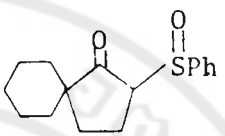
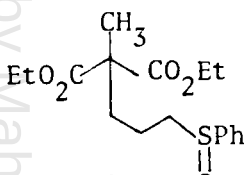
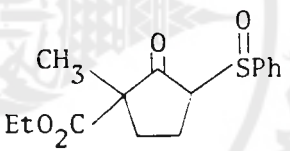
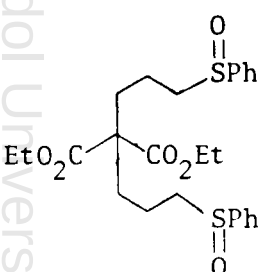
Sulfoxides 4	Reaction Conditions	β-Ketosulfoxides 6	Yields (%)
 4a	2.2 equiv. of LDA, THF:HMPA = 10:1, -78°C → RT overnight	 6a	88.25[a]
	2.2 equiv. of LDA, THF, -78°C → RT overnight		73.92[b]
 4b	2.2 equiv. of LDA, THF:HMPA = 10:1 -78°C → RT overnight	 6b	67.32[c]
	2.2 equiv. of LDA, THF, -78°C → RT overnight		50.39[c]
 4c	2.5 equiv. of LDA, THF, -78°C → RT overnight	 6c	68.97[d]
	2.5 equiv. of LDA, THF, -78°C 1 h, 0°C 2 h		73.66[d]

Table 2. (cont.)

Sulfoxides 4	Reaction Conditions	β-ketosulfoxides 6	Yields (%)
 4d	2.5 equiv. of LDA, THF, -78°C → RT overnight		69.54[b]
	2.5 equiv. of LDA, -78°C 1 h, 0°C 1 h	6d	95.85[a]
 4e	3.equiv. of LDA, THF, -78°C → RT overnight	 6e	24.8[d]
 4f	5 equiv. of LDA, THF, -78°C → RT overnight	a complex mixture	

a) % yields of crude product. b) % isolated yields by crystallisation.

c) % isolated yields by silica gel PLC based on recovered starting material.

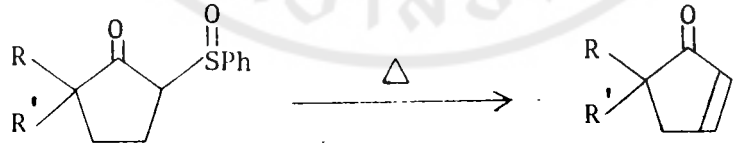
d) % isolated yields by silica gel PLC.

product obtained showed a complex mixture. However, the NMR spectrum of the crude product obtained showed the absence of the signals of ethoxyl groups (δ 1.17 (t, J=7 Hz, 6H, 2x-$OCH_2\underline{CH_3}$), 4.1 (q, J=7 Hz, 4H, 2x-$O\underline{CH_2}CH_3$). This indicated the possibilities that the expected intramolecular acylation reaction of the α-sulfinyl carbanion 5f derived from 4f had been taken place giving the initial cyclised product which decomposed slowly under the reaction conditions. Unfortunately, attempts to purify in order to receive any pure sample were unsuccessful. It must be mentioned here that the ketosulfoxides of type 6 decomposed slowly on standing, especially for the liquid.

3. Pyrolysis of the Ketosulfoxides 6: Preparation of Disubstituted Cyclopentenones (7).

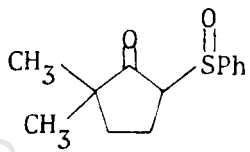
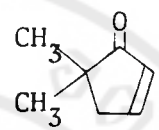
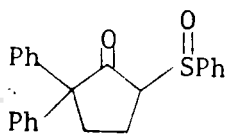
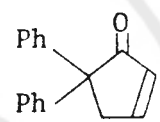
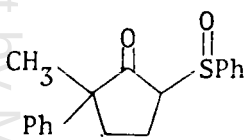
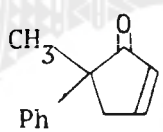
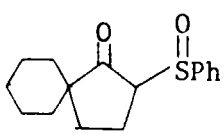
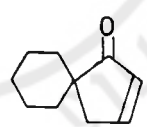
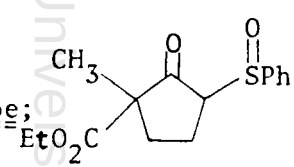
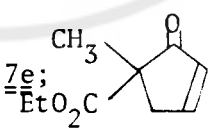
Numerous reports concerning the preparations of α,β-unsaturated carbonyl compounds via elimination of sulfenic acid under pyrolytic conditions have appeared in the literatures[58]. Having succeeded in preparation of the β-ketosulfoxides 6, we therefore expected that RS(O) group in compound 6 could be easily removed to afford disubstituted cyclopentenones (7). In an effort to remove phenylsulfinyl group we initially pyrolyzed 6a in refluxing CCl_4 for at least 18 h in order to complete the reaction as indicated by TLC. After removal of CCl_4, we tried to isolate the desired product 7a from phenylsulfinic acid by careful chromatography (PLC), but it was unsuccessful. This problem could be overcome by performing the neat pyrolysis of 6a at 180°C for 20 min followed by direct distillation under reduced pressure to give

76% of the cyclopentenone 7a. More conveniently, when the neat pyrolytic method was carried out under reduced pressure, i.e. 6d, because the reaction was completed in a short period of time and the product could be directly distilled (the distillate must be trapped with dry ice-acetone bath for the low boiling cyclopentenones (see experimental section). It was observed that no decomposition of products had been occurred by this pyrolytic condition. From our investigation, it was apparent that the pyrolytic conditions as neat under reduced pressure was superior to the pyrolysis in refluxing CCl_4 as we used for 6b, 6c and 6e. An extensive decomposition was observed during the pyrolysis of 6e in refluxing CCl_4; only 41% of the desired 7e could be isolated.



6 7

Table 3. Preparation of 5,5-Dialkyl-2-cyclopentenones (7).

β-Ketosulfoxides 6	Reaction Conditions	Cyclopentenones 7	Yields (%)
6a; 	180°C for 20 min followed by distillation (20 Torr)	7a; 	75.67[a]
6b; 	CCl_4/reflux for 8 h	7b; 	quantitative[b]
6c; 	CCl_4/reflux for 15 h	7c; 	89.94[b]
6d; 	100°C, 0.07 mmHg	7d; 	67.45[a]
6e; 	CCl_4/reflux for 19 h	7e; 	40.67[b]

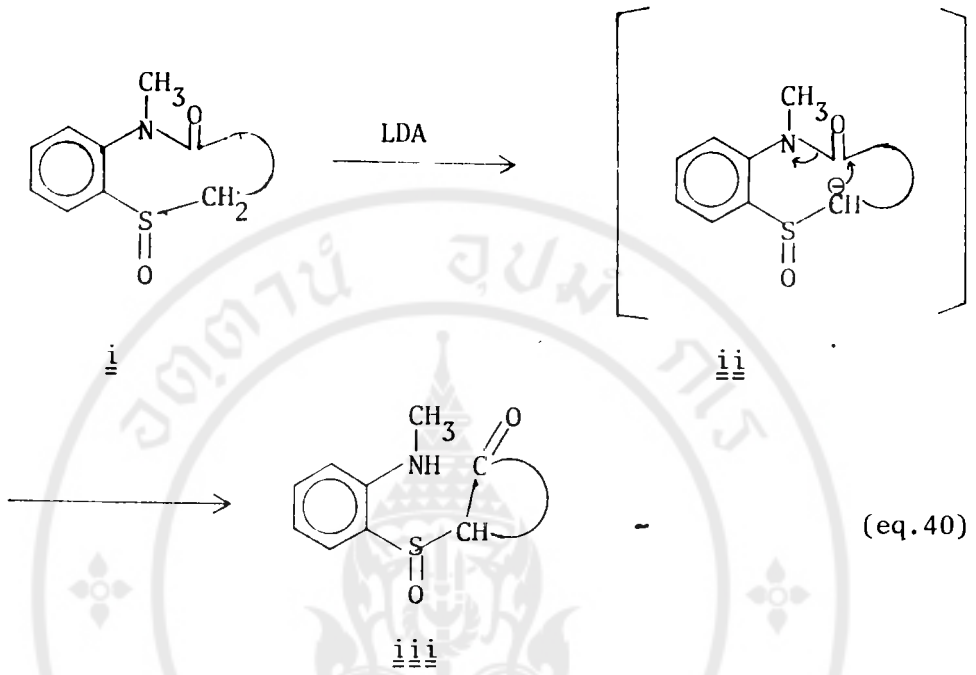
a) % isolated yields by distillation.

b) % isolated yields by preparative thin-layer chromatography (silica gel).

4. Preparation of 2-Monoalkylsubstituted-5-phenylsulfinylpentanamides (10).

Having succeeded in preparing the disubstituted cyclopentenones 7 by intramolecular acylation reaction followed by elimination of benzenesulfenic acid, we next investigated to acheive monosubstituted cyclopentenones of type A, which were potentially important intermediates in natural product syntheses. As shown above, the intramolecular acylation reaction of the α-sulfinyl carbanions 5a-d derived from 2,2-dialkylsubstituted-5-phenylsulfinylpentanoates (4a-d) proceeded clearly to 6a-d without any traces of other side products. It should be therefore expected that 5-alkylsubstituted-2-cyclopentenones would be synthesized by using the same reaction sequences as those for 7 starting from 2-alkyl-5-phenylsulfinylpentanoic esters. However, if one considers the acidities of both α-protons (α-proton adjacent to carbonyl group and α-proton with respect to phenylsulfinyl group), it would be found that they are closely the same[59]. This might lead to the difficulty to control the selectivity in proton abstraction with base such as LDA which we normally used in our standard cyclisation conditions. *N-N*-disubstituted amides, possesses α-protons with lower acidity in comparing with those of the esters and alkylsulfoxides. This fact has been supported by recent reports[55,56] that lactam sulfoxide such as i could be selectively deprotonated at -78°C by using LDA at α-proton adjacent to sulfinyl group leading to α-sulfinyl carbanion ii. This anion underwent readily intramolecular acylation reaction on slowly warming up to reach room temperature giving α-arylsulfinylcycloalkanones iii

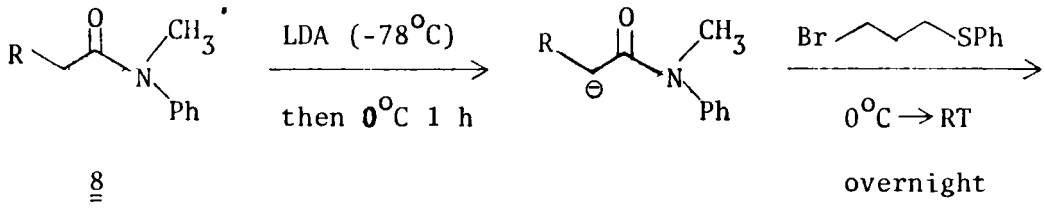
in good yields (eq.40).



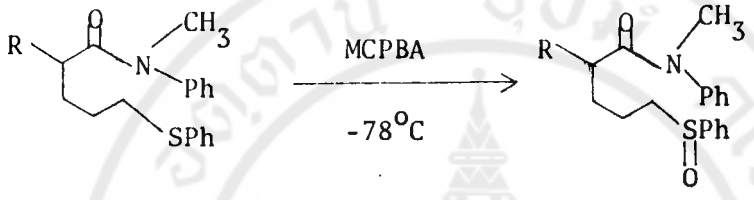
i ii iii (eq.40)

According to such reports, we therefore decided to synthesize the amide-sulfoxides 10 as the starting materials for our study concerning the intramolecular acylation reaction. It was hoped that the stardard reaction conditions using for the generation of α-sulfinyl carbanions 5 would be suitable for our present study. If this could be realized, 5-alkylsubstituted-2-cyclopentenones 12 would be readily synthesized.

The amide-sulfoxides 10 could be easily synthesized by utilizing the reaction sequence that for the ester sulfoxides 4. Thus, on treatment of the amide enolate anions derived from the amides 8 with 1-bromo-3-phenylthiopropane at $0^{o}C$ to room temperature overnight provided sulfides 9 after acidic work up. The crude products 9 were



8



9 10

further oxidised with 90% m-chloroperbenzoic acid at -78°C to give the desired sulfoxides 10 after purification either by preparative thin-layer chromatography (silica gel) or recrystallization. The results were collected in Table 4.

5. Intramolecular Acylation of α-Sulfinyl Carbanions derived from Sulfoxides 10.

Having amide sulfoxides 10 in hand, we then further investigated the intramolecular acylation reaction in the same way as the sulfoxides 4 shown previously in section 2. But the efficiency for cyclisation of the amide sulfoxides 10 might be different from the ester sulfoxides 4 because of their having another acidic proton at α-carbon adjacent to carbonyl group. However, this would not be the problem because the acidity of those two α-protons are different as mentioned previously. Therefore, we expected that treatment of the amide sulfoxides 10 with

Table 4. Preparation of 2-Alkyl-5-phenylsulfinylpentanamides (10).

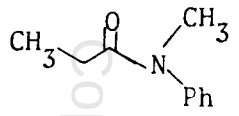
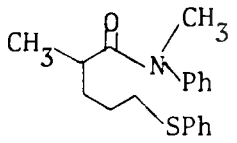
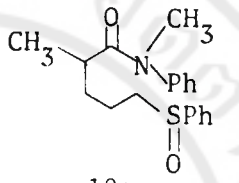
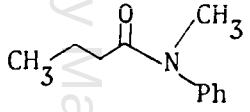
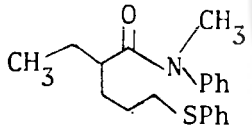
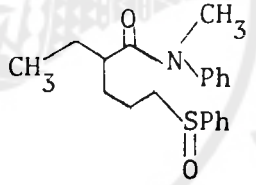
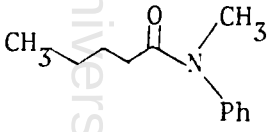
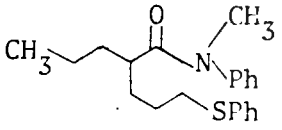
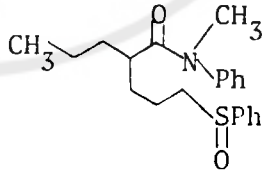
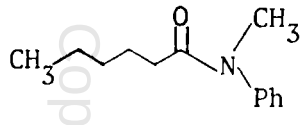
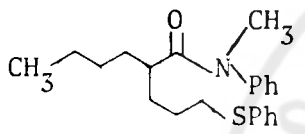
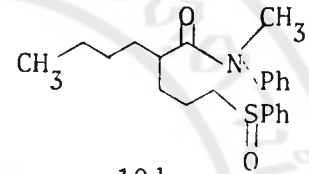
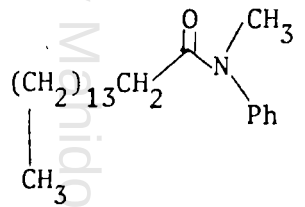
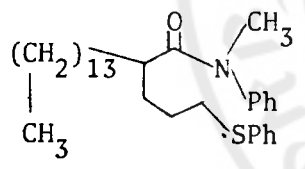
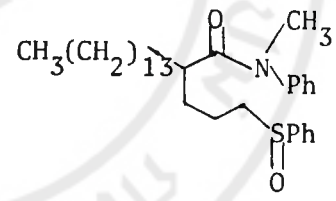
Amides 8	Sulfides 9	Yields (%)[a]	Sulfoxides 10	Yields (%)
 8a	 9a	quantitative	 10a	79.48[b]
 8b	 9b	quantitative	 10b	74.67[c]
 8c	 9c	quantitative	 10c	68.35[d]

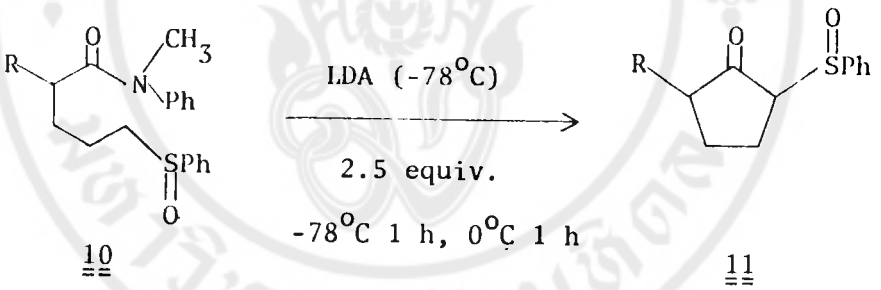
Table 4. (cont.)

Amides 8	Sulfides 9	Yields (%)[a]	Sulfoxides 10	Yields (%)
 8d	 9d	quantitative	 10d	77.08[d]
 8e	 9e	quantitative	 10e	69.0[e]

a) % yields of crude product.
b) % isolated yields by silica gel PLC.
c) % isolated yields by quick-column chromatography.
d) % isolated yields by column chromatography (SiO_2).
e) % isolated yields by crystallization.

an appropriate base would afford firstly the α-sulfinyl carbanion and readily undergo intramolecular acylation reaction yielding the desired monosubstituted β-ketosulfoxides 11.

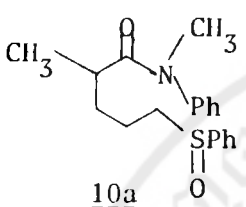
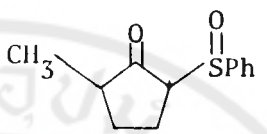
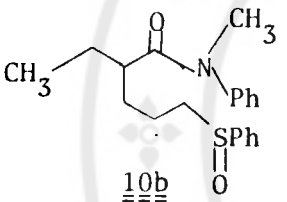
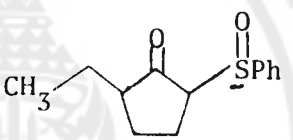
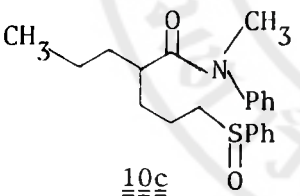
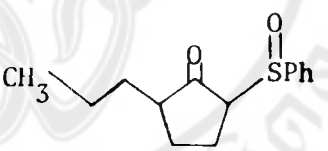
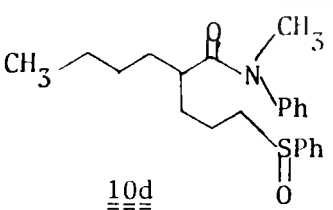
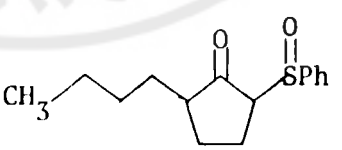
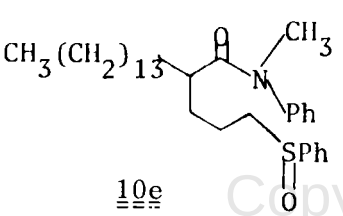
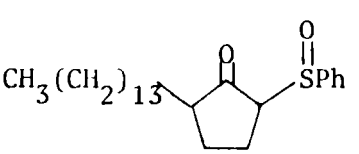
Thus, treatment of the amide sulfoxides 10 with 2.5 equivalents of lithium diisopropylamide in THF at -78°C for 1 h and at 0°C for 1 h afforded the monosubstituted β-ketosulfoxides 11 after acidic work up. Purification of the crude products so obtained by preparative thin-layer chromatography gave excellent yields of pure β-ketosulfoxides 11. The results were summarized in Table 5.



10 11

It was noticed that the β-ketosulfoxides 11 decomposed slowly on standing at room temperature as shown by TLC analysis. They must be kept in a cool place for the next step. Furthermore, having quenched the reaction mixture with excess stronger acid such as dilute HCl, decomposition of the desired product was observed. In order to avoid this trouble, aqueous ammonium chloride solution was used.

Table 5. Preparation of 5-Alkyl-2-phenylsulfinylcyclopentanones (11).

Sulfoxides 10	β-Ketosulfoxides 11	Yields (%)[a]
 10a	 11a	80.25
 10b	 11b	73.73
 10c	 11c	90.86
 10d	 11d	98.98
 10e	 11e	83.32

a) % isolated yields by preparative thin-layer chromatography (silica gel).

6. Preparation of 5-Alkylsubstituted Cyclopentenones (12).

It has been shown in section 3 that 5,5-disubstituted-2-cyclopentenones 7 could be readily obtained either by pyrolysis of the ketosulfoxides 6 as neat under reduced pressure or in refluxing CCl_4. Similarly, the β-ketosulfoxides 11 were pyrolyzed as neat substance under reduced pressure as indicated in Table 6. The cyclopentenones 12a-d were obtained in high yields by direct distillation under reduced pressure from the pyrolyzed vessel (see in experimental section), and the distillate were trapped at -78°C using dry ice-acetone bath. It has been interesting to note that decomposition of product and double bond isomerisation to the thermodynamically more stable 2-alkyl-2-cyclopentenones were not observed.

11 12

Table 6. Preparation of 5-Alkyl-2-cyclopentenones (12).

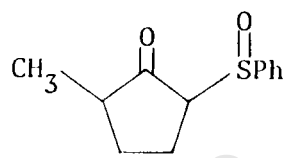
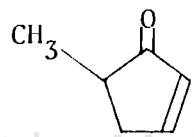
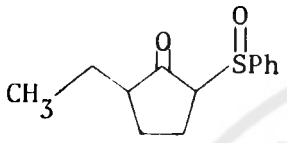
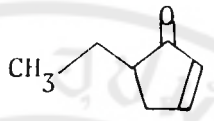
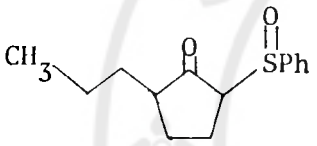
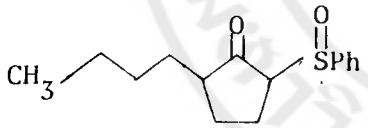
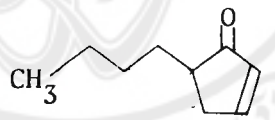
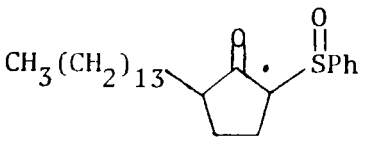
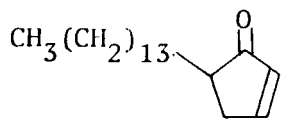
β-Ketosulfoxides 11	Cyclopentenones 12	Yields (%)
		quantitative[a]
11a	12a	

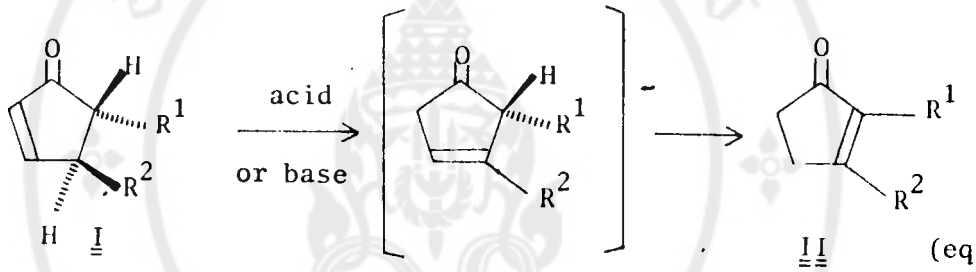
Table 6. (cont.)

β-Ketosulfoxides 11	Cyclopentenones 12	Yields (%)
 11b	 12b	94.56[a]
 11c	 12c	72.2[a]
 11d	 12d	74.1[a]
 11e	 12e	85.3[b]

a) % isolated yields by distillation.

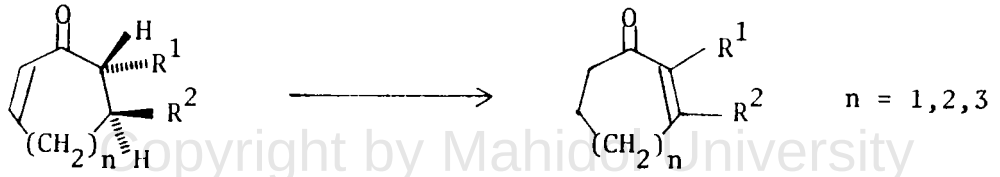
b) % isolated yields by preparative thin-layer chromatography (silica gel).

Our results clearly demonstrated that both 5,5-dialkylsubstituted-2-cyclopentenones 7 and 5-monoalkylsubstituted-2-cyclopentenones 12 could be prepared by intramolecular acylation reactions of the anions derived from 4 and 10 following by pyrolysis of the resulting β-ketosulfoxides 6 and 11, respectively. Especially, 5-alkyl-2-cyclopentenones are of interest due to the ability to be isomerised to the thermodynamically more stable cyclopentenones of type II (eq.41).



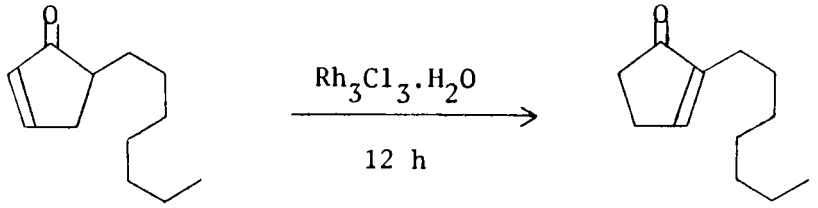
I II (eq.41)

It has been known that Δ^2-cyclopentenones of type I are versatile intermediates in organic synthesis because of their readily to equilibrate to cyclopentenones of type II. Isomerization of I to the more stable cyclopentenone II can be effected by heating in the presence of acid[60] or base[61]. P.A.Grieco and co-workers[49] have reported the smooth conversion of cycloalkenone III to its more stable isomer IV via rhodium catalysis which constitutes a synthetically useful new enone transposition.



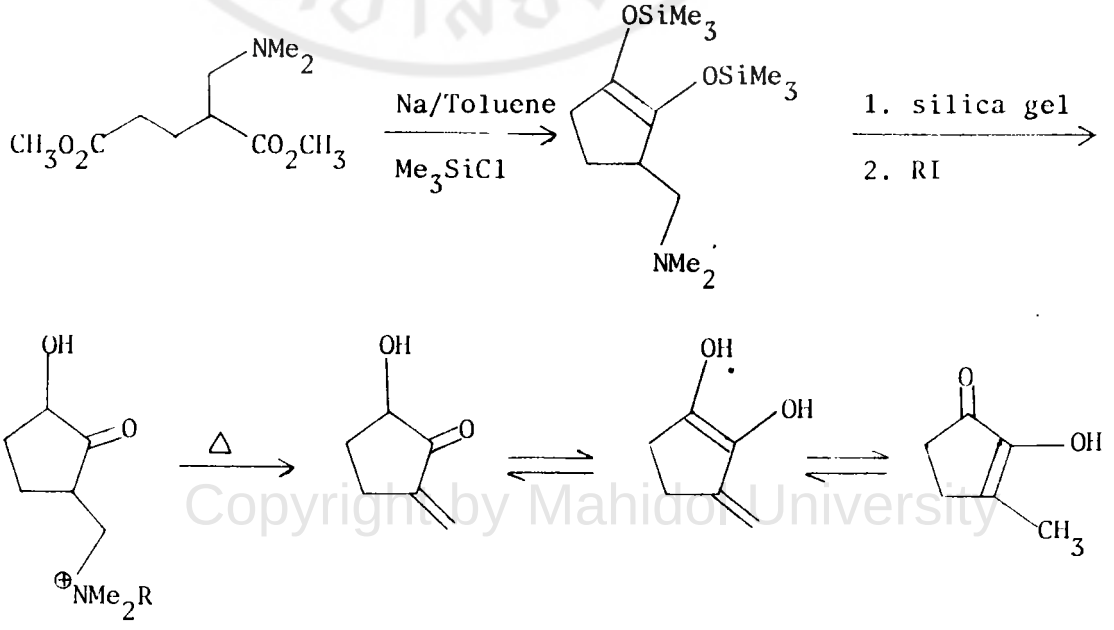
n = 1,2,3

III IV

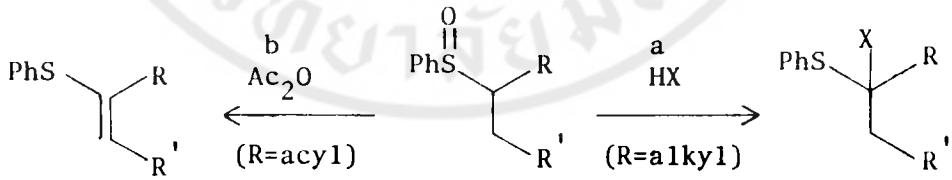


7. Attemptted Preparation of 2-Hydroxy-3-alkyl-2-cyclopentenones (Diosphenols).

Diosphenols are of interest because some of them have been used as intermediates in prostaglandin synthesis[62]. Especially, 2-hydroxy-3-methylcyclopent-2-en-1-one was an important perfumery and flavoring material possessing a sweet and very powerful spicy-coffee--caramel odour. In recent years many syntheses of this and similar structures have been published[63-66]. For an example, Cookson and Smith[66] have described a simple synthesis of this compound in high yield in three steps as shown below.



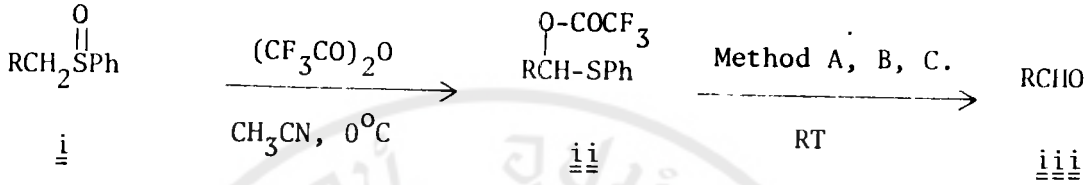
Our interest in this area prompted us to investigate the possibility to use the intramolecular acylation reactions of α-sulfinyl carbanions as a route for synthesis of 1-alkyl-2-hydroxy-3-oxocyclopentenes. Our previous results demonstrated that β-ketosulfoxides 6 and 11 could be readily obtained in high yields. To make an advantage of the β-ketosulfoxides such as 11 in organic synthesis, we therefore tried to convert them into hydroxycyclopentenones 15. It has been known that sulfoxides bearing at least one α-proton undergo the Pummerer rearrangement. The rearrangement involves treatment of the sulfoxides with acid or electrophilic agent leading to products in which the oxygen atom is lost from sulfur and a new functional group appears on the neighbouring carbon atom (e.g.X=OH) (see eq.42, pathway a). This reaction sequence has been used as a method for conversion of phenyl alkyl sulfoxides into the corresponding carbonyl compounds as



(eq.42)

demonstrated, for example, by Kaji et al.[67] (eq.43). The β-ketosulfoxides, on the other hand, lead to α-phenylthio-α,β-unsaturated carbonyl compounds under the standard conditions for the Pummerer rearrangement. The reaction uses normally acetic anhydride as the

electrophile with a catalytic amount of methanesulfonic acid at low temperature[68] (eq.42, pathway b).



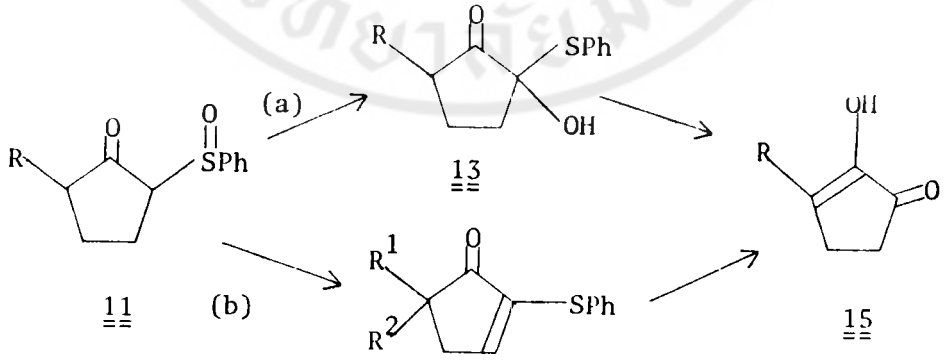
A = $NaHCO_3/H_2O/CH_3CN$

B = $CuCl_2/H_2O/CH_3CN$

C = $HgCl_2/H_2O/CH_3CN$

(eq.43)

Having considered both synthetic patways a and b in equation 42, we expected that Pummerer rearrangement of the β-ketosulfoxides 11 should furnish the desired α-hydroxycyclopentenones 15 via intermediates 13 or 14. Treatment of 11a with strong acid, for example, 6N HCl, conc.



14a; $R^1 = CH_3-$, $R^2 = H$

14b; $R^1—R^2 = -(CH_2)_5-$

HCl or $HClO_4$ resulted in the recovery of the starting material accompanying with a minor product possessing an olefinic proton at 6.73 ppm in the NMR spectrum which presumably indicated the presence of compound 14.

Again, the reaction of 11a with $CuCl_2.2H_2O$ in refluxing THF for a long period of time led to the same result. It was apparent to us that β-ketosulfoxide 11 could lead to compound 14 readily if proper reaction conditions was used. As expected, on treatment of the β-ketosulfoxide 11a with freshly distilled trifluoroacetic anhydride in CH_3CN at 0^oC for a short period of time, the compound 14 was obtained in good yields. By using the same reaction conditions, the β-ketosulfoxide 6d furnished 14b. Having succeeded in preparing of 14a, we then next investigated the hydrolytic conditions for transformation of 14a into the desired product 15 ($R=CH_3$). A large number of methods for hydrolysis of vinylsulfides to the corresponding carbonyl compounds has been reviewed[69], for example, $CuCl_2$, $AgNO_3$, CF_3CO_2H, $TiCl_4$, $Hg(OAc)_2$ in HCO_2H and $HgCl_2$ etc. However, our attempts to convert 14a into 15 ($R=CH_3$) under varieties of reaction conditions as given in Table 7 were unsuccessful. In most cases, complex mixtures were obtained. The only two conditions, that we observed the desired NMR signal at δ 2 ppm belonging to the methyl group of 15 ($R=CH_3$) were the reactions using $TiCl_4$ and $Hg(OAc)_2$ in HCO_2H. It is apparently that the difficulty for hydrolysis of the vinylsulfide moiety in compound 14a to the desired product 15 ($R=CH_3$) may be due to the electron-withdrawing power of the carbonyl group which therefore decreases the electron density in the vinylsulfide function. This effect presumably retards the complexation ability of the vinylsulfide function with hydrolytic reagents. Surprisingly, up to now, there are no available reports concerning the hydrolysis of the vinylsulfides possessing electron withdrawing group at α-position.

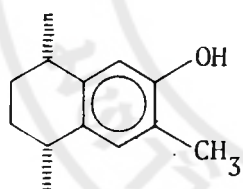
Table 7. Attempted Preparation of 2-Hydroxy-3-methyl-2-cyclopentenone.

Vinyl sulfides 14	Reagents and Solvents	Reaction Conditions	Results
14a	$CuCl_2.2H_2O$ THF:H_2O = 9.5:0.5	reflux 3 h	complex mixture
14a	$TiCl_4$/AcOH	RT 1 h and 15 min, oil bath 50°C for 1.5 h	crude product containing signal at δ = 2 ppm(s)
14a	$AgNO_3$, THF:H_2O= 9.5:0.5	0°C 1 h, RT 10 min	complex mixture
14a	$HgCl_2$, CH_3CN:H_2O = 9.5:0.5	reflux 9 h	14a
14a	$Hg(OAc)_2$/HCOOH	reflux 10 h	crude product containing signal at δ = 2 ppm (s)

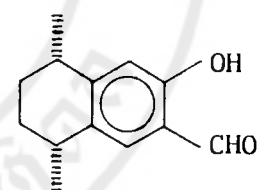
This is still to be a subject of further investigation.

8. Attempted Phenol-Annulation via the Intramolecular Acylation Reaction Of α-Sulfinyl Carbanions.

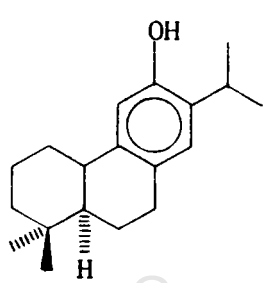
At the outset of our works, we were also interested in the possibility that this intramolecular acylation reaction of α-sulfinyl carbanions might serve as a powerful tool for six-membered ring annulation reactions. Particularly, substituted phenols are important moiety of many natural occurring commpounds[70], for example. 7-hydroxycalamenene, 7-hydroxycalamenenal, ferruginol and hinokiol.



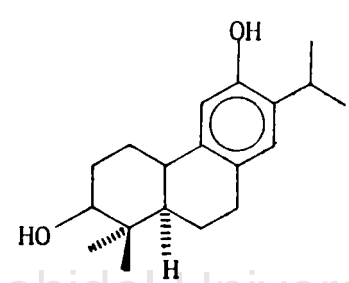
7-hydroxycalamenene



7-hydroxycalamenenal

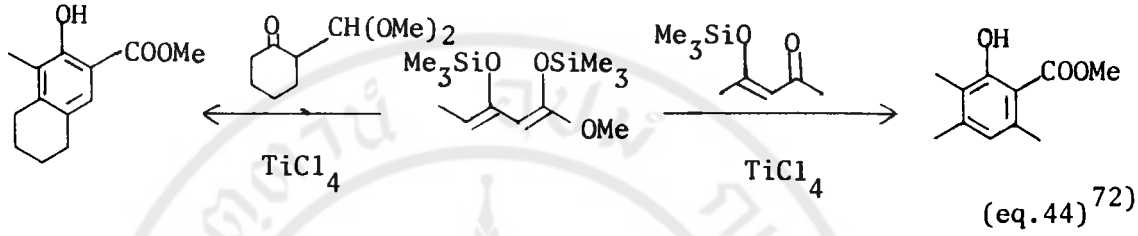


ferruginol

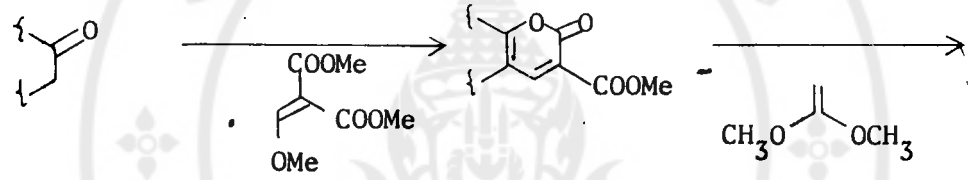


hinokiol

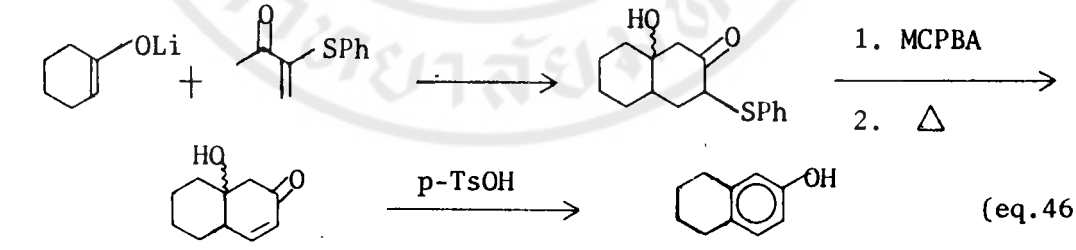
Numerous phenol annulation reactions have been reported. One of the representative and attractive routes to substituted phenols involves the Diels-Alder reaction[71-74]. Many other synthetic routes have been summarized in equation 44-47.



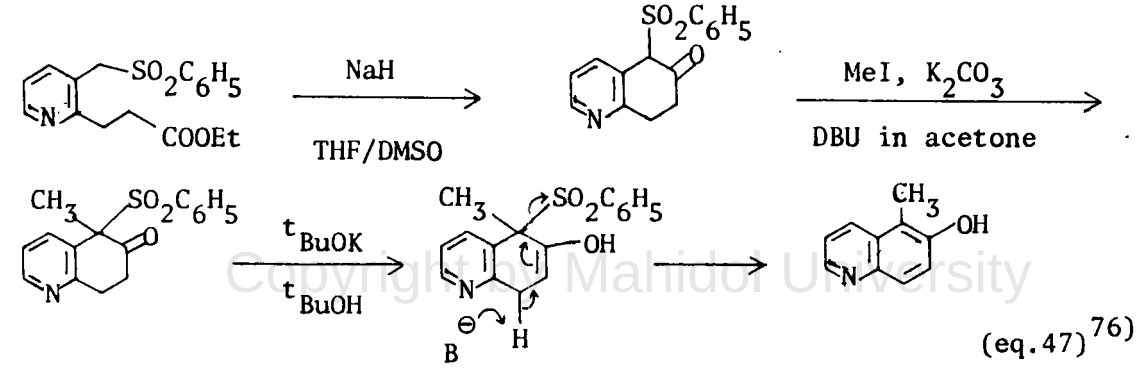
(eq.44)[72]



(eq.45)[74]

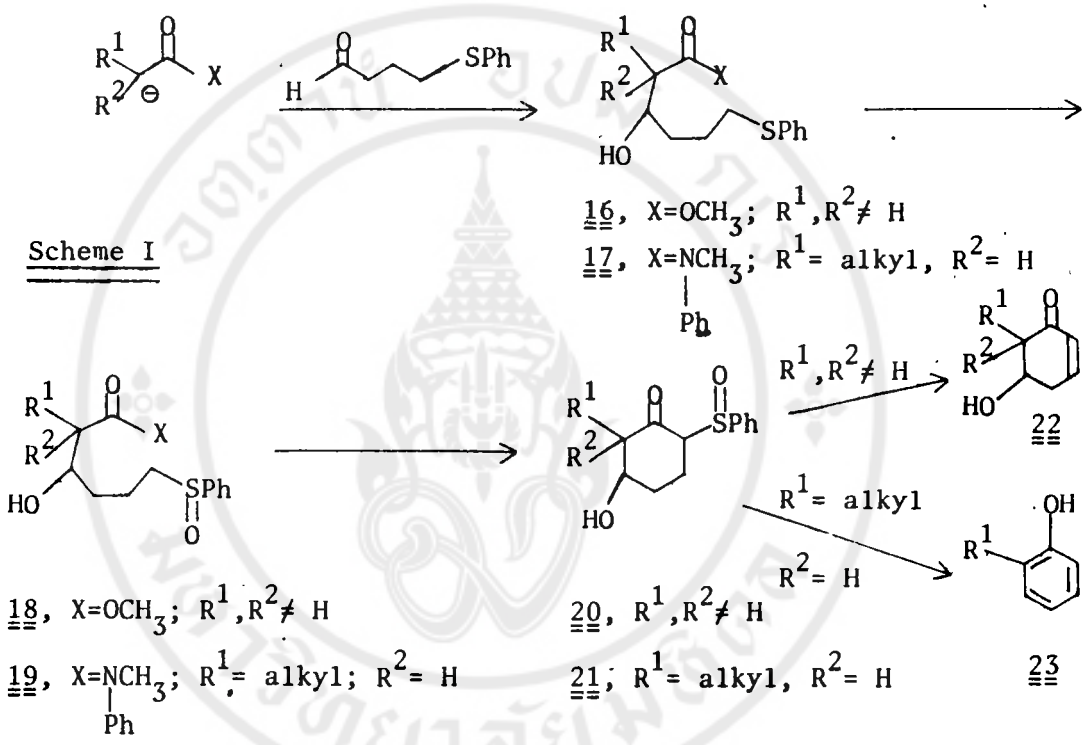


(eq.46)[75]



(eq.47)[76]

To illustrate the synthetic usefulness of the intramolecular acylation of the α-sulfinyl carbanions, we therefore subjected to investigate the cyclohexenone annulation reaction including the phenol annulation as depicted in scheme I. We first studied the method to



Scheme I

prepare compound of type 22, an interested class of highly substituted cyclohexenones, by starting from the sulfoxide 18. The ester sulfoxides 18 could be easily prepared as follows. Treatment of the corresponding ester enolate anions with 4-phenylsulfenyl-1-butanal in THF at -78°C for 2.5 h afforded the crude ester sulfides 16 which were readily purified by thin-layer chromatography. The ester sulfides 16 were subjected to oxidation using 90% m-chloroperbenzoic acid leading to the ester sulfoxides 18 in high yields after chromatography (see Table 8).

Table 8. Preparation of Methyl 2,2-Dialkyl-3-hydroxy-5-phenylsulfinylhexanoates (18).

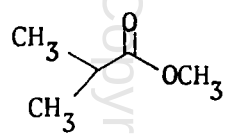
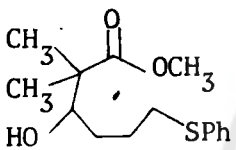
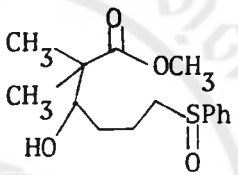
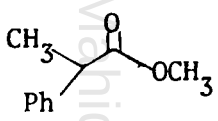
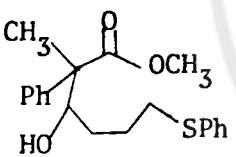
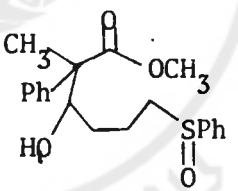
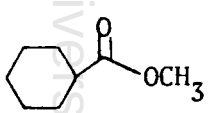
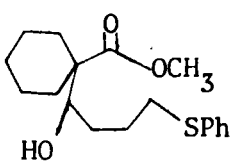
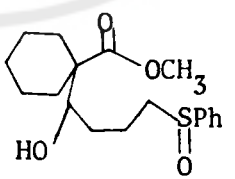
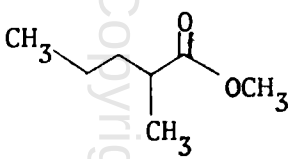
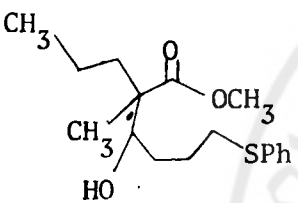
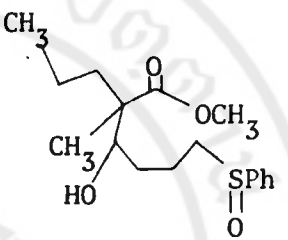
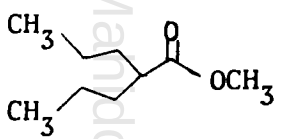
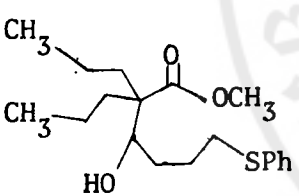
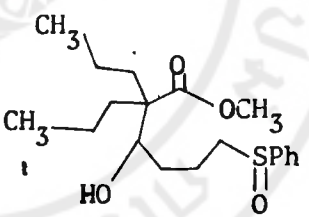
Esters	Sulfides 16	Yields (%)[a]	Sulfoxides 18	Yields (%)[a]
	 16a	53.6	 18a	68.0
	 16b	55.2	 18b	66.1
	 16c	54.4	 18c	69.67

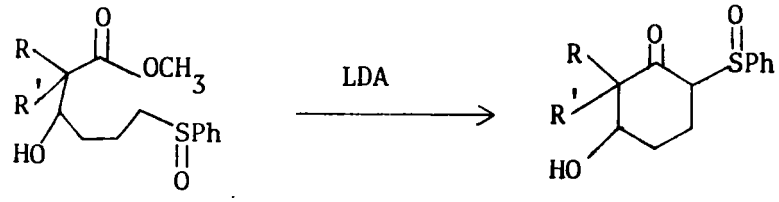
Table 8. (cont.)

Esters	Sulfides 16	Yields (%)[a]	Sulfoxides 18	Yields (%)[a]
	 16d	60.34	 18d	77.37
	 16e	63.4	 18e	84.71

a) % isolated yields by preparative thin-layer chromatography (silica gel).

It can be seen in Table 8 that addition of the ester enolate anions to 4-phenylsulfenylbutanal occured in moderate yields. This might be due to the purity of 4-phenylsulfenylbutanal, prepared from oxidation of 4-phenylsulfenyl-1-butanol[77]; distillative or chromatographic purification was unsuccessful. We have noticed that 4-phenylsulfenylbutanal could be easily air oxidised to the corresponding acid although it was kept in refrigerator under an argon for more than a few days. Another reason for having low yields of the sulfides 16 might be due to the reversibillity of the addition reaction (Retro-aldol).

Having succeeded in preparing of the sulfoxides 18, we then tried to cyclise them into the expected β-ketosulfoxides 20 via intramolecular acylation reaction of α-sulfinyl carbanions. Thus treatment of the sulfoxides 18 with 4.5 equivalents of lithium diisopropylamide in THF at -78°C for 1 h and 0°C for 1.5 h afforded the β-ketosulfoxides 20 after acidic work up. The crude products obtained were purified by preparative thin-layer chromatography (silica gel) to give the pure sulfoxides 20 in moderate to good yields as shown in Table 9.



18 20

Table 9. Preparation of 6,6-Dialkyl-5-hydroxy-2-phenylsulfinylcyclohexanones (20).

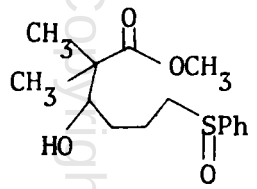
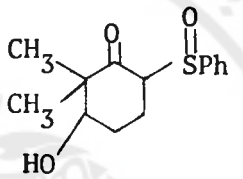
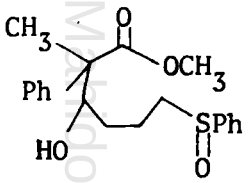
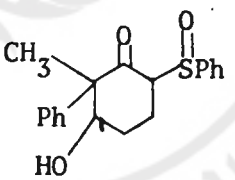
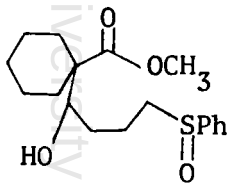
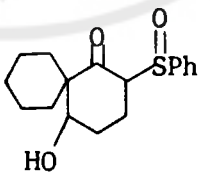
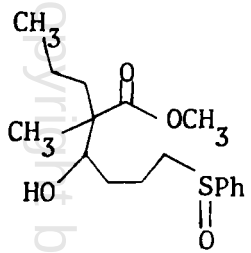
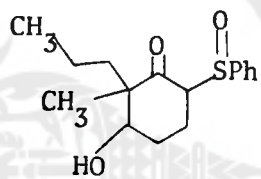
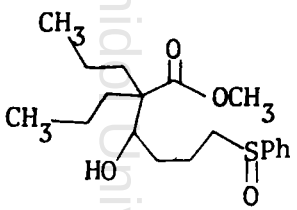
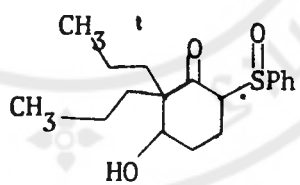
Sulfoxides 18	Reaction Conditions	β-Ketosulfoxides 20	Yields (%)[a]
 18a	4.5 equiv. of LDA, THF, -78°C 1 h, 0°C 1.5 h	 20a	69.8
	4.5 equiv. of LDA, THF, 1 equiv. of HMPA, -78°C 1 h, 0°C 1.5 h		61.8
 18b	4.5 equiv. of LDA, THF, -78°C 1 h, 0°C 1.5 h	 20b	60.43
 18c	4.5 equiv. of LDA, THF, -78°C 1 h, 0°C 1.5 h	 20c	79.56

Table 9. (cont.)

Sulfoxides 18	Reaction Conditions	β-Ketosulfoxides 20	Yields (%)[a]
 18d	4.5 equiv. of LDA, THF, -78°C 1 h, 0°C 1.5 h	 20d	71.19
 18e	4.5 equiv. of LDA, THF, -78°C 1 h, 0°C 1.5 h	 20e	75.4

a) % isolated yields by preparative thin-layer chromatography (silica gel).

To our delight, that we easily obtained the β-ketosulfoxides 20 in good yields, we therefore next investigated the pyrolysis of such compounds. Thus, heating of the pure β-ketosulfoxides, for example 20a at 100-120°C under reduced pressure (o.2 mmHg) afforded cyclohexenone 22a in high yield after preparative chromatography. Similarly, the cyclohexenone derivatives 22b-e were prepared under the given conditions as shown in Table 10.

20 22

According to the results shown in Table 10, it must be noted that under the pyrolysis conditions, no other side product has been observed. Compounds 22b and 22d were obtained as mixtures of diastereomers. In case of the cyclohexenone 22b, two pure diastereomers could be isolated by careful preparative thin-layer chromatography.

Using the same synthetic approach as for the cyclohexenones 22, we therefore tried to realize our phenol-annulation reaction. It was hoped that intramolecular acylation of α-sulfinyl carbanions derived from the amide sulfoxides 19 would furnish the cyclised products 21 which were expected by converted into the desired phenolic compounds 23 by benzenesulfenic acid elimination followed by dehydration under pyrolytic conditions. The requisite amide sulfoxides 19a and 19b were conveniently prepared by the reaction of the amide enolate anions with 4-phenylsulfenylbutanal following by subsequent oxidation with m-chloro-

Table 10. Preparation of 6,6-Dialkyl-5-hydroxy-2-cyclohexenones (22).

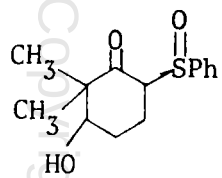
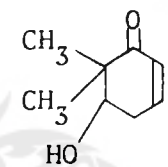
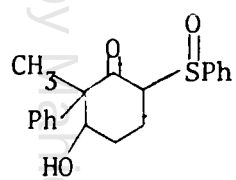
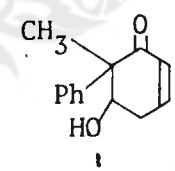
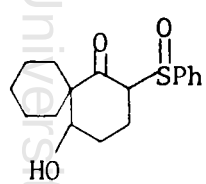
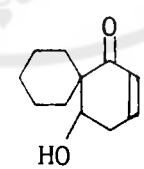
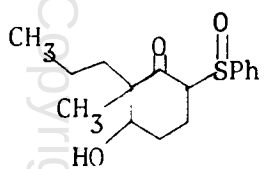
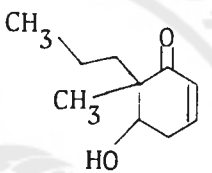
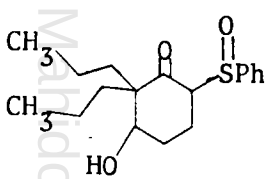
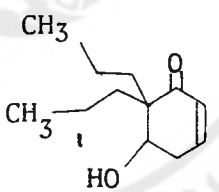
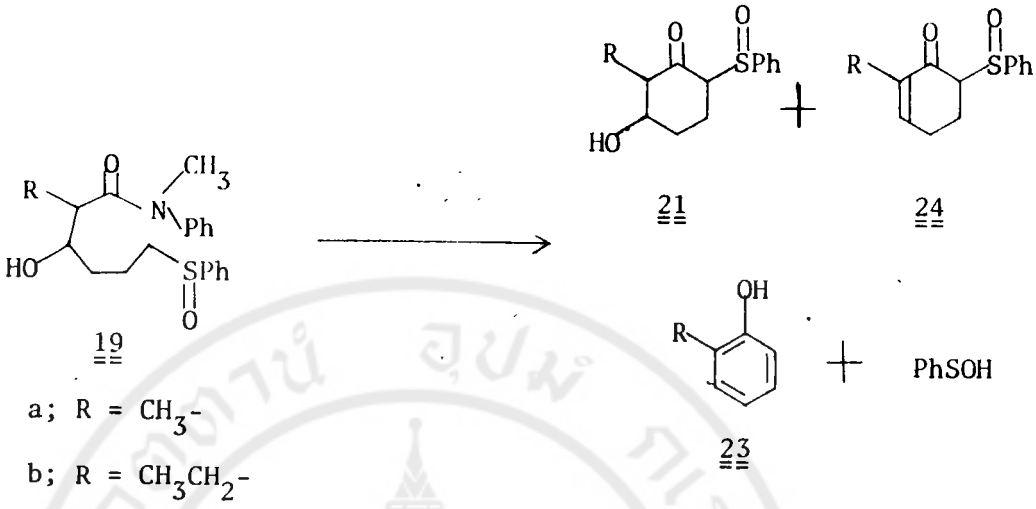
β-Ketosulfoxides 20	Reaction Conditions	Cyclohexenones 22	Yields (%)[a]
 20a	100-120°C, 0.2 mmHg for 1 h	 22a	84.45
 20b	120°C, 0.1 mmHg for 2 h	 22b	79.29[b]
 20c	100-120°C, 0.1 mmHg for 3.5 h	 22c	70.9

Table 10. (cont.)

β-Ketosulfoxides 20	Reaction Conditions	Cyclohexenones 22	Yields (%)[a]
 20d	120°C, 0.03 mmHg for 1.5 h	 22d	75.9
 20e	110°C, 0.03 mmHg for 2 h	 22e	71.87

a) % isolated yields by preparative thin-layer chromatography (silica gel).

b) % isolated yields of two stereoisomers.



19

a; R = CH_3-

b; R = CH_3CH_2-

21 24 23 PhSOH

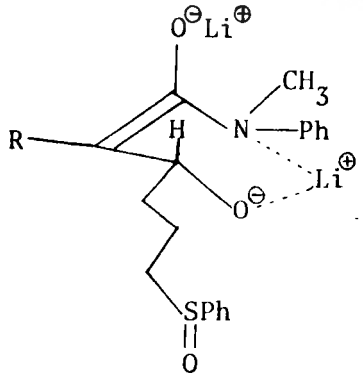
perbenzoic acid as parallel to those described for the ester sulfoxides 18. Treatment of the amide sulfoxides 19a or 19b with excess equivalents of lithium diisopropylamide under variety of reaction conditions as given in Table 11 led to a mixture of 5 products. The same ratio of products has been observed from all conditions as estimated by NMR and TLC analyses. The NMR and TLC analyses showed that the complex mixture obtained were consisted of unreacted starting material 19a or 19b, cyclised product 21, cyclohexenone 24, phenolic compound 23 and benzensulfenic acid, whose ratios could not be determined. The formation of 23 was arisen from dehydration of the cyclised product 21 leading to the cyclohexenone 24 which then lose benzensulfenic acid during work up. It was apparent to us that about 50% of the starting amide sulfoxide 19a or 19b was still unreacted. Attempts to isolate all components in the mixture were found to be very difficult. Especially, the starting amide sulfoxide 19 seemed to have almost the same polarity as the cyclised product 21: we have tried to use many developing systems for PLC. Moreover, the cyclised product 21 was dehydrated slowly on

Table 11.

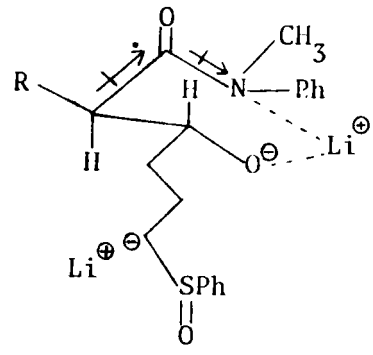
Sulfoxides 19	Reagents and Reaction Conditions	Results	Pyrolysis Conditions	Results
crude 19a	4 equiv. of LDA -78°C 1 h, 0°C 1 h	19a and a complex mixture	-	-
pure 19a	4 equiv. of LDA -78°C→RT overnight	19a and a complex mixture	heat at 120°C 4 h in CCl_4	pure 23a in low yield
pure 19b	5 equiv. of LDA; 1 equiv. of HMPA -78°C→RT overnight	19b and a complex mixture	-	-
pure 19b	5 equiv. of LDA -78°C→RT overnight	19b and a complex mixture	reflux 2 h in CCl_4, p-TsOH reflux 3 h	crude 23b (~44%)
crude 19a	8 equiv. of LDA -78°C→RT overnight	19a and a complex mixture	reflux in CCl_4 5 h	crude 23a (~43%)

standing leading to the cyclohexenone 24 which then aromatized by lose of benzenesulfenic acid giving the phenolic compound 23. This had been observed during our attempted purification by PLC. This observation prompted us to use the crude reaction mixture for further reaction. Thus, pyrolysis of the crude mixture obtained from LDA-catalyzed cyclisation of 19 in refluxing CCl_4 for 1 h in the presence or absence of catalytic amount of p-toluenesulfonic acid yielded very low yield of 23 (~43%) after basic work up (10% NaOH). The NMR spectra of the crude phenols 23a and 23b were consistent with the assigned structures.

Much to our surprise, LDA-catalyzed cyclisation of the amide sulfoxide 19 to produce the ketosulfoxide 21 could not be completely effected, although many reaction conditions were tried. We believed that the incomplete cyclisation of the amide sulfoxide 19 to the ketosulfoxide 21 could be due to the competitive proton abstraction by LDA of the α-proton adjacent to phenylsulfinyl group and the α-proton with respect to the carbonyl function leading to an intermediate 25



25



26

which could not cyclise to the expected β-ketosulfoxide 21. The ease of α-proton abstraction adjacent to the amide function might be presumably accelerated by complexation of the lithium cation of the initially formed alkoxide with the nitrogen atom of the amide moiety, as shown in figure 26. This chelation effect could therefore result in the higher degree of the α-proton adjacent to the amide function. Furthermore, such conformation of the intermediate 26 could hinder the cyclisation.

Conclusion

Our results clearly demonstrated that α-sulfinyl carbanions could undergo the internal (intramolecular) acylation affording the α-phenylsulfinyl-cyclopentanones and cyclohexanones, which upon pyrolysis yielded cyclopentenone and cyclohexenone derivatives. Considering the high yields, the present technique would appear to constitute the method of choice for the preparation of 5-monoalkylsubstituted, 5,5-disubstituted cyclopentenones and cyclohexenone derivatives. Moreover, the present method appears to possess the synthetic potential for the preparation of some highly substituted-cyclopentenones, -cyclopentanones or -cyclohexanones or even some simple prostanoid natural products.

Experimental Section

General

^{1}H-NMR spectra were recorded on Varian EM 360L spectrometer. Chemical shifts (δ) are reported in parts per million relative to the internal standard, tetramethylsilane (δ = 0). IR spectra were taken with a Perkin Elmer model 137E, Perkin Elmer model SP 2000 and Beckman model IR 20A spectrometers. The mass spectra were recorded on Du Pont 21-490. Melting points were determined by an Electrothermal Melting Point apparatus and were uncorrect. Merck (Kieselgel 60 PF_{254}) silica gel was used for PLC, TLC and Quick Column Chromatography. The molarity of n-BuLi (in hexane) was determined by titration with diphenylacetic acid[78]. Dry THF was obtained by distillation from Na/benzophenone. HMPA, DMF, dimethylsulfoxide, acetonitrile and triethylamine were distilled from CaH_2. Methylene chloride was distilled from P_2O_5.

Preparation of 1-Bromo-3-phenylsulfenylpropane (2).

A solution of thiophenol (20.5 ml, 200 mmol) in methanol (50 ml) was added dropwise at 0^{o}C to a solution of sodium methoxide (225 mmol) in methanol (350 ml) followed by a solution of 1,3-dibromopropane (20.2 ml, 200 mmol). The resulting reaction mixture was stirred at 0^{o}C to room temperature overnight before being poured onto a mixture of H_2O and hexane and extracted with hexane. The combined extracts were washed with 10% aqueous $NaHCO_3$, H_2O, brine and dried over anhydrous $MgSO_4$. Filtration followed by evaporation to dryness afforded a crude colourless liquid (37.8467 gm, 82.2%). Fractional

distillation under reduced pressure yielded 18.5587 gm (40.3%) of pure 2 (b.p.=85°C, 0.015 mmHg). [-IR(neat): 1585, 1480, 1435, 1240,1015, 735, 690 cm^{-1}. -NMR(CCl_4): δ 2.1 (quint, J=6,6 Hz, 2H, $-CH_2\underline{CH_2}CH_2-$); 3.0 (t, J=6 Hz, 2H, $-\underline{CH_2}SPh$); 3.45 (t, J=6 Hz, 2H,$-\underline{CH_2}Br$); 7.0-7.41 (m, 5H, aromatic protons)], 1.0291 gm of 2 and 1,3-diphenylsulfenylpropane, and 18.1582 gm of pure 1,3-diphenylsulfenylpropane (b.p.=150°C, 0.15 mmHg).

Preparation of Methyl 2,2-dialkyl-5-phenylsulfinylpentanoates (4).

General Procedure:

Methyl 2,2-dimethyl-5-phenylsulfinylpentanoate (4a)

n-BuLi (19.2 ml, 30 mmol) was added to a cooled (-78°C) THF (50 ml) solution of diisopropylamine (4.25 ml, 30 mmol under an argon atmosphere. The resulting mixture was stirred at -78°C for 15 min, then stirred at 0°C for 10 min and cooled again at -78°C at which was added dropwise methyl isobutanoate (3.4 ml, 30 mmol). After stirring at 0°C 1 h, HMPA (4.4 ml, 25 mmol) was added dropwise. To the cooled (-78°C) reaction mixture was added dropwise a THF (10 ml) solution of 1-bromo-3-phenylsulfenylpropane (5.7544 gm, 25 mmol). After being stirred at -78°C to room temperature overnight, the resulting yellow solution was quenched with saturated aqueous NH_4Cl solution and extracted with hexane. The combined extracts were washed with H_2O, brine and dried over anhydrous $MgSO_4$. Filtration followed by evaporation to dryness afforded a crude yellow liquid of methyl 2,2-dimethyl-5-phenylsulfenylpentanoate (3a) (6.4670 gm, quantitative

yield). -NMR(CCl_4): δ 1.1 (s, 6H, methyl protons); 1.3-1.63 (m, 4H, -CH_2CH_2-CH_2SPh); 2.7-3.0 (m, 2H, -CH_2SPh); 3.53 (s, 3H, -OCH_3); 7.0-7.4 (m, 5H, aromatic protons).

The crude product 3a was used without purification for further oxidation as follows: A solution of methyl 2,2-dimethyl-5-phenylsulfenylpentanoate (3a) (6.467 gm, 25.7 mmol) in 120 ml of methylene chloride was cooled to -78°C, and a solution of 90% m-chloroperbenzoic acid (4.8516 gm, 25.5 mmol) in 60 ml of methylene chloride was added dropwise from dropping funnel. After completion of the addition, the reaction was monitored by TLC until the reaction had been completed. The cold reaction mixture was then poured into a seporatory funnel containing 100 ml of saturated aqueous $NaHCO_3$ solution and 100 ml of ethyl acetate. The organic layer was separated, extracted with ethyl acetate, washed with saturated aqueous $NaHCO_3$ solution, H_2O, brine and dried over anhydrous $MgSO_4$, filtered and evaporated to give a crude yellow liquid (6.897 gm). It was purified by quick-column chromatography (silica gel) to give 3.6313 gm of a mixture of sulfone and sulfoxide 4a, and 2.9140 gm (42.3%) of pure sulfoxide 4a as viscous liquid. -IR(neat): 1720, 1465, 1440, 1160, 1035, 740, 685 cm^{-1}. -NMR($CDCl_3$): δ 1.15 (s, 6H, methyl protons); 1.65 (m, 4H methylene protons); 2.6-2.95 (m, 2H, -CH_2SOPh); 3.62 (s, 3H, -OCH_3); 7.38-7.75 (m, 5H aromatic protons).

Methyl 2,2-diphenyl-5-phenylsulfinylpentanoate (4b)

A reaction of LDA (30 mmol) in THF (40 ml), methyl diphenyl acetate (6.7912 gm, 30 mmol) in THF (10 ml), HMPA (4.39 ml, 25 mmol)

and a THF (10 ml) solution of 1-bromo-3-phenylsulfenylpropane (5.6393 gm, 24.5 mmol) gave a crude yellow liquid of methyl 2,2-diphenyl-5-phenylsulfenyl-pentanoate (3b) (8.2799 gm, 89.88%). -NMR(CCl_4): δ 1.1-2.7 (m, 2H, methylene protons); 2.26-2.63 (m, 2H, methylene protons); 2.77 (br.t, J≅7 Hz, 2H, -CH_2SPh); 3.6 (s, 3H, -OCH_3); 7.0-7.4 (m, 15H, aromatic protons).

The crude product 3b (5.490 gm, 14.6 mmol) in 80 ml of methylene chloride was treated with a solution of 90% m-chloroperbenzoic acid (2.519 gm, 14.6 mmol) in 50 ml of methylene chloride giving a crude yellow liquid (5.8576 mg, quantitative yield). It was purified by quick-column chromatography (silica gel) to give 0.6075 gm of sulfone, 1.711 gm of sulfone and sulfoxide 4b, and 2.829 gm (49.43%) of pure sulfoxide 4b as a viscous liquid. -IR(neat): 1725, 1490, 1445, 1235, 1060, 740, 690 cm^{-1}. -NMR(CCl_4): δ 1.1-1.76 (m, 2H, methylene protons); 2.3-2.86 (m, 4H, methylene protons); 3.65 (s, 3H, -OCH_3); 7.3 (s, 10H, Ph_2-); 7.5 (s, 5H, PhSO). -MS: m/e(%) = 392(M^+, 77.36), 267(100), 225(56.26), 218(5.95), 207(6.23), 197(29.88), 189(10.27), 178(15.82), 165(45.71), 149(10.94), 129(80.87), 126(16.50), 125(18.52), 121(22.22), 78(15.8), 77(31.65), 65(8.42), 59(10.27), 51(13.3).

Methyl 2-methyl-2-phenyl-5-phenylsulfinylpentanoate (4c)

A reaction of LDA (20 mmol) in THF (30 ml), methyl methyl-phenylacetate (3.2955 gm, 20 mmol) in THF (5 ml), HMPA (3.51 ml, 20 mmol) and a THF (5 ml) solution of 1-bromo-3-phenylsulfenylpropane (4.318 gm, 18.77 mmol) gave a crude yellow liquid of methyl 2-methyl-2-phenyl-5-

-phenylsulfenylpentanoate (3c) (5.7914 gm, 98.26%). -NMR($CDCl_3$):δ 1.5 (s) and 1.2-1.8 (m) (s, 3H, CH_3- and m,2H, methylene protons); 1.9-2.33 (m, 2H, methylene protons); 2.97 (br.t, J≅7 Hz, 2H, -CH_2SPh); 3.57 (s, 3H, -OCH_3); 7.2-7.4 (m, 10H, aromatic protons).

The crude product 3c (5.79 gm, 18.4 mmol) in 100 ml of methylene chloride was treated with a solution of 90% m-chloroperbenzoic acid (3.5072 gm, 18.4 mmol) in 50 ml of methylene chloride affording a crude yellow liquid (5.4166 gm, 89.21%). It was purified by quick-column chromatography (silica gel) to give 3.1157 gm of pure sulfoxide 4c as viscous liquid (51.31%). -IR(neat): 1725, 1600, 1580, 1500, 1445, 1270, 1150, 1090, 1040, 750, 695 cm^{-1}. -NMR($CDCl_3$):δ 1.33-1.86 (m) and 1.55 (s) (m, 2H, methylene protons and s, 3H, methyl protons); 1.86-2.6 (br.m, 2H, methylene protons); 2.73 (t, J=7 Hz, 2H, -CH_2SOPh); 3.61 (s, 3H, -OCH_3); 7.26 (br.s, 5H, Ph-); 7.5 (br.s, 5H, PhSO). -MS: m/e(%) = 330(M^+, 10.67), 312(1.46), 251(3.3), 205(100), 163(8.15), 145(91.4), 135(17.20), 131(9.12), 126(9.61), 121(10.77), 117(19.36), 105(13.98), 103(21.50), 91(24.73), 78(12.90), 77(18.28), 59(14.85), 51(9.42).

Methyl α-(3-phenylsulfinylpropyl)cyclohexanecarboxylate (4d)

A reaction of LDA (13 mmol) in THF (5 ml), methyl cyclohexanecarboxylate (1.7104 gm, 12 mmol) in THF (5 ml), HMPA (2.1 ml, 12 mmol) and a THF (5 ml) solution of 1-bromo-3-phenylsulfenylpropane (2.2997 gm, 10 mmol) gave a crude yellow liquid of methyl α-(3-phenylsulfenylprophyl)cyclohexanecarboxylate (3d) (3.0834 gm, quantitative yield). -IR(neat): 1725, 1580, 1450, 1440, 1210, 1135, 740, 690 cm^{-1}.

-NMR($CDCl_3$):δ 0.95-1.8 (m, 14H, methylene protons); 2.76 (br.t, J≅5 Hz, 2H, -CH_2SPh); 3.55 (s, 3H, -OCH_3); 6.9-7.33 (m, 5H, aromatic protons).

The crude product 3d (3.0834 gm, 10.5 mmol) in 100 ml of methylene chloride was treated with a solution of 90% m-chloroperbenzoic acid (1.9095 gm, 10 mmol) in 50 ml of methylene chloride. A crude yellow liquid (3.0857 gm, 100%) thus obtained was purified by quick-column chromatography (silica gel) to give 0.3202 gm of sulfone, 0.4429 gm of sulfone and sulfoxide 4d, and 1.9365 gm (62.87%) of pure sulfoxide 4d as viscous liquid. -IR(nujol): 1720, 1220, 1195, 1100, 1050, 740, 690 cm^{-1}. -NMR(CCl_4):δ 0.83-1.76 (m) and 1.83-2.23 (m) (m, 14H, methylene protons); 2.3-2.83 (m, 2H, -CH_2SOPh); 3.58 (s, 3H, -OCH_3); 7.2-7.63 (m, 5H, aromatic protons). -MS: m/e(%) = 308(M^+, 15.44), 290(7.35), 249(5.88), 184(18.38), 183(100), 151(5.15), 126(8.83), 124-(7.35), 123(55.88), 109(8.09), 95(8.82), 81(50.73), 78(8.09), 77(10.29), 67(27.20), 59(20.59), 55(13.23).

Preparation of Ethyl 2-carboethoxy-2-methyl-5-phenylsulfinylpentanoate (4e).

To a DMF (20 ml) solution of NaH (0.6026 gm, 25 mmol) was added dropwise diethyl methylmalonate (1.7 ml, 10 mmol) at room temperature. After stirring for 1 h a DMF (10 ml) solution of 1-bromo-3-phenylsulfenylpropane (2.303 gm, 10 mmol) was added, and the resulting mixture was stirred at room temperature overnight. The reaction mixture was heated at 40°C for 30 min and then cooled to room temperature. An excess of NaH was destroyed by the addition of ethanol and the resulting

mixture was extracted with hexane. The combined hexane extracts were washed with H_2O, brine and dried over anhydrous $MgSO_4$, evaporated to give a crude yellow liquid of ethyl 2-ethylcarboxylate-2-methyl-5-phenylsulfenylpentanoate (3e) (2.2368 gm, 69.04%). -NMR(CCl_4): δ 1.0-1.47 (m, 9H, methyl protons); 1.47-2.13 (m, 4H, methylene protons); 2.83 (br.t, J≅7 Hz, 2H, $-CH_2SPh$); 4.05 (q, J=7 Hz, 4H, 2x-OCH_2-); 6.93-7.73 (m, 5H, aromatic protons).

The crude product 3e was used without purification for further oxidation as follows: A solution of 3e (4.3129 gm, 13.3 mmol) in 100 ml of methylene chloride was cooled to -78°C and a solution of 90% m-chloroperbenzoic acid (2.795 gm, 14.5 mmol) in 60 ml of methylene chloride was added dropwise from dropping funnel. Upon completion of the addition, the reaction was monitored by TLC until it had been completed. The cold reaction mixture was then poured into a seporatory funnel containing 100 ml of ethyl acetate and 100 ml of saturated aqueous $NaHCO_3$ solution. The organic layer was separated, extracted with ethyl acetate, washed with saturated aqueous $NaHCO_3$ solution, H_2O, brine and dried over, anhydrous $MgSO_4$, filtered and evaporated to dryness to give a crude yellow liquid (4.3125 gm, 95.37%). Purification by quick-column chromatography (silica gel) afforded 0.5954 gm of sulfone and sulfoxide 4e, 2.884 gm of pure sulfoxide 4e (63.78%). -IR(neat): 1730, 1445, 1250, 1020, 750, 690 cm^{-1}. -NMR($CDCl_3$): δ 1.1-1.53 (m, 9H, methyl protons); 1.53-2.17 (m, 4H, methylene protons); 2.85 (br.t, J≅7 Hz, $-CH_2SOPh$); 3.97-4.43 (m, 4H, 2x-OCH_2-); 7.47-7.87 (m, 5H, aromatic protons). -MS: m/e(%) = 340(M^+, 26.87), 294(16.62), 214(100), 187(17.73), 141(42.11), 123(15.51), 113(28.25), 95(24.38), 85(27.15), 78(12.19), 77(8.86), 69(49.31), 55(16.07).

Preparation of 5,5-Dialkyl-2-phenylsulfinylcyclopentanones (6).

General Procedure:

5,5-Dimethyl-2-phenylsulfinylcyclopentanone (6a)

n-BuLi (3.52 ml, 5.5 mmol) was added to a cooled (-78°C) THF (18 ml) solution of diisopropylamine (0.78 ml, 5.5 mmol) under an argon atmosphere. The resulting mixture was stirred at -78°C for 15 min, then stirred at 0°C for 10 min and cooled again at -78°C at which was added dropwise a THF (7 ml) solution of sulfoxide 4a (0.6715 gm, 2.5 mmol), during which a yellow colour was developed. After being stirred at -78°C to room temperature overnight the resulting yellow solution was quenched with saturated aqueous NH_4Cl and extracted with ethyl acetate. The combined extracts were washed with saturated aqueous NH_4Cl, H_2O, brine, dried over anhydrous $MgSO_4$, filtered and evaporated to give a crude pale brown solid (0.5175 gm, 78%). Purification by recrystallisation from a mixture of hexane and methylene chloride afforded a pure pale brown solid of 6a (0.4361 gm, 73.92%) as a mixture of diastereomers (80:20), m.p.=102-104°C. -IR(nujol): 1725, 1320, 1300, 1030, 740, 730, 690 cm^{-1}. -NMR($CDCl_3$): δ 1.06 and 1.1 (2xs, 6H, methyl protons); 1.43-2.0 (m) and 2.0-2.67 (m) (m, 4H, methylene protons); 3.2-3.53 and 3.7-4.0 (m, 1H, methine proton); 7.33-7.73 (m, 5H, aromatic protons).

5,5-Diphenyl-2-phenylsulfinylcyclopentanone (6b)

A reaction of LDA (6 mmol) in THF (18 ml), HMPA (2.5 ml, HMPA: THF = 1:10) and a THF (7 ml) solution of sulfoxide 4b (0.8617 gm, 2.39

mmol) gave a crude brown liquid (0.7396 gm, 85.96%). Purification by silica gel PLC (40% ethyl acetate in hexane) afforded 0.1178 gm of the starting material, 0.4581 gm (53.24%) of 6b as a white solid (m.p.= 128-130°C) and as a mixture of diastereomers (73:27) (67.32% based on recovered starting material). -IR(nujol): 1725, 1490, 1090, 1035, 755, 695 cm^{-1}. -NMR($CDCl_3$): δ 1.57-2.57 (m, 2H, methylene protons); 2.57-2.97 (m, 2H, methylene protons); 3.3-3.67 (dd, J=10,8 Hz) and 3.8-4.13 (br.t, J≅8 Hz) (1H, methine proton); 6.73-7.7 (m, 15H, aromatic protons). -MS: m/e (%) = 234(M^+, 58.67), 205(40.53), 191(17.07), 178(26.67), 165(37.87), 157(16.0), 126(38.93), 109(23.47), 91(39.47), 78(66.67), 77(36.88), 65(19.73), 55(100).

5-Methyl-5-phenylsulfinylcyclopentanone (6c)

A reaction of LDA (6.25 mmol) in THF (18 ml) and a THF (7 ml) solution of sulfoxide 4c (0.8287 gm, 2.5 mmol) at -78°C for 1 h and 0°C for 2 h gave a crude brown liquid (0.7439 gm, 99.85%). Purification by silica gel PLC (30% ethyl acetate in hexane) afforded 0.5488 gm (73.66%) of 6c as a yellow liquid (diastereomeric mixture). -IR(neat): 1730, 1600, 1580, 1500, 1440, 1375, 1305, 1080, 1040, 1100, 750, 700 cm^{-1}. -NMR($CDCl_3$): δ1.0 and 1.43 (each s, 3H, methyl protons); 1.6-2.9 (m, 4H, methylene protons); 3.2-3.66 and 3.66-4.2 (2xm, 1H, methine proton); 7.1-7.8 (m, 10H, aromatic protons). -MS: m/e(%) = 300(M^++2, 18.09), 280(61.90), 188(20.95), 172(97.62), 157(100), 136(78.57), 125(92.86), 118(64.28), 110(78.57), 103(38.09), 91(33.33), 77(76.19), 55(57.14).

1-Oxo-2-phenylsulfinyl-spiro[4,5]decane (6d)

A reaction of LDA (6.25 mmol) in THF (18 ml) and a THF (7 ml) solution of sulfoxide 4d (0.7696 gm, 2.5 mmol) gave a crude brown solid (0.6465 gm, 93.7%). Recrystallisation from a mixture of ether, methylene chloride and hexane afforded a pure white solid 6d (0.4798 gm, 69.54%), m.p.=143-144°C. -IR(nujol); 1725, 1085, 1045, 740, 690 cm^{-1}. -NMR($CDCl_3$): δ1.03-1.93 (m, 12H, methylene protons); 1.93 (m, 2H, methylene protons); 3.36 (m, 1H, methine proton); 7.37-7.77 (m, 5H, aromatic protons). -MS: m/e(%) = 276(M^+, 4.03), 260(24.26), 204(8.24), 166(10.98), 151(64.53), 136(64.99), 125(31.12), 123(20.59), 121(18.31), 110(58.58), 95(49.43), 81(100), 78(41.19), 77(54.46), 67(84.99), 55(89.98).

5-Carboethoxy-5-methyl-2-phenylsulfinylcyclopentanone (6e)

A reaction of LDA (6 mmol) in THF (15 ml) and a THF (5 ml) solution of sulfoxide 4e (0.6569 gm, 1.9 mmol) gave a crude brown liquid (0.3425 gm). Purification by silica gel PLC (50% ethyl acetate in hexane) afforded 6e (0.1348 gm, 24.8%) as a yellow liquid. -IR(neat): 1730, 1440, 1270, 1170, 1140, 750, 690 cm^{-1}. -NMR($CDCl_3$):δ 0.9-1.47 (m, 6H, methyl protons); 1.63-2.8 (m, 4H, methylene protons); 3.13-3.73 (m, 1H, methine proton); 3.9-4.4 (m, 2H, $-OCH_2-$); 7.3-7.73 (m, 5H, aromatic protons).

Preparation of 5,5-Dialkyl-2-cyclopentenones (7)

General Procedure:

5,5-Dimethyl-2-cyclopentenone (7a)

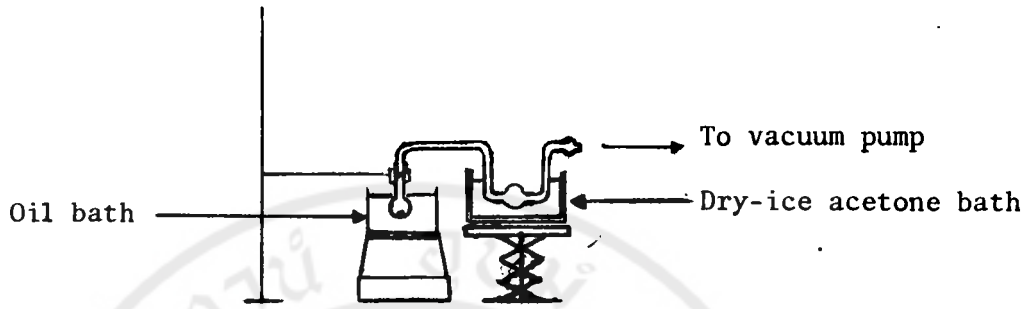


Figure 1.

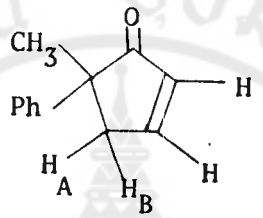
5,5-Dimethyl-2-phenylsulfinylcyclopentanone (6a) (0.174 gm, 0.73 mmol) was placed in round bottom flask fillted to the U-shape tube which is placed in dry ice-acetone bath as shown in Figure 1. The flask containing the ketosulfoxide 6a was heated at 180°C for 20 min, during which it was distilled under reduced pressure using water pump. Distilled product was trapped in U-shape tube. A colourless liquid of 7a (0.6613 gm, 75.67%) was obtained. -IR($CDCl_3$): 1700, 1590 cm^{-1}. -NMR(CCl_4): δ 1.07 (s, 6H, methyl protons); 2.5 (dd, J=3,2 Hz, 2H, methylene protons); 6.03 (dt, J=6,2 Hz, 1H, -CH=CHCO-); 7.5 (dt, J=6,3 Hz, 1H, -CH=CHCO-).

5,5-Diphenyl-2-cyclopentenone (7b)

A solution of pure 6b (0.6714 gm, 1.86 mmol) in CCl_4 (30 ml) was refluxed under an argon atmosphere for 8 h. After removal of CCl_4, the crude product was purified by silica gel PLC (20% methylene chloride in hexane) to give a white solid 7b (0.4547 gm, quantitative yield), m.p.=85-87°C. -IR(nujol): 1690, 1590, 1160 cm^{-1}. -NMR($CDCl_3$): δ 3.36

(dd, J=2.5,2 Hz, 2H, methylene protons); 6.11 (dt, J=6,2 Hz, 1H, -CH=CHCO-); 6.97-7.57 (br.s, 10H, aromatic protons); 7.67 (dt, J=6, 2.5 Hz, 1H, -CH=CHCO-). -MS: m/e(%) = 234(M^+, 100), 205(37.5), 191(13.21), 178(12.60), 165(16.67), 157(11.58), 128(13.41), 91(16.06).

5-Methyl-5-phenyl-2-cyclopentenone (7c).



7c

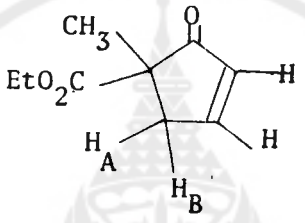
A solution of pure 6c (0.5973 gm, 2.0 mmol) in toluene (30 ml) was refluxed under an argon atmosphere for 15 h. After removal of CCl_4, the crude product was purified by silica gel PLC (20% ethyl acetate in hexane) to give a yellow liquid of 7c (0.3094 gm, 89.94%). -IR(neat): 1700, 1590, 1440, 1340, 700, 670 cm^{-1}. -NMR(CCl_4): δ 1.4 (s, 3H, $-CH_3$); 2.67 (ddd, J=19.5,2.5,2 Hz, 1H, H_A or H_B); 3.08 (ddd, J=19.5,2.5,2 Hz, 1H, H_B or H_A); 6.05 (dt, J=6,2 Hz, 1H, -CH=CHCO-); 6.97-7.47 (br.s, 5H, aromatic protons); 7.56 (dt, J=6,2.5 Hz, 1H, -CH=CHCO-). -MS: m/e(%) = 172(M^+, 32.64), 157(38.89), 129(100), 117(17.36), 115(27.78), 103(19.44), 95(18.40), 91(15.62), 78(12.5), 77(24.30), 51(15.97).

1-Oxo-spiro [4,5] dec-2-ene (7d)

The crude product of 6d (0.6614 gm, 2.39 mmol) was heated at 100°C under reduced pressure (0.07 mmHg), using the apparatus as shown in Figure 1. Distilled product 7d was trapped in U-shaped tube as colourless liquid (0.2418 gm, 67.45%). -IR(neat): 1690, 1590, 1450,

1350, 1190, 810 cm^{-1}. -NMR(CCl_4):δ 1.0-2.0 (m, 10H, methylene protons); 2.51 (dd, J=3,2 Hz, 2H, -CH_2CH=CHCO-); 6.0 (dt, J=5.5,2 Hz, 1H, -CH=CHCO-); 7.51 (dt, J=5.5,3 Hz, 1H, -CH=CHCO-). -MS: m/e(%) = 150(M^+, 19.05), 135(4.76), 108(19.73), 95(86.39), 82(36.73), 79(21.77), 68(100), 67(44.90), 55(30.61).

5-Carboethoxy-5-methyl-2-cyclopentenone (7e)



7e

A solution of pure 6e (0.2654 gm, 0.9 mmol) in CCl_4 (20 ml) was refluxed under an argon atmosphere for 19 h. After removal CCl_4, the crude product obtained was purified by silica gel PLC (50% chloroform in hexane) to give a pure brown liquid 7e (0.0615 gm, 40.67%). -IR(neat): 1740, 1710, 1590, 1270, 1190, 750 cm^{-1}. -NMR(CCl_4):δ 1.2 (t, J=7 Hz, 3H, CH_3CH_2-); 1.3 (s, 3H, CH_3C-); 2.45 (ddd, J=19,2.5,2 Hz, 1H, H_A or H_B); 3.2 (ddd, J=19,2.5,2 Hz, 1H, H_B or H_A); 6.03 (dt, J=5.5,2 Hz, 1H, -CH=CHCO-); 7.68 (dt, J=5.5,2.5 Hz, 1H, -CH=CHCO-).

Preparation of *N*-Methyl-*N*-phenyl-2-alkyl-5-phenylsulfinylpentanamides (10).

General Procedure:

N-Methyl-*N*-phenyl-2-methyl-5-phenylsulfinylpentanamide (10a).

n-BuLi (6.6 ml, 10 mmol) was added to a cooled (-78°C) THF

(10 ml) solution of diisopropylamine (1.42 ml, 10 mmol) under an argon atmosphere. The mixture was stirred at -78°C for 15 min then stirred at 0°C for 10 min at which was added dropwise a THF (5 ml) solution of *N*-methyl-*N*-phenylpropanamide (1.4195 gm, 8.7 mmol). After stirring at 0°C for 1 h, a THF (5 ml) solution of 1-bromo-3-phenylsulfenylpropane (1.8486 gm, 8 mmol) was added dropwise. After stirring at 0°C to room temperature overnight, the resulting pale yellow liquid was quenched with saturated aqueous NH_4Cl and extracted with hexane. The combined extracts were washed with saturated aqueous NH_4Cl, H_2O, brine and dried over anhydrous $MgSO_4$. Filtration followed by evaporation to dryness afforded a crude yellow liquid of *N*-methyl-*N*-phenyl-2-methyl-5-phenylsulfenylpentanamide (9a) (2.5285 gm, quantitative yield). -NMR(CCl_4): δ 0.95 (d, J=6 Hz, 3H, CH_3C-); 1.17-2.57 (m, 5H, methine proton and methylene protons); 2.7 (br.t, J≅6 Hz, 2H, -CH_2SPh); 3.17 (s, 3H, -NCH_3); 6.97-7.57 (m, 10H, aromatic protons).

The crude product 9a was used without purification for further oxidation: A solution of 9a (2.5285 gm, 8 mmol) in 80 ml of methylene chloride was cooled to -78°C, and a solution of 90% m-chloroperbenzoic acid (1.5355 gm, 8 mmol) in 50 ml of methylene chloride was added dropwise from dropping funnel. Upon completion of the addition, the reaction was monitored by TLC until it had been completed. The cold reaction mixture was then poured into a seporatory funnel containing 100 ml of ethyl acetate and 100 ml of saturated aqueous $NaHCO_3$ solution. The organic layer was separated, extracted with ethyl acetate, washed with saturated aqueous $NaHCO_3$ solution, H_2O, brine and dried over

anhydrous $MgSO_4$, filtered and evaporated to give a crude yellow liquid (2.7277 gm). Purification by silica gel PLC (50% ethyl acetate in hexane) gave 2.0905 gm of pure sulfoxide 10a (79.43%) as viscous liquid. -IR(neat): 1650, 1600, 1500, 1390, 1090, 1040, 750, 700 cm^{-1}. -NMR ($CDCl_3$): δ0.01 (d, J=7 Hz, 3H, CH_3C-); 1.17-2.03 (m, 4H, methylene protons); 2.17-2.83 (m, 3H, methine proton and -CH_2SPh); 3.2 and 3.23 (2xs, 3H, -NCH_3); 6.93-7.67 (m, 10H, aromatic protons). -MS: m/e(%) = 330(M^+, 2.12), 312(2.64), 223(11.64), 204(100), 195(8.46), 134(32.07), 107(37.73), 97(8.29), 91(6.52), 78(18.87), 77(41.51), 69(88.68), 65(10.58), 51(21.16).

N-Methyl-*N*-phenyl-2-ethyl-5-phenylsulfinylpentanamide (10b)

A reaction of LDA (12 mmol) in THF (10 ml), *N*-methyl-*N*-phenylbutanamide (1.9497 gm, 11 mmol) in THF (5 ml) and a THF (5 ml) solution of 1-bromo-3-phenylsulfenylpropane (0.3008 gm, 10 mmol) gave a crude yellow liquid of *N*-methyl-*N*-phenyl-2-ethyl-5-phenylsulfenylpentanamide (9b) (3.3953 gm, quantitative yield). -NMR(CCl_4): δ0.78 (t, J=7 Hz, 3H, CH_3CH_2-); 1.1-2.33 (m, 7H, methine proton and methylene protons); 2.7 (br.t, J≅6 Hz, 2H, -CH_2SPh); 3.2 (s, 3H, -NCH_3); 6.83-7.57 (m, 10H, aromatic protons).

The crude product 9b (3.3953 gm, 10.3 mmol) in 80 ml of methylene chloride was treated with a solution of 90% m-chloroperbenzoic acid (1.9642 gm, 10 mmol) in 50 ml of methylene chloride gave a crude yellow liquid (3.5795 gm, quantitative yield). It was purified by quick-column chromatography (silica gel) to give 0.3136 gm of sulfone,

0.1049 gm of sulfone and sulfoxide 10b, and 2.5611 gm of pure sulfoxide 10b (74.67%) as viscous liquid. -IR(neat): 1655, 1605, 1455, 1405, 1050, 705, cm^{-1}. -NMR(CCl_4): δ 0.75 (t, J=7 Hz, 3H, CH_3C-); 1.07-2.37 (m, 7H, methine proton and methylene protons); 2.37-2.8 (m, 2H, $-CH_2-$SOPh); 3.17 and 3.21 (2xs, 3H, $-NCH_3$); 6.83-7.7 (m, 10H, aromatic protons). -MS: m/e(%) = 345(M^++2, 13.48), 327(3.88), 238(18.03), 218(100), 209(10.87), 193(3.12), 149(2.86), 134(30.32), 127(3.79), 125(4.97), 123(4.21), 109(4.13), 108(8.34), 107(34.43), 106(17.86), 97(3.03), 83(36.06), 78(5.56), 77(13.73), 55(36.06).

N-Methyl-*N*-phenyl-5-phenylsulfinyl-2-propylpentanamide (10c)

A reaction of LDA (12 mmol) in THF (10 ml), *N*-methyl-*N*-phenyl-pentanamide (2.1071 gm, 11 mmol) in THF (5 ml) and a THF (5 ml) solution of 1-bromo-3-phenylsulfenylpropane (2.3028 gm, 10 mmol) gave a crude yellow liquid of *N*-methyl-*N*-phenyl-2-propyl-5-phenylsufenylpentanamide (9c) (3.4631 gm, quantitative yield). -IR(neat): 1650, 1590, 1495, 1390, 735, 700 cm^{-1}. -NMR(CCl_4): δ 0.53-1.0 (m, 3H, CH_3C-); 1.0-2.33 (m, 9H, methine proton and methylene protons); 2.65 (t, J=7 Hz, 2H, $-CH_2SPh$); 3.17 (s, 3H, $-NCH_3$); 6.77-7.63 (m, 10H, aromatic protons).

The crude product 9c (3.4631 gm, 10.15 mmol) in 80 ml of methylene chloride was treated with a solution of 90% m-chloroperbenzoic acid (1.8246 gm, 9.5 mmol) in 50 ml of methylene chloride gave a crude yellow liquid (3.6344 gm, quantitative yield). It was purified by column chromatography (SiO_2, 20% ethyl acetate in hexane, 25%, 30%, 35%, 40% and 50%) to give 0.3071 gm of sulfone, 0.1034 gm of sulfone and

sulfoxide 10c, and 2.4402 gm of pure sulfoxide 10c (68.35%) as viscous liquid. -IR(neat): 1655, 1605, 1505, 1455, 1050, 705 cm^{-1}. -NMR(CCl_4): δ 0.53-2.77 (m, 14H, CH_3C-, methylene protons and methine proton); 3.17 and 3.21 (2xs, 3H, $-NCH_3$); 6.97-7.67 (m, 10H, aromatic protons). -MS: m/e(%) = 357(M^+, 8.21), 310(3.97), 250(13.46), 232(100), 223(8.59), 134(22.31), 125(4.62), 107(25.0), 106(9.23), 97(16.15), 77(7.18), 55(20.9).

N-Methyl-*N*-phenyl-2-butyl-5-phenylsulfinylpentanamide (10d)

A reaction of LDA (12 mmol) in THF (10 ml), *N*-methyl-*N*-phenyl-hexanamide (2.3298 gm, 11.3 mmol) in THF (5 ml) and a THF (5 ml) solution of 1-bromo-3-phenylsulfenylpropane (2.3009 gm, 10 mmol) gave a crude yellow liquid of *N*-methyl-*N*-phenyl-2-butyl-5-phenylsulfenylpentanamide (9d) (3.8215 gm, quantitative yield). -NMR(CCl_4): δ 0.6-1.93 (br.m, 13 H, CH_3C- and methylene protons); 1.93-2.4 (br.m, 1H, methine proton); 2.68 (t, J=6 Hz, 2H, $-CH_2SPh$); 3.2 (s, 3H, $-NCH_3$); 6.87-7.43 (m, 10H, aromatic protons).

The crude product 9d (3.8215 gm, 10.7 mmol) in 80 ml of methylene chloride was treated with a solution of 90% m-chloroperbenzoic acid (1.8607 gm, 9.8 mmol) in 50 ml of methylene chloride gave a crude yellow liquid (4.0531 gm, quantitative yield). It was purified by column chromatography (SiO_2, 20% ethyl acetate in hexane, 25%, 30%, 35%, 40%, and 50%) to give 0.2900 gm of sulfone, 0.0143 gm of sulfone and sulfoxide 10d, and 2.8597 gm of pure sulfoxide 10d (77.08%) as viscous liquid. -IR(neat): 1645, 1590, 1495, 1440, 1390, 1085, 1040, 745, 700 cm^{-1}. -NMR($CDCl_3$): δ 0.6-2.03 (m, 13H, CH_3C- and methylene protons); 2.03-2.9 (m, 3H, methine

proton and -CH_2SOPh); 3.23 and 3.28 (2xs, 3H, -NCH_3); 6.97-7.8 (m, 10H, aromatic protons).

N-Methyl-*N*-phenyl-2-tetradecanyl-5-phenylsulfinylpentanamide (10e)

A reaction of LDA (12 mmol) in THF (10 ml), *N*-methyl-*N*-phenyl-hexadecanamide (3.9467 gm, 11.4 mmol) in THF (5 ml) and a THF (5 ml) solution of 1-bromo-3-phenylsulfenylpropane (2.3085 gm, 10 mmol) gave a crude yellow liquid of *N*-methyl-*N*-phenyl-2-tetradecanyl-5-phenylsulfenylpentanamide (9e) (5.3659 gm, quantitative yield). -IR(neat): 1655, 1595, 1495, 735, 700 cm^{-1}. -NMR(CCl_4):δ 0.67-2.33 (br.m, 34H, CH_3C-, methylene protons and methine proton); 2.5-2.83 (m, 2H, -CH_2SPh); 3.2 (s, 3H, -NCH_3); 6.9-7.5 (m, 10H, aromatic protons).

The crude product 9e (5.3659 gm, 10.8 mmol) in 80 ml of methylene chloride was treated with a solution of 90% m-chloroperbenzoic acid (1.8919 gm, 9.8 mmol) in 50 ml of methylene chloride gave a crude viscous yellow liquid (5.9008 gm, quantitative yield). Purification by crystallization from a mixture of hexane and ether afforded a pure white solid of 10e (3.5277 gm, 69.0%), m.p.=51-53°C. IR(neat): 1650, 1595, 1040, 760, 690 cm^{-1}. -NMR($CDCl_3$):δ 0.6-2.43 (m, 34H, CH_3C-, methylene protons and methine proton); 2.43-2.83 (m, 2H, -CH_2SOPh); 3.21 and 3.27 (2xs, 3H, -NCH_3); 6.93-7.63 (m, 10H, aromatic protons).

Preparation of 5-Alkyl-2-phenylsulfinylcyclopentanones (11).

General Procedure:

5-Methyl-2-phenylsulfinylcyclopentanone (11a)

n-BuLi (4.12 ml, 6.25 mmol) was added to a cooled (-78°C) THF (18 ml) solution of diisopropylamine (0.88 ml, 6.25 mmol) under an argon atmosphere. The resulting mixture was stirred at -78°C for 15 min, then stirred at 0°C for 10 min and cooled again at -78°C at which was added dropwise a THF (7 ml) solution of pure sulfoxide 10a (0.8310 gm, 2.5 mmol) during which a yellow colour developed. After being stirred at -78°C for 1 h and at 0°C for 1 h, the resulting yellow solution was quenched with saturated aqueous NH_4Cl and extracted with ethyl acetate. The combined extracts were washed with saturated aqueous NH_4Cl, H_2O, brine and dried over anhydrous $MgSO_4$, filtered and evaporated to give a crude orange liquid (0.7133 gm, quantitative yield). Purification by silica gel PLC (chloroform) afforded 0.4469 gm of pure 11a (80.52%) as viscous liquid. -IR(neat): 1740, 1445, 1150, 1090, 1050, 750, 690 cm^{-1}. -NMR($CDCl_3$): δ 1.11 (d, J=6 Hz, 3H, CH_3C-); 1.31-2.77 (m, 5H, -CHC- and methylene protons); 3.07-3.6 (m, 1H, -CHSOPh); 7.55 (br.s, 5H, aromatic protons). -MS: m/e(%) = 222(M^+, 54.02), 206(16.07), 136(20.54), 126(100), 125(80.94), 97(71.43), 78(42.86), 77(18.30), 55(23.21), 53(25.45), 51(25.89).

5-Ethyl-2-phenylsulfinylcyclopentanone (11b)

A reaction of LDA (6.25 mmol) in THF (18 ml) and a THF (7 ml) solution of sulfoxide 10b (0.8622 gm, 2.5 mmol) gave a crude orange liquid (0.7041 gm, quantitative yield). Purification by silica gel PLC (chloroform) afforded a pure white solid of 11b, m.p.=50-54°C (0.435 gm, 73.73%). -IR(nujol): 1730, 1480, 1450, 1440, 1150, 1080,

1030, 750, 720, 690 cm^{-1}. NMR(CCl_4): δ 0.91 (t, J=7 Hz, 3H, $\underline{CH_3}C$-); 1.17-2.7 (m, 7H, -C$\underline{H}$C- and methylene protons); 3.0-4.0 (m, 1H, -C$\underline{H}$SOPh); 7.2-7.8 (m, 5H, aromatic portons). -MS:m/e(%) = 236(M^+, 15.58), 218(100), 154(12.27), 136(19.09), 126(25.32), 125(29.41), 109(78.71), 98(9.74), 96(7.4), 83(12.27), 82(14.61), 81(12.85), 78(21.04), 77(27.66), 55(100).

2-Phenylsulfinyl-5-propylcyclopentanone (11c)

A reaction of LDA (6.25 mmol) in THF (18 ml) and a THF (7 ml) solution of sulfoxide 10c (0.8936 gm, 2.5 mmol) gave a crude orange liquid (0.8365 gm, quantitative yield). Purification by silica gel PLC (chloroform) afforded a pure yellow liquid of 11c (0.5679 gm, 90.86% as viscous liquid. -IR(neat): 1735, 1445, 1085, 1045, 750, 690 cm^{-1}. -NMR(CCl_4): δ 0.9 (t) and 0.63-2.63 (m) (t, J=5 Hz; 3H, $\underline{CH_3}C$- and m, 9H, -C$\underline{H}$C- and methylene protons); 3.03-3.63 (m, 1H, -C$\underline{H}$SOPh); 7.2-7.73 (m, 5H, aromatic protons). -MS: m/e(%) = 250(M^+, 1.64), 232(1.85), 218 (8.56), 190(1.17), 154(0.91), 149(0.64), 141(0.89), 136(1.37), 125(11.38), 110(12.59), 95(7.26), 82(60.97), 77(32.51), 67(49.59), 55 (100), 53(49.96), 51(39.84).

5-Butyl-2-phenylsulfinylcyclopentanone (11d)

A reaction of LDA (6.25 mmol) in THF (18 ml) and a THF (7 ml) solution of sulfoxide 10d (0.9452 gm, 2.5 mmol) gave a crude yellow liquid (0.8530 gm, quantitative yield). Purification by silica gel PLC (chloroform) afforded a pure yellow liquid of 11d (0.6632 gm, 98.98%). -IR (neat): 1730, 1440, 1080, 1040, 750, 690 cm^{-1}. -NMR(CCl_4): δ 0.62-1.08

(br.t, J≅4 Hz, 3H, CH_3C-), 1.08-2.63 (m, 11H, -CHC-and methylene protons); 3.02-3.52 and 3.53-3.98 (2xm, 1H, -CHSOPh); 7.25-7.82 (m, 5H, aromatic protons). -MS: m/e(%) = 250(M^+, 0.56), 218(5.35), 139(3.86), 109(12.19), 95(13.67), 82(100), 77(7.28), 68(13.67), 67(11.89), 58(28.33), 53(23.33).

5-Tetradecanyl-2-phenylsulfinylcyclopentanone (11e)

A reaction of LDA (6.24 mmol) in THF (18 ml) and a THF solution of sulfoxide 10e (1.1532 gm, 2.25 mmol) gave a crude brown liquid (1.1252 gm, quantitative yield). Purification by silica gel PLC (3:2:5 = $CHCl_3$:CH_2Cl_2:hexane) afforded a pure pale solid of 11e (0.7574 gm, 83.32%). -IR(mujol): 1725, 1040, 745, 690 cm^{-1}. -NMR($CDCl_3$): δ 1.03-2.73 (m, 34H, CH_3C-, -CHC- and methylene protons); 3.03-3.53 (m, 1H, -CHSOPh); 7.4-7.8 (m, 5H, aromatic protons). -MS: m/e(%) = 348(M^+-O, 0.76), 280(14.58), 235(1.74), 218(2.01), 186(2.64), 126(18.05), 125 (18.05), 110(13.19), 109(22.22), 97(11.80), 96(13.19), 95(77.78), 83 (38.19), 82(100), 81(20.83), 78(20.14), 77(15.97), 69(11.11), 68(9.72), 67(11.11), 65(11.11), 55(20.83).

Preparation of 5-Alkyl-2-cyclopentenones (12).

General Procedure:

5-Methyl-2-cyclopentenone (12a)

Pyrolysis of the ketosulfoxide 11a (0.3624 gm, 1.6 mmol) as neat was performed by using the apparatus as shown in Figure 1 (page 70) under reduced pressure (80°C, 0.5 mmHg, 30 min). A distilled product 12a (0.1678 gm, quantitative yield) as a colorless liquid was trapped

in U-shaped tube which was cooled with dry ice-acetone bath. -IR(neat): 1705, 1590, 1340, 790 cm^{-1}. -NMR(CCl_4): δ 1.11 (d, J=7 Hz, 3H, CH_3C-); 1.8-2.53 (m, 2H, CH_3CHCO- and -CH_2-CH=CHCO); 2.94 (part of ABXZ, J=19,7, 3, 2.5 Hz, 1H -CH_2CH=CHCO-); 6.05 (dt, J=6, 2 Hz, 1H, -CH=CHCO-); 7.53 (dt, J=6,3 Hz, 1H, -CH=CHCO-).

5-Ethyl-2-cyclopentenone (12b)

Pyrolysis of pure ketosulfoxide 11b (0.2192 gm, 0.9 mmol) at 100-130°C for 1 h using the apparatus shown in Figure 1 afforded 0.0957 gm (94.56%) of 12b as a colorless liquid after distillation at 80°C (1.0 mmHg), and the distillate was trapped in the U-shaped tube which was cooled at -78°C (dry ice-acetone bath). -IR(neat): 1700, 1590, 1350, 1180, 770 cm^{-1}. NMR(CCl_4): δ 0.93 (t, J=7 Hz, 3H, CH_3 C-); 1.13-2.57 (m, 4H, -CHCO, methylene protons and -CH_2CH=CHCO); 2.9 (part of ABXZ, J=18,4,3,2 Hz, 1H, -CH_2CH=CHCO); 6.06 (dt, J=6,2 Hz, 1H, -CH=CHCO-); 7.58 (dt, J=6,3 Hz, 1H, -CH=CHCO-). -MS: m/e(%) = 100)M^+, 22.32), 82(100), 81(59.27), 78(33.53), 77(32.32), 53(62.95).

5-Propyl-2-cyclopentenone (12c)

Pyrolysis of pure ketosulfoxide 11c (0.5090 gm, 2 mmol) was performed at 100°C for 1 h by the usual manner as described for 12a. Distillation at 58-62°C (0.07 mmHg) furnished a colorless liquid of 12c (0.1791 gm, 72.2%). -IR(neat): 1700, 1590, 1340 cm^{-1}. -NMR(CCl_4): δ 0.73-2.63 (m, 9H, $CH_3CH_2CH_2$-, $CH_3(CH_2)_2CHCO$, -CHCO and -CH_2CH=CHCO-); 2.9 (part of ABXZ, J=19,7,3,2.5 Hz, 1H, -CH_2CH=CHCO-); 6.05 (dt, J=6, 2.5 Hz, 1H, -CH=CHCO-); 7.58 (dt, J=6,3 Hz, 1H, -CH=CHCO-). -MS: m/e(%)

= 124(M^+, 5.37), 95(10.07), 82(100), 81(29.53), 78(19.46), 77(23.49), 53(50.33).

5-Butyl-2-cyclopentenone (12d)

Pyrolysis of pure ketosulfoxide 11d (0.6300 gm, 2.38 mmol) at 130°C for 1 h followed by distillation at 100-120°C (0.1 mmHg) using the apparatus shown in Figure 1 gave 12d (0.2431 gm, 74.1%) as colorless liquid. -IR(neat): 1700, 1590, 1340, 1170, 770 cm^{-1}. -NMR(CCl_4): δ 0.7-1.93, 1.93-2.33 and 2.33-2.6 (m, 11H, methyl protons, methylene protons, -CHCO- and -CH_2CH=CHCO-); 2.93 (part of ABXZ, J=19,7,3,2.5 Hz, 1H, -CH_2CH=CHCO); 6.07(dt, J=6, 2.5 Hz, 1H, -CH=CHCO-); 7.57 (dt, J=6, 3 Hz, 1H, -CH=CHCO-). -MS: m/e(%) = 138(M^+, 4.6), 95(12.56), 82(100), 68(12.82), 67(11.79), 53(19.99).

5-Tetradecanyl-2-cyclopentenone (12e)

Pyrolysis of pure ketosulfoxide 11e (0.3998 gm, 0.98 mmol) was done at 100-110°C for 5 h. The crude pyrolysate was furified by silica gel PLC (70% methylene chloride in hexane) afforded a pure pale yellow solid of 12e (0.2346 gm, 85.31%). -IR(nujol): 1690, 1590, 1350, 1160, 950, 770, 740 cm^{-1}. -NMR($CDCl_3$):δ 0.7-2.57 (m, 31H, methyl protons and methylene proton, -CHCO and -CH_2CH=CHCO); 2.57-2.9 and 2.9-3.2 (part of ABXZ, 1H, -CH_2CH=CHCO); 6.11 (dt, J=6, 2 Hz, 1H, -CH=CHCO-); 7.61 (dt, J=6.3 Hz, -CH=CHCO-). -MS: m/e(%) = 280(M^++2, 100), 123(7.38), 109(18.12), 98(21.48), 97(53.02), 94 (63.09), 83(35.57), 81(36.24).

Preparation of 5-Methyl-2-phenylsulfenyl-2-cyclopentenone (14a).

To an acetonitrile (12 ml) solution of ketosulfoxide 11a (0.4497 gm, 2 mmol) was added neat trifluoroacetic anhydride (0.56 ml, 4 mmol) at 0°C under an argon atmosphere. After stirring at 0°C for 1 h and at room temperature for 1 h, TLC analysis showed complete loss of the starting material, the crude product was evaporated to dryness and purified by silica gel PLC (80% methylene chloride in hexane) to give a pure brown liquid 14a (0.2707 gm, 66.35%). -IR(neat); 1695, 1575, 1475, 1440, 1280, 980, 750, 690 cm^{-1}. -NMR(CCl_4): δ 1.17(d, J=8 Hz, 3H, CH_3C-); 1.9-2.03, 2.13-2.83 and 2.9-3.1 (m, 3H, methine proton and methylene protons); 6.73 (t, J=3 Hz, 1H, olefinic proton); 7.13-7.63 (m, 5H, aromatic protons).

Preparation of 1-Oxo-2-phenylsulfenyl-spiro [4,5] dec-2-ene (14b)

To an acetonitrile (9 ml) solution of ketosulfoxide (6d) (0.4207 gm, 1.5 mmol) was added dropwise neat trifluoroacetic anhydride (0.42 ml, 3 mmol) at 0°C under an argon atmosphere. After 10 min was added neat CH_3SO_3H (0.1 ml) and stirred at 0°C for 30 min. The crude product was diluted with methylene chloride, extracted with methylene chloride, washed with H_2O, 5% aqueous $NaHCO_3$ solution, H_2O, brine and dried over anhydrous $MgSO_4$. Filtration followed by evaporation to dryness afforded a crude orange solid (0.4413 gm). Purification by silica gel PLC (70% methylene chloride in hexane) afforded a pure yellow solid 14b (0.3053 gm, 78.89%); m.p.=123-125°C. IR(nujol): 1690, 1580, 1290, 760, 690 cm^{-1}. -NMR($CDCl_3$): δ 0.97-2.03 (m, 10H,

methylene protons); 2.45 (d, J=3 Hz, 2H, -$\underline{CH_2}$C=C-); 6.83 (t, J=3 Hz, 1H, olefinic proton); 7.1-7.6 (m, 5H, aromatic protons). -MS: m/e(%) = 258(M^+, 100), 204(15.51), 149(7.01), 134(8.39), 121(5.63), 115(5.52), 115(7.54), 105(6.53), 93(5.31), 91(7.27), 79(7.75), 77(4.88), 71(6.42), 67(6.58).

Preparation of 4-phenylsulfenylbutanal

To an acetonitrile (170 ml) solution of THF (20.3 ml, 250 mmol) and sodium iodide (45.3 gm, 302 mmol) was added acetonitrile (80 ml) solution of acetyl chloride (17.7 ml, 250 mmol) at 0°C. After 21 h of stirring the reaction mixture at an ambient temperature, reaction was quenched by the addition of aqueous $NaHSO_3$, extracted with methylene chloride. The combined extracts were washed with brine and dried over anhydrous $MgSO_4$. Filtration followed by evaporation to dryness afforded a crude yellow liquid of 4-iodobutyl acetate (62.0 gm, quantitative yield). -NMR(CCl_4): δ 1.5-2.2 (m, 4H, methylene protons); 1.97 (s, 3H, -C$\underline{CH_3}$); 3.2 (br.t, J≅6 Hz, 2H, -$\underline{CH_2}$O-); 4.05 (br.t, J≅6 Hz, 2H, -$\underline{CH_2}$I).

The crude product of 4-iodobutyl acetate was used without purification for further reaction as follows: To an ethanol (250 ml) solution of ethoxide of sodium (7.338 gm, 319 mmol) was added dropwise an ethanol (20 ml) solution of thiophenol (25 ml, 250 mmol) at 0°C. To the resulting clear solution was added dropwise an ethanol (50 ml) solution of 4-iodobutyl acetate at 0°C. After being stirred at 0°C to room temperature overnight, 50% aqueous solution of NaOH (10.1516 gm)

was added dropwise and stirred at room temperature for 2 h. The reaction mixture was poured onto a mixture of H_2O and methylene chloride. The organic layer was separated, and the aqueous layer was acidified by 5 N HCl, extracted with methylene chloride. The combined extracts were washed with H_2O, brine and dried over anhydrous $MgSO_4$. Filtration followed by evaporation to dryness afforded a crude pale yellow liquid of 4-phenylsulfenylbutanol (38.4 gm, 84.4%) which is crystallised on standing in a refrigerator (-0°C). -NMR($CDCl_3$): δ 1.47-1.97 (m, 4H, methylene protons); 2.73 (s, 1H, -OH); 2.91 (t, J=7 Hz, 2H, $-CH_2O-$); 3.58 (t, J=6 Hz, 2H, $-CH_2SPh$); 7.03-7.63 (m, 5H, aromatic protons). -MS: m/e(%) = 182(M^+, 62.39), 123(45.88), 110(100), 77(9.22), 73(22.02), 66(10.41), 58(11.16), 55(45.88).

The crude product of 4-phenylsulfenylbutanol was used without purification for further oxidation as follows: To a stirred solution of dimethyl sulfoxide (1.4 ml, 20 mmol) in methylene chloride (40 ml, 0.5 M) under and argon atmosphere at -78°C was added neat oxalyl chloride (1.7 ml, 20 mmol) to produce a homogeneous solution. After 25 min a solution of 4-phenylsulfenylbutanol (1.8328 gm, 10 mmol) in methylene chloride (40 ml, 0.25 M) was added, stirring was continued at -78°C for 10 min and neat Et_3N (5.6 ml, 40 mmol) was added. The solution was allowed to warm to room temperature, quenched with 10% H_2SO_4 solution, and extracted with methylene chloride. The combined extracted were washed with 10% H_2SO_4, H_2O, saturated aqueous $NaHCO_3$ solution, brine and dried over anhydrous $MgSO_4$ and concentrated to afford a crude 4-phenylsulfenylbutanal (1.9182 gm, quantitative yield).

-NMR(CCl_4): δ 1.57-2.33 (m, 2H, methylene protons); 2.37-2.7 (m, -CH_2-CO-); 2.9 (t, J=7 Hz, 2H, -CH_2-SPh); 7.0-7.47 (m, 5H, aromatic protons); 9.7-9.87 (m, 1H, aldehydic proton).

Preparation of Methyl 2,2-dialkyl-3-hydroxy-5-phenylsulfinylhexanoates (18).

General Procedure:

Methyl 2,2 dimethyl-3-hydroxy-5-phenylsulfinylhexanoate (18a)

n-BuLi (5.36 ml, 8 mmol) was added to a cooled (-78°) THF (10 ml) solution of diisopropylamine (1.13 ml, 8 mmol) under an argon atmosphere. The resulting mixture was stirred at -78°C for 15 min, then stirred at 0°C for 10 min and cooled again at -78°C at which was added dropwise methyl isobutanoate (1.0 ml, 8 mmol). After stirring at 0°C for 1 h, a THF (5 ml) solution of 4-phenylsulfenylbutanal (1.097 gm, 6 mmol) was added dropwise to a cooled (-78°C) reaction mixture. Stirring was continued at -78°C for 2.5 h, then the resulting yellow solution was quenched with saturated squeous NH_4Cl and extracted with methylene chloride. The combined extracts were washed with saturated aqueous NH_4Cl, H_2O, brine and dried over anhydrous $MgSO_4$. Filtration followed by evaporation to dryness afforded a crude yellow liquid of methyl 2,2-dimethyl-3-hydroxy-5-phenylsulfenylhexanoate (16a) (1.315 gm, 77.3%). It was purified by silica gel PLC (30% methylene chloride in hexane, 3 times and 40% methylene chloride in hexane, 2 times) to give pure 16a (0.9115 gm, 53.6%). -NMR(CCl_4): δ 1.1 (s, 6H, $(CH_3)_2C$-); 0.91-2.1 (m, 4H, methylene protons); 2.57-3.1 (m, 3H, -OH

and -CH_2SPh); 3.3-3.77 (m, 1H, -CHO-); 3.5 (s, 3H, -OCH_3); 6.93-7.73 (m, 5H, aromatic protons).

A solution of pure 16a (1.7535 gm, 6.2 mmol) in 60 ml of methylene chloride was cooled to -78°C, and a solution of 90% m-chloroperbenzoic acid (1.1804 gm, 6.2 mmol) in 30 ml methylene chloride was added dropwise from dropping funnel. Upon completion of the addition, the reaction was monitored by TLC analysis until it had been completed. The cold reaction mixture was then poured into a seporatory funnel containing 50 ml of ethyl acetate and 50 ml of saturated aqueous sodium bicarbonate solution. The organic layer was separated, extracted with ethyl acetate, washed with saturated $Na_2S_2O_3$ solution, saturated aqueous $NaHCO_3$ solution, H_2O, brine and dried over anhydrous $MgSO_4$, filtered and evaporated to give a crude yellow liquid (1.6891 gm). Purification by silica gel PLC (70% ethyl acetate in hexane) afforded 1.2526 gm of pure 18a as a white solid (68.07%), m.p.=77-78°C. -IR(nujol): 3320, 1745, 1255, 1130, 1025, 995 cm^{-1}. -NMR($CDCl_3$): δ1.13 (s, 6H, $(CH_3)_2C$-); 1.27-2.23 (m, 4H, methylene protons); 2.85 (br.t, J≅7 Hz, 2H, -CH_2SOPh); 3.23-3.77 (m, 2H, -CHO- and -OH); 3.63 (s, 3H, -OCH_3); 7.2-7.7 (m, 5H, aromatic protons). -MS:m/e(%) = 300(M^++2, 26.09), 280(5.75), 197(13.33), 173(14.49), 141(31.88), 126(17.38), 113(100), 102(34.78), 95(60.87), 87(16.38), 85(16.38), 78(42.03), 77(34.78), 69(33.33), 59(21.30), 55(21.01).

Methyl 3-hydroxy-2-methyl-2-phenyl-5-phenylsulfinylhexanoate (18b).

A reaction of LDA (8 mmol) in THF (8 ml), methyl methyl-

phenylacetate (1.2770 gm, 7.7 mmol) in THF (4 ml) and a THF (4 ml) solution of 4-phenylsulfenylbutanal (1.1425 gm, 6.3 mmol) gave a crude orange liquid of methyl 3-hydroxy-2-methyl-2-phenyl-5-phenylsulfenyl-hexanoate (16b) (2.0289 gm). Purification by silica gel PLC (30% chloroform in hexane and 40% chloroform in hexane, 2 times) afforded a pure orange liquid of 16b (1.2153 gm, 55.2%). -IR(neat): 1710, 1435, 1245, 1060, 740, 700 cm^{-1}. -NMR(CCl_4): δ 0.9-2.0 (m, 4H, methylene protons); 1.51 and 1.55 (2xs, 3H, CH_3C-); 2.53-3.03 (m, 3H, -CH_2SPh and -OH); 3.58 and 3.61 (2xs, 3H, -OCH_3); 3.83-4.33 (m, 1H, -CHO-); 6.93-7.47 (m, 10H, aromatic protons). -MS: m/e(%) = 344(M^+, 24.39), 326(8.54), 182(18.70), 181(100), 164(73.98), 132(56.91), 123 (18.70), 110(36.59), 109(9.76), 105(17.07), 104(14.63), 103(12.60), 77(10.98), 71(60.16), 55(25.20).

A solution of pure 16b (1.1114 gm, 3.2 mmol) in 40 ml of methylene chloride was treated with a solution of 90% m-chloroperbenzoic acid (0.6107 gm, 3.2 mmol) in 30 ml of methylene chloride gave a crude yellow liquid (1.0184 gm). Purification by silica gel PLC (60% ethyl acetate in hexane) afforded a pure yellow liquid of 18b (0.7613 gm, 66.1%) as viscous liquid. -IR(neat): 3380, 1720, 1440, 1240, 1080, 1030, 750, 700 cm^{-1}. -NMR($CDCl_3$): δ 0.6-2.07 (m, 4H, methylene protons); 1.57 (s, 3H, CH_3C-); 2.37-3.03 (m, 3H, -CH_2SOPh and -OH); 3.63 and 3.67 (2xs, 3H, -OCH_3); 3.83-4.4 (m, 1H, -CHO-); 7.03-7.37 (m, 5H, PhC-); 7.37-7.7 (m, 5H, PhSO-). -MS: m/e(%) = 360(M^+, 48.16), 352(24.76), 235(22.20), 197(100), 181(24.59), 175(87.50), 164(47.30), 157(31.25), 132(54.17), 126(20.15), 105(49.18), 104(27.32), 103(31.76), 91(22.20),

78(33.47), 77(27.15), 71(37.23).

Methyl α-(1-hydroxy-4-phenylsulfinylbutyl)cyclohexanecarboxylate (18c)

A reaction of LDA (8 mmol) in THF (8 ml), methyl cyclohexanecarboxylate (1.1241 gm, 7.9 mmol) in THF (4 ml) and a THF (4 ml) solution of 4-phenylsulfenylbutanal (1.1069 gm, 6.1 mmol) gave a crude orange liquid of methyl α-(1-hydroxy-4-phenylsulfenylbutyl)cyclohexanecarboxylate (16c) (1.946 gm). Purification by silica gel PLC (40% chloroform in hexane, 3 times) afforded a pure orange liquid of 16c (1.0505 gm, 54.4%). -IR(neat): 3480, 1730, 1590, 1460, 1140, 740, 695 cm^{-1}. -NMR(CCl_4):δ 0.71-2.38 (m, 15H, methylene protons and -OH); 2.58-3.05 (br.t, J≅7 Hz, 2H, $-CH_2SPh$); 3.05-3.78 (m, 1H, -CHO); 3.65 (s, 3H, $-OCH_3$); 6.91-7.38 (m, 5H, aromatic protons). -MS: m/e(%) = 322(M^+, 100), 305(25.72), 291(31.67), 245(17.36), 182(29.74), 181(59.26), 163(16.72), 153(41.80), 142(62.95), 136(28.94), 135(16.40), 121(43.09), 110(46.30), 109(14.15), 81(13.67), 77(9.65), 73(11.9), 71(42.44), 55 (28.94).

A solution of pure 16c (0.9961 gm, 3.1 mmol) in 40 ml of methylene chloride was treated with a solution of 90% m-chloroperbenzoic acid (0.5683 gm, 3.1 mmol) in 30 ml of methylene chloride gave a crude yellow liquid (1.0181 gm). Purification by silica gel PLC (60% ethyl acetate in hexane) afforded a pure yellow liquid of 18c (0.730 gm, 69.67%) as viscous liquid. -IR(neat): 3380, 1740, 1470, 1235, 1050, 760, 700 cm^{-1}. -NMR($CDCl_3$):δ 0.9-2.67 (m, 15H, methylene protons and -OH); 2.83 (br.t, J≅7 Hz, 2H, $-CH_2SOPh$); 3.17-3.57 (m, 1H, -CHO-);

3.7 (s, 3H, $-OCH_3$); 7.33-7.8 (m, 5H, aromatic protons). -MS: m/e(%) = 338(M^+, 4.27), 322(3.96), 213(6.02), 197(21.22), 181(17.42), 153(69.70), 135(17.1), 126(12.03), 109(8.87), 93(15.20), 79(8.55), 78(11.72), 77 (7.92), 71(100), 67(16.15), 55(9.02).

Methyl 3-hydroxy-2-methyl-5-phenylsulfinyl-2-propylhexanoate (18d)

A reaction of LDA (8 mmol) in THF (8 ml), methyl 2-methyl-pentanoate (0.8472 gm, 6.5 mmol) in THF (4 ml) and a THF (4 ml) solution of 4-phenylsulfenylbutanal (1.0239 gm, 5.6 mmol) gave a crude oragne liquid of methyl 3-hydroxy-2-methyl-5-phenylsulfenyl-2-propylhexanoate (16d) (1.5918 gm). Purification by silica ge PLC (40% chloroform in hexane, 3 times) afforded a pure orange liquid of 16d (1.0475 gm, 60.34%) as viscous liquid. -IR(neat): 3500, 1720, 1590, 1440, 1230, 1150, 740, 690 cm^{-1}. -NMR(CCl_4): δ1.07 (s, 3H, $CH_3\overset{|}{C}$-); 0.63-2.13 (m, 11H, CH_3CH_2- and methylene protons); 2.13-2.6 (broad, 1H, -OH); 2.9 (t, J=6 Hz, $-CH_2SPh$); 3.33-3.77 (m, 1H, -CHO); 3.51 and 3.53 (2xs, 3H, $-OCH_3$); 6.93-7.4 (m, 5H, aromatic protons). -MS: m/e(%) = 310(M^+, 52.0), 294(6.11), 279(7.58), 250(5.05), 233(3.58), 201(6.32), 181 (42.02), 169(16.21), 163(17.47), 141(48.0), 136(32.0), 130(36.0), 123 (32.0), 110(28.0), 109(14.32), 101(70.11), 98(8.42), 81(8.0), 77(10.95), 71(100), 69(27.79), 66(8.0), 65(9.05), 59(9.26), 55(13.47).

A solution of pure 16d (0.9812 gm, 3.16 mmol) in 40 ml of methylene chloride was treated with a solution of 90% m-chloroperbenzoic acid (0.6076 gm, 3.16 mmol) in 30 ml of methylene chloride gave a crude orange liquid (0.9218 gm). Purification by silica gel PLC (65% ethyl

acetate in hexane) afforded a pure yellow liquid of 18d (0.7967 gm, 77.37%) as viscous liquid. -IR(neat): 3380, 1720, 1440, 1220, 1090, 1030, 750, 690 cm^{-1}. -NMR(CCl_4): δ0.63-2.2 (m, 11H, CH_3CH_2- and methylene protons); 1.03 and 1.07 (2xs, 3H, $CH_3\overset{|}{C}$-); 2.7 (br.t, J≅7 Hz, 2H, -CH_2SOPh); 3.43-3.8 (m, 1H, -CHO-); 3.6 and 3.63 (2xs, 3H, -OCH_3); 3.8-4.1 (broad, 1H, -OH); 7.3-7.8 (m, 5H, aromatic protons). -MS: m/e(%) = 326(M^+, 100), 308(8.98), 201(8.28), 197(12.24), 183(4.9), 169(9.33), 141(35.07), 126(7.0), 125(8.75), 123(8.57), 109(5.25), 101(10.73), 97(5.83), 81(6.41), 78(7.17), 77(7.35), 71(37.31), 69(10.49), 59(6.65), 55(6.53).

Methyl 2,2-dipropyl-3-hydroxy-5-phenylsulfinylhexanoate (18e)

A reaction of LDA (8 mmol) in THF (8 ml), methyl 2-propyl-pentanoate (1.2805 gm, 8.1 mmol) in THF (4 ml) and a THF (4 ml) solution of 4-phenylsulfenylbutanal (1.0689 gm, 5.9 mmol) gave a crude yellow liquid of methyl 2,2-dipropyl-3-hydroxy-5-phenylsulfenylhexanoate (16c) (2.0917 gm). Purification by silica gel PLC (40% chloroform in hexane, 2 times) afforded a pure yellow liquid of 16e (1.2612 gm, 63.4%). -IR (neat): 3500, 1710, 1590, 1430, 1210, 1130, 740, 690 cm^{-1}. -NMR(CCl_4): δ 0.6-1.7 (m) and 1.7-2.13 (m) (m, 18H, methyl protons and methylene protons); 2.53-3.1 (m, 3H, -CH_2SPh and -OH); 3.37-3.87 (m, 1H, -CHO-); 3.63 (s, 3H, -OCH_3); 6.93-7.4 (m, 5H, aromatic protons). -MS: m/e(%) = 338(M^+, 43.63), 321(5.77), 307(7.39), 197(6.23), 181(59.09), 169(37.40), 163 (8.31), 158(45.71), 136(30.47), 129(100), 123(22.16), 110(21.01), 109 (17.31), 97(17.08), 95(8.77), 77(6.92), 73(9.00), 71(93.17), 69(18.93), 59(9.23), 57(9.70), 55(18.47).

A solution of pure 16e (1.0956 gm, 3.2 mmol) in 40 ml of methylene chloride was treated with a solution of 90% m-chloroperbenzoic acid (0.6098 gm, 3.2 mmol) in 30 ml of methylene chloride gave a crude yellow liquid (1.1018 gm). Purification by silica gel PLC (60% ethyl acetate in hexane) afforded a pure yellow liquid of 18e (0.9596 gm, 84.71%) as viscous liquid. -IR(neat): 3300, 1720, 1440, 1210, 1140, 1020, 750, 690 cm^{-1}. -NMR(CCl_4): δ 0.57-2.13 (m, 18H, $(CH_3)_2C$- and methylene protons); 2.81 (br.t, J≅7 Hz, 2H, $-CH_2SOPh$); 3.2-3.87 (m, 2H, -CHO- and -OH); 3.63 (s, 3H, $-OCH_3$); 7.27-7.77 (m, 5H, aromatic protons). -MS: m/e(%) = 354(M^+, 82.67), 336(9.67), 229(7.67), 197(42.67), 169 (70.0), 151(8.67), 129(15.33), 126(11.67), 109(11.67), 96(11.33), 95 (10.67), 78(11.33), 77(7.67), 71(100), 69(24.0), 59(21.33), 57(31.33), 55(51.33).

Preparation of 6,6-Dialkyl-5-hydroxy-2-phenylsulfinylcyclohexanones (20).

General Procedure:

6,6-Dimethyl-5-hydroxy-2-phenylsulfinylcyclohexanone (20a)

n-BuLi (5.25 ml, 7.83 mmol) was added to a cooled (-78°C) THF (14 ml) solution of diisopropylamine (1.11 ml, 7.83 mmol) under an argon atmosphere. The resulting mixture was stirred at -78°C for 15 min, then stirred at 0°C for 10 min and cooled again at -78°C at which was added dropwise a THF (4 ml) solution of pure sulfoxide 18a (0.5203 gm, 1.74 mmol) during which a yellow colour was developed. After being stirred at -78°C for 1 h and at 0°C for 1.5 h, the resulting yellow

solution was quenched with saturated aqueous NH_4Cl and extracted ethyl acetate. The combined extracts were washed with saturated aqueous NH_4Cl, H_2O, brine and dried over anhydrous $MgSO_4$, filtered and evaporated to dryness to give a crude yellow foam (0.4037 gm, 87.7%). Purification by silica gel PLC (60% ethyl acetate in hexane) afforded a pure white foam of 20a (0.3211 gm, 69.8%). -IR($CHCl_3$): 3400, 1730, 1410, 1100, 1040, 1020, cm^{-1}. -NMR($CDCl_3$): δ 0.9-1.43 (m, 6H, $(CH_3)_2C$-); 1.43-2.23 (m, 4H, methylene protons); 3.2-4.3 (m, 3H, -CHSOPh, -CHO- and -OH); 7.3-7.8 (m, 5H, aromatic protons). -MS: m/e(%) = 250(M^+-0, 10.56), 234(3.64), 218(9.86), 186(15.49), 154(2.82), 141 (16.67), 125(100), 110(28.57), 109(61.90), 97(33.33), 78(14.28), 77 (60.72), 65(23.80).

5-Hydroxy-6-methyl-6-phenyl-2-phenylsulfinylcyclohexanone (20b)

A reaction of LDA (8.2 mmol) in THF (14 ml) and a THF (4 ml) solution of pure sulfoxide 18b (0.6560 gm, 1.82 mmol) gave a crude yellow foam (0.5539 gm). Purification by silica gel PLC (60% ethyl acetate in hexane) afforded a pure white foam of 20b (0.3608 gm, 60.43%). -IR($CHCl_3$): 3360, 1720, 1450, 1250, 1030 cm^{-1}. -NMR($CDCl_3$): δ 1.27- -1.73 (m, 3H, CH_3C-); 1.73-2.67 (m, 4H, methylene protons); 3.4-4.3 (m, 2H, -CHO- and -CHSOPh); 4.6-4.87 (m, 1H, -OH); 6.83-7.87 (m, 10H, aromatic protons). -MS: m/e(%) = 325(M^+-3, 2.47), 309(12.36), 218 (11.12), 202(20.18), 185(14.42), 157(9.47), 135(11.12), 134(100), 131 (16.27), 126(15.65), 125(27.80), 110(15.24), 109(23.06), 105(44.89), 97(24.71), 91(22.86), 78(30.89), 77(31.51), 69(9.47), 65(15.65), 51 (15.44).

1-Oxo-3-hydroxy-2-phenylsulfinyl-spiro [5,5] undecane (20c).

A reaction of LDA (8.46 mmol) in THF (14 ml) and a THF (4 ml) solution of pure sulfoxide 18c (0.6373 gm, 1.88 mmol) gave a crude yellow foam (0.5156 gm). Purification by silica gel PLC (60% ethyl acetate in hexane) afforded a pure white foam of 20c (0.4535 gm, 79.56%). -IR($CHCl_3$): 3370, 1710, 1450, 1025 cm^{-1}. -NMR($CDCl_3$): δ 0.53-3.17 (m, 15H, -OH and methylene protons); 3.17-4.2 (m, 2H, -CHO- and -CHSOPh); 7.3-7.87 (m, 5H, aromatic protons). -MS: m/e(%) = 306(M^+, 6.9), 235 (32.86), 218(32.62), 186(10.0), 181(19.52), 163(100), 136(47.62), 125 (71.43), 111(26.19), 109(52.38), 97(30.59), 81(30.95), 77(15.71), 69 (33.33), 67(30.95), 65(59.52), 55(45.24), 53(52.38).

5-Hydroxy-6-methyl-6-propyl-2-phenylsulfinylcyclohexanone (20d)

A reaction of LDA (8.1 mmol) in THF (12 ml) and a THF (4 ml) solution of pure sulfoxide 18d (0.5030 gm, 1.62 mmol) gave a crude yellow liquid (0.4082 gm). Purification by silica gel PLC (60% ethyl acetate in hexane) afforded a pure yellow liquid of 20d (0.3389 gm, 71.19%). -IR(nujol): 3350, 1690, 1440, 1240, 1080, 1020, 740, 690 cm^{-1}. -NMR($CDCl_3$): δ 0.53-2.3 (m, 14H, methyl protons and methylene protons); 3.0-4.0 (m, 3H, -OH, -CHO- and -CHSOPh); 7.1-7.8 (m, 5H, aromatic protons). -MS: m/e(%) = 295(M^++1, 0.31), 278(0.59), 218(0.47), 186 (0.69), 169(6.55), 151(2.24), 126(87.93), 111(28.45), 109(44.83), 100 (24.14), 97(34.48), 78(100), 77(56.89), 69(91.38), 65(51.72), 55(63.79).

6,6-Dipropyl-5-hydroxy-2-phenylsulfinylcyclohexanone (20e).

A reaction of LDA (12 mmol) in THF (20 ml) and a THF (5 ml) solution of pure sulfoxide 18e (0.8752 gm, 2.47 mmol) gave a crude orange liquid (0.6800 gm). Purification by silica gel PLC (60% ethyl acetate in hexane) afforded a pure yellow liquid of 20e (0.5992 gm, 75.4%). -IR(nujol): 3350, 1690, 1240, 1020, 740, 690 cm^{-1}. -NMR ($CDCl_3$):δ 0.5-2.73 (m, 18H, methyl protons) and methylene protons); 3.03-3.43 (br.s, 1H, -OH); 3.43-4.2 (m, 2H, -CHO- and -CHSOPh); 7.2-7.83 (m, 5H, aromatic protons). -MS: m/e(%) = 323(M^++1, 3.17), 306(6.67), 197(46.67), 179(17.78), 154(56.51), 126(67.94), 125(65.40), 111(100), 109(73.02), 99(76.82), 97(58.41), 95(33.02), 85(14.60), 83 (24.76), 82(34.28), 78(95.87), 77(68.57), 71(78.73), 69(68.25), 65 (52.70), 57(60.32), 55(79.36).

Preparation of 6,6-Dialkyl-5-hydroxy-2-cyclohexenones (22).

General Procedure:

6,6-Dimethyl-5-hydroxy-2-cyclohexenone (22a)

The pure ketone 20a (0.1934 gm, 0.727 mmol) was heated in a round-bottomed flask connected with a condenser under reduced pressure (at 100-120°C, 0.2 mmHg) for 1 h. The crude brown liquid was purified by silica gel PLC (chloroform) to give a pure brown liquid of 22a (0.0860 gm, 84.45%). -IR(neat): 3400, 1670, 1400, 1060, 820 cm^{-1}. -NMR(CCl_4):δ 1.0 and 1.07 (2xs,2x3H, methyl protons); 2.23-2.63 (m, 2H, $-CH_2CHO-$); 3.0-3.33 (br.s, 1H, -OH); 3.47-3.93 (m, 1H, -CHO-); 5.83 (dt, J=10,2 Hz, 1H, -CH=CHCO-); 6.71 (dt, J=10,4 Hz, 1H, -CH=CHCO-). -MS: m/e(%) = 140(M^+, 25.82), 123(7.79), 122(7.79), 97(54.51),

79(23.36), 72(100), 69(41.39), 68(50.0), 57(77.26).

5-Hydroxy-6-methyl-6-phenyl-2-cyclohexenone (22b)

The pure ketone 20b (0.1800 gm, 0.548 mmol) was pyrolysed at 120°C under reduced pressure (0.1 mmHg) for 2 h. The crude brown liquid was purified by silica gel PLC (20% ethyl acetate in hexane, 3 times) to give two pure stereoisomers 22b (A) and 22b (B) (0.0877 gm, 79.29%, 22b (A): 22b (B) = 3:5).

22b (A)(as brown liquid): -IR(neat): 3420, 1665, 1390, 1250, 700 cm^{-1}. -NMR(CCl_4): δ1.47 (s, 3H, CH_3C-); 2.1-2.5 (m, 2H, methylene protons); 2.63-3.03 (m, 1H, -OH); 2.67-4.07 (m, 1H, -CHO-); 6.07 (br.d, J≅5 Hz, 1H, -CH=CHCO-); 6.53-6.93 (m, 1H, -CH=CHCO-); 6.93-7.43 (m, 5H, aromatic protons).

22b (B)(as brown solid, m.p.=98-100°C): -IR(nujol): 3500, 3420, 1670, 1320, 1210, 905, 705 cm^{-1}. -NMR(CCl_4): δ 1.37 (s, 3H, CH_3C-); 2.2-2.53 (m, 2H, methylene protons); 2.87-3.2 (br.s, 1H, OH); 4.31 (t, J=5 Hz, 1H, -CHO-); 5.97 (br.d, J≅10 Hz, 1H, -CH=CHCO-); 6.57 (dt, J=10,4 Hz, 1H, -CH=CHCO-); 7.0-7.5 (m, 5H, aromatic protons).

-MS: m/e(%) = 202(M^+, 30.44), 184(7.33), 134(100), 105(17.77), 97(8.44), 78(4.22), 77(5.33).

5-Hydroxy-1-oxo-spiro [5,5] undec-3-ene (22c)

The pure ketone 20c (0.2251 gm, 0.7 mmol) was pyrolyzed at 100-120°C under reduced pressure (0.1 mmHg) for 3.5 h. The crude brown liquid was purified by silica gel PLC (chloroform) to give a pure yellow solid of 22c (0.0893 gm, 70.9%), m.p.=70-71°C. -IR

(nujol): 3360, 1650, 1300, 940 cm^{-1}. -NMR($CDCl_3$): δ 1.13-1.93 (m, 8H, methylene protons); 1.93-2.4 (br.s, 1H, -OH); 2.4-2.73 (m, 2H, $-CH_2CHO-$); 4.13 (br.t, J≅4 Hz, 1H, -CHO-); 5.88 (dt, J=10,2 Hz, 1H, -CH=CHCO-); 6.47-6.8 (m, 1H, -CH=CHCO-). -MS: m/e(%) = 180(M^+, 43.15), 162(43.15), 136(87.98), 111(100), 97(56.26), 95(45.69), 81 (67.98), 68(36.38), 67(43.99), 55(40.19).

5-Hydroxy-6-methyl-6-propyl-2-cyclohexenone (22d)

The pure ketone 22d (0.1313 gm, 0.45 mmol) was pyrolyzed at 120°C under reduced pressure (0.03 mmHg) for 1.5 h. The crude brown liquid was purified by silica gel PLC (chloroform) to give a pure yellow liquid of 22d (0.0574 gm, 75.9%). -IR(neat): 3425, 1660, 1450, 1380, 1050 cm^{-1}. -NMR(CCl_4): δ 0.6-2.83 (m, 7H, $-CH_2-CH_2CH_3$); 2.33-2.67 (m, 2H, -CHCHO-); 3.27-3.67 (broad, 1H, -OH); 3.67-4.17 (m, 1H, -CHO-); 5.83 (br.d, J≅10 Hz, 1H, -CH=CHCO-); 6.7 (dt, J=10,4 Hz, -CH=CHCO-). -MS: m/e(%) = 169(M^++1, 9.83), 126 (59.32), 111(32.20), 100(33.90), 97(26.27), 71(100), 69(37.29), 68 (20.34), 58(33.9).

6,6-Dipropyl-5-hydroxy-2-cyclohexenone (22e).

The pure ketone 20e (0.2581 gm, 0.8 mmol) was pyrolyzed at 110°C under reduced pressure (0.03 mmHg) for 2 h. The crude brown liquid was purified by silica gel PLC (chloroform) to give a pure yellow liquid of 22e (0.1127 gm, 71.87%). -IR(neat): 3425, 1650, 1450, 1380, 1220, 1055 cm^{-1}. -NMR(CCl_4): δ 0.55-1.95 (m, 14H, $(CH_3CH_2CH_2)_2C-$);

2.35-2.65 (m, 2H, -$\underline{CH_2}$CHO-); 2.65-3.35 (broad, 1H, -$\underline{OH}$; 4.07 (br.t, J≅6 Hz, 1H, -$\underline{CH}$O-); 5.8 (dt, J=11,1.5 Hz, 1H, -CH=$\underline{CH}$CO-); 6.65 (dt, J=11, 4 Hz, 1H, -$\underline{CH}$=CHCO-). -MS: m/e(%) = 197(M^++1, 92.98), 179(17.89), 154(42.10), 111(100), 99(40.35), 97(19.29), 81(15.09), 71(35.09), 69(26.31), 55(19.28),

Preparation of *N*-methyl-*N*-phenyl-2-alkyl-3-hydroxy-6-phenylsulfinyl-hexanamides (19).

General Procedure:

N-methyl-*N*-phenyl-3-hydroxy-2-methyl-6-phenylsulfinylhexanamide (19a).

n-BuLi (8.32 ml, 13 mmol) was added to a cooled (-78°C) THF (18 ml) solution of diisopropylamine (1.84 ml, 13 mmol) under an argon atmosphere. The resulting mixture was stirred at -78°C for 15 min and at 0°C for 10 min, to which was added a THF (4 ml) solution of *N*--methyl-*N*-phenylpropanamide (2.1293 gm, 13 mmol). After stirring at 0°C for 1 h, a THF (3 ml) solution of 4-phenylsulfenylbutanal was added at -78°C and stirred at -78°C for 1.5 h. The resulting yellow solution was quenched with saturated aqueous NH_4Cl and extracted with ethyl acetate. The combined extracts were washed with saturated aqueous NH_4Cl, H_2O, brine and dried over anhydrous $MgSO_4$. Filtration to dryness afforded a crude brown liquid (3.7418 gm, quantitative yield). It was purified by column chromatography (20% chloroform in hexane, 25%, 30% and 35%) to give a pure yellow liquid of *N*-methyl-*N*-phenyl-3-hydroxy--2-methyl-6-phenylsulfenylhexanamide (17a)(2.4865 gm, 72.5%). -IR(neat): 3420, 1630, 1590, 1500, 1390, 740, 700 cm^{-1}. NMR(CCl_4):δ 1.05(d, J=6

Hz, 3H, -CHC$\underline{H}_3$); 1.2-2.03 (m, 4H, methylene protons); 2.03-2.6 (m, 1H, -C$\underline{H}$CO-); 2.9 (br.t, J≅7 Hz, 2H, -C$\underline{H}_2$SPh); 3.21 (s) and 2.13-3.67 (m) (s, 3H, -NC$\underline{H}_3$ and m, 1H, -C$\underline{H}$O-); 4.17-4.43 (br.s, 1H, -O$\underline{H}$); 6.97-7.67 (m, 10H, aromatic protons).

A solution of pure $\underline{\underline{\underline{17a}}}$(2.4865 gm, 7.2 mmol) in 60 ml of methylene chloride was cooled to -78°C, and a solution of 90% m-chloroperbenzoic acid (1.3480 gm, 7.2 mmol) in 40 ml of methylene chloride was added from dropping funnel. Upon completion of the addition, the reaction monitored by TLC until it had been completed. The cold reaction mixture was then poured into a seporatory funnel containing 80 ml of ethyl acetate and 80 ml of saturated aqueous sodium bicarbonate solution. The organic layer was separated, extracted with ethyl acetate, washed with saturated $Na_2S_2O_3$, saturated $NaHCO_3$, H_2O, brine and dried over anhydrous $MgSO_4$, filtered and evaporated to give a crude yellow liquid of $\underline{\underline{\underline{19a}}}$ (2.1619 gm, 83.79%). -NMR($CDCl_3$): δ 0.8-1.97 (m, 7H, C$\underline{H}_3$-C- and methylene protons); 2.13-2.53 (m, 2H, -C$\underline{H}$CO- and -O$\underline{H}$); 2.53-3.03 (m, 2H, -C$\underline{H}_2$SOPh); 3.23 (s, 3H, -NC$\underline{H}_3$); 2.53-4.0 (m, 1H, -C$\underline{H}$O-); 6.9-7.7 (m, 10H, aromatic protons).

N-methyl-*N*-phenyl-2-ethyl-3-hydroxy-6-phenylsulfinylhexanamide ($\underline{\underline{\underline{19b}}}$)

A reaction of LDA (10.5 mmol) in THF (15 ml), *N*-methyl-*N*-phenylbutanamide (1.7985 gm, 10.16 mmol) in THF (5 ml) and a THF (5 ml) solution of 4-phenylsulfenylbutanal (1.6900 gm, 9.38 mmol) gave a crude yellow liquid of *N*-methyl-*N*-phenyl-2-ethyl-3-hydroxy-6-phenylsulfenylhexanamide ($\underline{\underline{\underline{17b}}}$)(3.2746 gm). It was purified by column chromatography

(SiO_2, 15% chloroform in Hexane, 20%, 25%, 30% and 35%) to give a pure yellow liquid of 17b (2.2578 gm, 67.4%). -IR(neat): 3400, 1640, 1590, 1490, 1430, 1390, 1270, 1110, 730, 700 cm^{-1}. -NMR(CCl_4):δ0.88 (t, J=7 Hz, 3H, $-CCH_3$); 1.1-1.98 (m, 6H, methylene protons); 1.97-2.4 (m, 1H, -CHCO-); 2.8-3.07 (m, 2H, $-CH_2SPh$); 3.2 (s) and 3.2-3.9 (m) (s, 3H, $-NCH_3$ and m, 2H, -CHO- and -OH); 6.97-7.5 (m, 10H, aromatic protons).

A solution of pure 17b (1.2511 gm, 3.5 mmol) in 40 ml of methylene chloride was treated with a solution of 90% m-chloroperbenzoic acid (0.628 gm, 3.5 mmol) in 30 ml of methylene chloride gave a crude yellow liquid of 19b (1.1727 gm, 90.2%). Purification by silica gel PLC (70% ethyl acetate in hexane, 2 times) afforded a pure yellow liquid 19b (0.9872 gm, 75,9%). -IR(neat): 3420, 1680, 1600, 1500, 1455, 1290, 1040, 700 cm^{-1}. -NMR($CDCl_3/CCl_4$): δ 0.57-1.03 and 1.23-2.0 (m, 9H, $-CCH_3$ and methylene protons); 2.0-2.5 (m, 1H, -CHCO-); 2.57-3.0 (m, 2H, $-CH_2SOPh$); 3.27 (s) and 3.0-3.93 (m) (s, 3H, $-NCH_3$ and m, 2H, -CHO- and -OH); 7.0-7.7 (m, 10H, aromatic protons).

Attempted preparation of 6-alkyl-5-hydroxy-2-phenylsulfinylcyclohexanone (21).

General Procedure:

Attempted preparation of 5-hydroxy-6-methyl-2-phenylsulfinylcyclohexanone (21a).

n-BuLi (8.04 ml, 12 mmol) was added to a cooled (-78°C) THF (8 ml) solution of diisopropylamine (1.7 ml, 12 mmol) under an argon

atmosphere. The resulting mixture was stirred at -78°C for 15 min, then stirred at 0°C for 10 min and cooled again at -78°C at which was added dropwise a THF (4 ml) solution of crude sulfoxide 19a (0.5458 gm, 1.5 mmol). After being stirred at -78°C to room temperature overnight, the resulting green solution was quenched with 0.5 N HCl. The reaction mixture was then poured into a seporatory funnel and then acidified by 0.5 N HCl to pH 5, extracted with ethyl acetate, washed with 0.5 N HCl, H_2O, brine and dried over anhydrous $MgSO_4$. Filtration followed by evaporation to dryness afforded a crude orange liquid (0.2536 gm). The crude product (0.2536 gm, 1 mmol) in CCl_4 (2 ml) was refluxed under an argon atmosphere for 5 h. The crude brown liquid was evaporated to dryness and diluted with ether, basified with 10% aqueous NaOH, then the aqueous layer was acidified by 6 N HCl and extracted with ether. The combined extracts were washed with H_2O, brine, and dried over anhydrous $MgSO_4$. Filtration followed by evaporation to dryness afforded a crude brown liquid of 23a (0.0466 gm, 43.15%). -NMR($CDCl_3$): δ2.13 (s, 3H, $-CH_3$); 4.3-5.13 (broad, 1H, -OH); 6.5-7.63 (m, 4H, aromatic protons).

Attempted preparation of 6-ethyl-5-hydroxy-2-phenylsulfinylcyclohexanone (21b).

A reaction of LDA (6.15 mmol) in THF (6 ml) and a THF (3 ml) solution of a pure sulfoxide 19b (0.4607 gm, 1.23 mmol) gave a crude brown liquid (0.3376 gm). The crude product (0.3132 gm, 1.17 mmol) in CCl_4 (1.5 ml) was refluxed under an argon atmosphere for 4 h. p-Toluenesulfonic acid was then added and refluxed for 3 h. The

crude product was evaporated to dryness and diluted with $CHCl_3$, basified with 8% aqueous NaOH, then the aqueous layer was acidified by 6 N HCl and extracted with $CHCl_3$. The combined extracts were washed with H_2O, brine and dried over anhydrous $MgSO_4$. Filtration followed by evaporation to dryness afforded a crude brown liquid of 23b (0.063 gm, 44.37%). -NMR($CDCl_3$): δ 1.17 (br.t, J≅8 Hz, 3H, $-CCH_3$); 2.58 (br.q, J≅8 Hz, 2H $-CH_2CH_3$); 3.57-5.1 (broad, 1H, -OH); 6.27-7.63 (m, 4H, aromatic protons).

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