A New 4C + 2C Annelation Reaction Based on Tandem Michael-Claisen Condensation. 1. General Scope

Tak Hang Chan* and C. V. C. Prasad

Department of Chemistry, McGill University, Montreal, Quebec, Canada H3A 2K6

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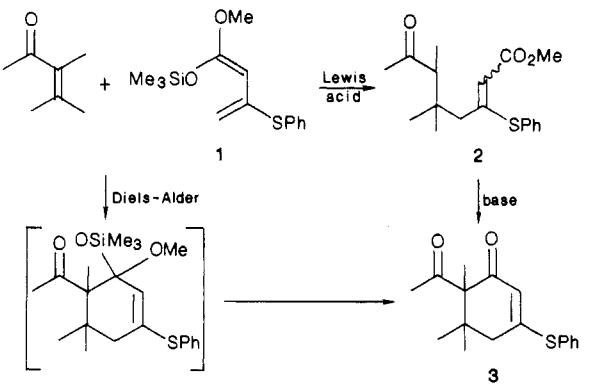
A new 4C + 2C annelation reaction based on the propensity of 3-(phenylthio)-1-(trimethylsiloxy)-1-methoxy-1,3-butadiene to undergo Michael reaction with α,β-unsaturated ketones under Lewis acid catalyzed conditions has been developed. The Michael adducts in turn were cyclized either with potassium *tert*-butoxide or with lithium thiophenoxide. Further, the tandem Michael–Claisen annelation reaction can be controlled to give either the cis- or trans-fused 9-methyldecalin system with three carbonyl groups that are differently masked. The chemoselective transformations of the three carbonyl groups are described.

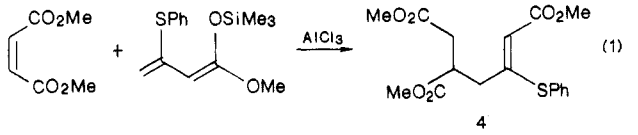
Reactions leading to the formation of six-membered rings are of great importance in organic synthesis.[1] The Diels–Alder reaction and the Robinson annelation have served remarkably well for this purpose, but they are not without limitations. In the Diels–Alder reaction, both the diene and dienophile components must be appropriately activated.[2] For example, cyclohexenone undergoes cycloaddition with most dienes readily, whereas 2- or 3-substituted cyclohexenones react sluggishly or not at all.[3] The Robinson annelation is essentially a two carbon plus four carbon (2C + 4C) tandem Michael–aldol condensation. The reaction is critically dependent on the ability of the two-carbon fragment to act as Michael donor and the four-carbon fragment to be Michael acceptor under the basic reaction conditions. Various modifications of the Robinson annelation reaction have been introduced to address these problems.[4] We report here a new 2C + 4C annelation reaction based on tandem Michael–Claisen condensation. It is based on the fact that 3-(phenylthio)-1-(trimethylsiloxy)-1-methoxy-1,3-butadiene (**1**)[5] behaves as a remarkably facile Michael donor in its reactions with α,β-unsaturated carbonyl compounds under Lewis acid catalyzed conditions to give the adduct **2**. An intramolecular Claisen condensation of **2** under basic conditions gives the annelated product **3**. The reaction thus differs from the classical Robinson annelation in that the Michael reaction is carried out under acidic conditions. Furthermore, the Michael acceptor α,β-unsaturated ketone serves as the two-carbon component in this reaction, and the Michael donor serves as the four-carbon component. In a formal way, it is equivalent to the Diels–Alder reaction of the diene **1** with the α,β-unsaturated carbonyl compound (Scheme I). It offers certain advantages over the Diels–Alder reaction, however, in that the stereochemistry of the ring junction is amenable to control by this two-step sequence. Finally, the product **3** has three carbonyl groups that are differently masked and can be manipulated separately. It can serve as the entry point to an array of multifunctional targets.

Scheme I



Results and Discussion

1. Conjugative Addition Reactions of 3-(Phenylthio)-1-(trimethylsiloxy)-1-methoxy-1,3-butadiene. We have recently described the preparation and reactions of 3-(phenylthio)-1-(trimethylsiloxy)-1-methoxy-1,3-butadiene (**1**).[5] In a general study of its reactivity as a Diels–Alder diene, its reactions with a number of dienophiles were studied. While the reaction of **1** with dimethyl acetylenedicarboxylate did give the Diels–Alder adduct, its reaction with dimethyl maleate under thermal conditions gave no adducts at all. Under Lewis acid catalyzed conditions, **1** reacted with dimethyl maleate to give the Michael adduct **4** instead (eq 1). This preference of Michael

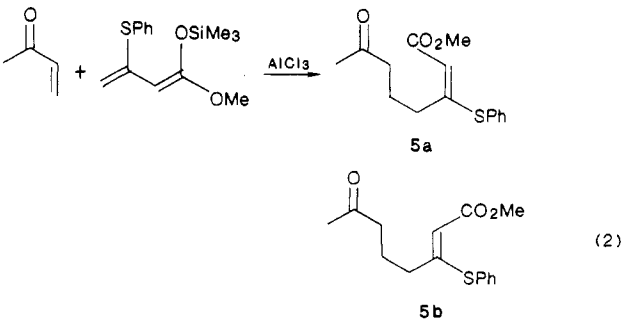


(1)

4

reaction over cycloaddition led us to examine the reaction of **1** with a number of α,β-unsaturated carbonyl compounds.

Indeed, **1** reacted with methyl vinyl ketone under $AlCl_3$-catalyzed conditions to give the *E* and *Z* isomers of **5** (eq 2). The diene also reacted with cyclohexenone under



(2)

(1) Jung, M. E. *Tetrahedron* **1976**, *32*, 3.
(2) Wollweber, H. *Diels–Alder Reakton*; Verlag: Stuttgart, 1972, and references therein.
(3) Das, J.; Kakushima, M.; Valenta, Z.; Jankowski, K.; Luce, R. *Can. J. Chem.* **1984**, *62*, 411.
(4) (a) Marshall, J. A.; Fanta, W. I. *J. Org. Chem.* **1964**, *29*, 2501. (b) Heathcock, C. H.; Ellis, J. E.; McMurry, J. E.; Coppolino, A. *Tetrahedron Lett.* **1971**, 4995. (c) Boeckmann, R. K. *J. Am. Chem. Soc.* **1973**, *95*, 6867; **1976**, *96*, 6179. (d) Stork, G.; Ganem, B. *Ibid.* **1973**, *95*, 6152. (e) Stork, G.; Singh, J. *Ibid.* **1974**, *96*, 6181. (f) Mander, L. N.; Hamilton, R. J. *Tetrahedron Lett.* **1981**, *22*, 4115. (g) Stork, G.; Danishefsky, S.; Ohasi, M. *J. Am. Chem. Soc.* **1967**, *89*, 5459. (h) Stork, G.; McMurry, J. E. *Ibid.* **1967**, *89*, 5463, 5464. (i) Ziegler, F. E.; Hwang, K.-J. *J. Org. Chem.* **1983**, *48*, 3349. (j) Huffman, J. W.; Potnis, S. M.; Satish, A. V. *J. Org. Chem.* **1985**, *50*, 4266.
(5) Chan, T. H.; Prasad, C. V. C. *J. Org. Chem.* **1986**, *51*, 3012.

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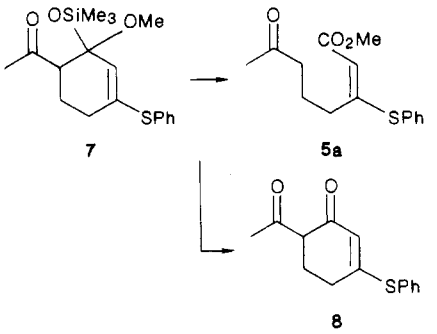
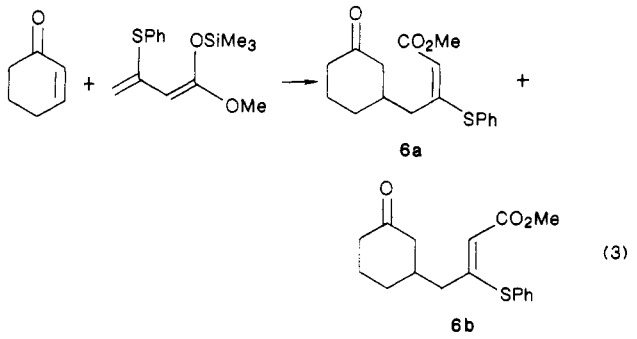
Scheme II



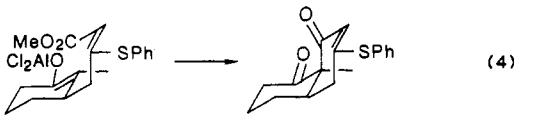
$TiCl_4$–$Ti(O\text{-}i\text{-}Pr)_4$-catalyzed conditions to give the *E* and *Z* isomers of **6** (eq 3).



It is clear from these reactions that the diene **1** reacts exclusively at its γ-position and in a 1,4-manner. Another interesting observation is the fact that the products **5** and **6** retain the enethiol structure in both *E* and *Z* isomers of the Michael adducts with the *E* isomer (**a**) predominating over the *Z* isomer (**b**). This raises the possibility that the reaction may have proceeded through a Diels–Alder cycloaddition pathway followed by ring opening of the adduct **7** during hydrolytic workup. While this may account for the formation of **5a**, it cannot lead to the *Z* isomer **5b**. We have proved that under the reaction conditions, **5a** does not isomerize to **5b**. We have also not detected any of the compound **8**, which would have been the more likely hydrolytic product (Scheme II).

The diene also reacted with cyclopentenone, 2-methylcyclohexenone, and 3-methylcyclohexenone under Lewis acid catalyzed conditions to give the Michael adducts in modest to good yields (Table I). In each case, *E* and *Z* isomers of the Michael adduct were obtained. The yields in many of these reactions have not been optimized.

When the diene **1** reacted with 2-methylcyclohexenone under $TiCl_4$–$Ti(O\text{-}i\text{-}Pr)_4$ conditions, only the *E* and *Z* isomers of the Michael adducts **10** were isolated. But when the reaction was catalyzed by $AlCl_3$ at room temperature, the bicyclic compound **14** was also isolated in 23% yield.



We have made efforts to increase the yield of **14** by changing the catalyst to $EtAlCl_2$ and/or by changing the solvent, but we could not improve the yield significantly.

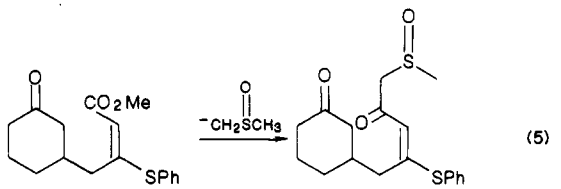
We have also used the diene **1a** to effect the Michael addition with 4,4-dimethylcyclohexenone. It is noteworthy that the diene **1a** is less reactive than **1** and gives a lower ratio of *E*/*Z* in the Michael adduct **13**.

In addition to $AlCl_3$ and $TiCl_4$–$Ti(O\text{-}i\text{-}Pr)_4$, the following acids, BF_3, $SnCl_4$, and $TiCl_4$, also catalyze the Michael addition reactions.

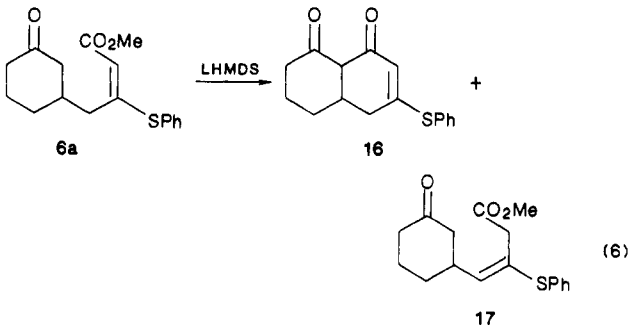
Effect of Solvent. The solvent effect on this reaction was briefly studied by treating the diene **1** with equimolar amounts of 4,4-dimethylcyclohexenone and titanium tetrachloride in various solvents. The results show (Table II) that in methylene chloride a higher ratio *E*/*Z* was obtained in addition to better yield. It is the solvent of choice.

Effect of the Amount of Lewis Acid. The amount of Lewis acid was also varied from equimolar to 2 mol of titanium tetrachloride to α,β-unsaturated compound. In all cases, we did not find any noticeable change in terms of yield and *E*/*Z* ratio. In cases where $Ti(O\text{-}i\text{-}Pr)_4$ was also used in conjunction with $TiCl_4$, the ratio of $TiCl_4$ to $Ti(O\text{-}i\text{-}Pr)_4$ was varied from 1:0.5 to 1:1. The ratio of 1 mol of $TiCl_4$ to 0.8 mol of $Ti(O\text{-}i\text{-}Pr)_4$ appeared to be the best for the reaction in terms of yield.

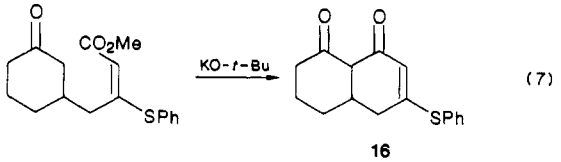
2. Intramolecular Claisen Condensation of the *E* Isomers. In order to cyclize the *E* isomers of the Michael adducts, one needs to generate the enolate anion from the ketone carbonyl group. We tried the reaction using NaH in THF but without much success. We then turned our attention to dimsyl anion to effect the Claisen condensation. The adduct **6a** on reaction with dimsyl anion gave product **15** instead of generating the enolate and cyclization (eq 5).



Nitrogen bases such as lithium hexamethyldisilazide (LHMDS) was tried next. We were gratified to isolate the cyclized product **16**, but the low yield of the reaction made us look for improved conditions. The low yield of the reaction is presumably due to a side reaction, where LHMDS is abstracting the γ-hydrogen of the ester functionality, thereby isomerizing the double bond to give **17** (eq 6).

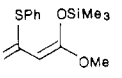
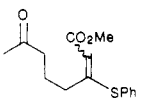
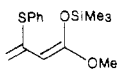
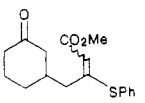
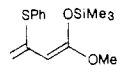
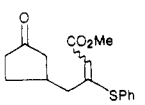
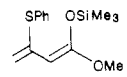
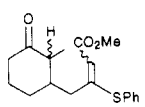
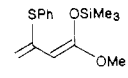
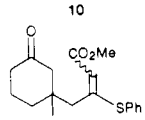
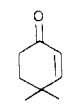
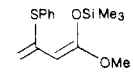
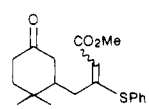
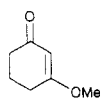
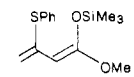
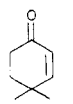
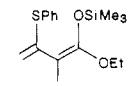
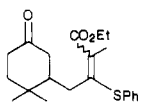
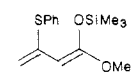
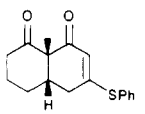


We therefore examined weaker oxygen bases like potassium *tert*-butoxide. When the *E* isomer **6a** was treated with K^+O^--*t*-Bu in THF, the compound smoothly cyclized to give the bicyclic compound **16** in 89% yield (eq 7). The



^1H NMR spectrum of compound **16** in deuteriochloroform shows a sharp singlet at 15.06 ppm, which indicates that the compound exists predominantly in the enol form. We were able to cyclize the other Michael adducts in the

Table I. Michael Reactions of 1 and 1a with α,β-Unsaturated Ketones

Michael acceptor	silyl ether	Lewis acid	E/Z	product	yield, %
		$AlCl_3$	1.1	 **5**	52
		$TiCl_4$–$Ti(O\text{-}i\text{-}Pr)_4$	1.4	 **6**	79
		$TiCl_4$–$Ti(O\text{-}i\text{-}Pr)_4$	1.1	 **9**	55[a]
		$TiCl_4$–$Ti(O\text{-}i\text{-}Pr)_4$	1.05	 **10**	86
		$TiCl_4$–$Ti(O\text{-}i\text{-}Pr)_4$[b]		 **11**	23
		$TiCl_4$	3.0	 **12**	68
		$TiCl_4$–$Ti(O\text{-}i\text{-}Pr)_4$		no reaction	
	 **1a**	$TiCl_4$	0.36	 **13**	35
		$AlCl_3$		 + 10a + 10b	23[c]

[a] Yield calculated on the basis of 20% recovered cyclopentenone. [b] Yield of the recovered *E* isomer. The *Z* isomer might have been formed, but we could not purify it. [c] Yield of the bicyclic compound. It was separated from the *Z* isomer of the Michael adduct by preparative TLC (eluant, 14% *tert*-butyl alcohol–carbon tetrachloride).

Table II. Effect of the Solvent on the Reaction between 4,4-Dimethylcyclohexenone and 1

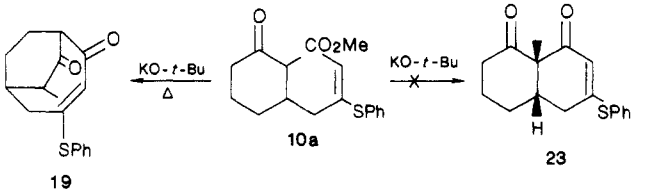
solvent	temp, °C	Lewis acid	E/Z	yield, %
CH_3CN	−23	$TiCl_4$	1.56	34
CH_2Cl_2	−78	$TiCl_4$	3.0	68
hexane	−78	$TiCl_4$	1.1	38

presence of K^+O^--*t*-Bu. The Michael adducts **9a**, **11a**, **12a**, and **13a** all cyclized in the presence of K^+O^--*t*-Bu to give the bicyclic compounds **18**, **20**, **21**, and **22**, respectively, in 72–89% yield (Table III).

From the ^1H NMR spectra of these bicyclic compounds, it is clear that the three bicyclic compounds **20**, **21**, and **22** exist in their enol forms. Compound **18**, however, exists in both the enol and keto forms in $CDCl_3$ but only in the keto form in CD_3OD.

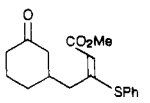
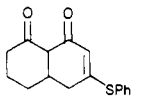
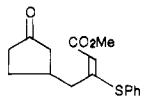
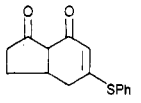
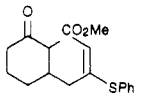
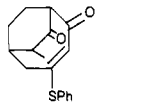
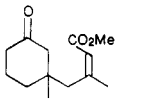
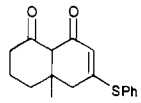
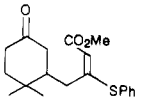
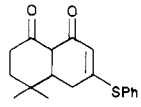
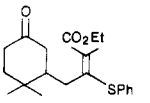
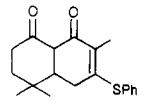
Cyclization of Michael adduct **10a** gave different results. The diene **1** in its reactions with 2-methyl-2-cyclohexen-1-one in the presence of Lewis acid gave a mixture of the

Scheme III



cis and trans isomers of the *E* Michael adduct **10a** as well as the cis and trans isomers of *Z* Michael adduct **10b**. Our efforts to separate the cis and trans isomers of each Michael adduct were not successful. Cyclization of **10a** was attempted under K^+O^--*t*-Bu conditions (Scheme III) at room temperature. No cyclized product was obtained. However, when the reaction was carried out in refluxing THF, compound **10a** did undergo cyclization because the isolated product **19** did not show the presence of the methoxy group. On the other hand, compound **19** showed a doublet (J = 11 Hz) for the methyl group, which is

Table III. Cyclization of Michael Adducts with Potassium *tert*-Butoxide

entry	Michael adduct	product	yield, %
1		 **16**	89
2		 **18**	72
3		 **19**	63
4		 **20**	83
5		 **21**	86
6		 **22**	79

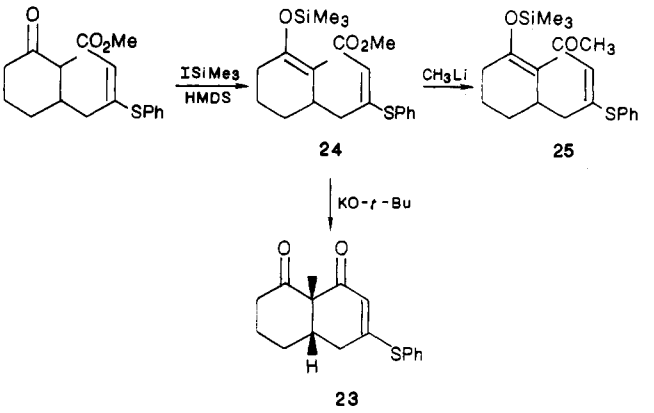
contrary to the expected singlet for the methyl group of compound **23**. We assigned the [4.2.2]bicyclo structure to compound **19** from its ^{13}C NMR, ^{1}H NMR, and infrared spectra (Scheme III).

Presumably, our inability to cyclize **10a** to compound **23** is due to generation of the kinetically favored enolate instead of the needed thermodynamically favored enolate. Recently, active Fe(0) has been used for effectively generating the thermodynamically favored enolate from 2-methylcyclohexanone.[6] The cyclization of **10a** was attempted with active Fe(0), but in our hands, the cyclization to **23** was still not successful. Only starting material **10a** was recovered.

Conversion of **10a** to its enol silyl ether was then attempted under NEt_3–DMF/chlorotrimethylsilane as described by House et al.[7] No enol silyl ether was formed under these conditions. The silylation of **10a** was finally achieved under iodotrimethylsilane–hexamethyldisilazane conditions[8] to give the thermodynamically favored enol silyl ether **24** (Scheme IV).

There are several well-established methods for generating the corresponding enolate anion from an enol silyl ether. Among them are treatment of the silyl enol ether either with CH_3Li[9] or with fluoride ion.[10] When the enol silyl ether **24** in THF was treated with CH_3Li, not unexpectedly, reaction with the ester functionality occurred to

Scheme IV

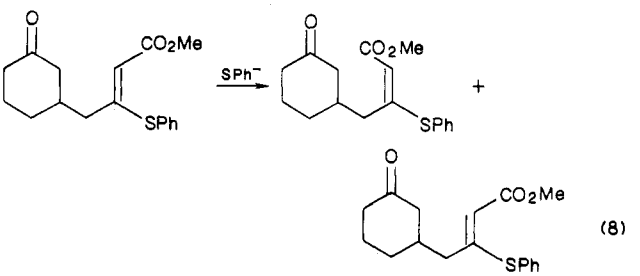


give compound **25** (Scheme IV).

One of the inherent problems in using tetraalkylammonium fluorides to generate enolate anions is that these fluoride salts are highly hygroscopic.[11] After taking all possible precautions in drying benzyltrimethylammonium fluoride (BTAF),[12] the silyl enol ether was treated with BTAF in THF. None of the cyclized compound **23** was obtained. We have tried with other fluoride ion sources like TASF,[13] KF–18-crown-6 ether,[14] also but without any success. In all cases, the Michael adduct **10a** was recovered.

We were therefore very pleased to find that the enol silyl ether **15** on reaction with K^+O^--*t*-Bu did undergo cyclization in THF–DMF to give compound **23** in 63% yield (Scheme IV).

3. Thiophenoxide-Induced Cyclization of the Michael Adducts. In the reaction of diene **1** with α,β-unsaturated carbonyl compounds, both the *E* and *Z* isomers of the Michael adducts were obtained. In some cases the ratio of *E* to *Z* isomer is as high as 1:1. While the *E* isomer of the Michael adducts smoothly cyclized in the presence of K^+O^--*t*-Bu to the bicyclic compounds in good yield, the tandem Michael–Claisen annelation reaction would be synthetically more useful if it is possible to convert the *Z* isomer to the annelated compound as well. Accordingly, the isomerization of *Z* isomer to *E* isomer was attempted. In principle, the *Z* isomer of the Michael adduct should undergo isomerization of the double bond in the presence of SPh^- (eq 8) to give an equilibrium mixture of *E* and *Z*

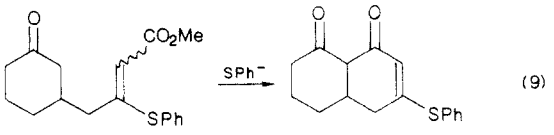


(8)

isomers of the Michael adduct. To our pleasant surprise, the thiophenoxide anion not only caused isomerization of the double bond but also cyclization to generate the annelated compound in one operation (eq 9).

Thus, the Michael adducts **6b**, **9b**, and **12b** were converted to the corresponding bicyclic compounds **16**, **18**, and **21**, respectively, in excellent yields (Table IV).

(6) Krafft, M. E.; Holton, R. A. *J. Org. Chem.* **1984**, *49*, 3669.
(7) House, H. O.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1971**, *36*, 2361.
(8) Miller, R. D.; McKean, D. R. *Synthesis* **1979**, 730.
(9) (a) Stork, G.; Hudrlik, P. F. *J. Am. Chem. Soc.* **1968**, *90*, 4464. (b) House, H. O.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1971**, *36*, 2361.
(10) Noyori, R.; Yokoyama, K.; Sakata, J.; Kuwajima, I.; Nakamura, E.; Shimizu, M. *J. Am. Chem. Soc.* **1977**, *99*, 1265.
(11) Phillip Cox, D.; Terpinski, J.; Lawrynowicz, W. *J. Org. Chem.* **1984**, *49*, 3216.
(12) Kuwajima, I.; Nakamura, E. *J. Am. Chem. Soc.* **1975**, *97*, 3257.
(13) (a) Noyori, R.; Nishida, I.; Sakata, J.; Nishizawa, M. *J. Am. Chem. Soc.* **1980**, *102*, 1223. (b) RajanBabu, T. V. *J. Org. Chem.* **1984**, *49*, 2083.
(14) Liotta, C. L.; Harris, H. P. *J. Am. Chem. Soc.* **1974**, *96*, 2250.



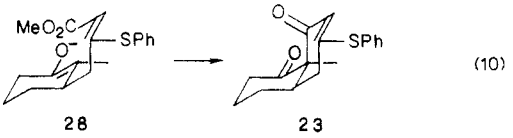
(9)

The exception is the cyclization of **13b**, which was attempted under thiophenoxide conditions, but we were not able to isolate any bicyclic compound **22** presumably due to the reluctance of the double bond to undergo isomerization under these conditions. The next question we must face is the stereoselectivity of the annelation reaction. Obviously, it would be most desirable if the annelation reaction can be controlled to yield either the cis- or the trans-fused products. So far, in the case of compound **23**, only one stereoisomer was obtained with stereochemistry yet to be established. In cases (compound **16**, **18**, **20**, **21**, and **22**) where one of the ring-junction hydrogens is situated between the two carbonyl groups, either the compound exists in the enol form or enolization is so facile that separation of the stereoisomers would not be practical. We thus turned our attention to this question.

4. Stereoselectivity of the Annelation Reaction. We begin by establishing the stereochemistry of compound **23**. In principle, NOE can be used to distinguish between the cis and the trans isomers. Positive enhancement should be observed for the ring-junction proton H_a on irradiation of the methyl protons for the cis compound (Scheme V). Unfortunately, its chemical shift is such that it is part of a broad multiplet at 2.38–2.13 ppm. The NOE experiment gave equivocal results and no definitive assignment was possible.

Chemical correlation was next tried according to Scheme VI. Compound **23** was first converted to the enol methyl ether **26**. Lithium aluminum hydride reduction of **26** followed by acid hydrolysis gave the known compound **27** with cis ring junction.[15] It establishes clearly that compound **23** has the cis stereochemistry.

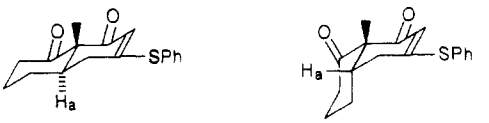
The cis stereochemistry of **23** is not unexpected. In the intramolecular cyclization of the enolate anion **28** derived from the enol silyl ether **24**, the electrophile is expected to come from the axial direction, thus leading to the cis stereochemistry (eq 10).



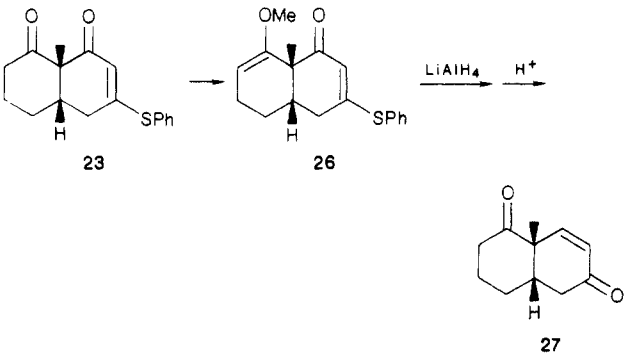
(10)

The prefered axial approach of the electrophile can be used advantageously to obtain the trans isomer of compound **23**. In the cyclization of **6a** to give **16**, the intermediate must be the anion **29**. If, instead of quenching the reaction mixture with water, methyl iodide is used, compound **23** should be obtained with the trans isomer as the prefered product. This was found to be the case. On treatment of **6a** with K^+O^--*t*-Bu in THF followed by CH_3I, a mixture of *trans*- and *cis*-**23** was obtained in 72% yield with a trans/cis ratio of 9:4 (Scheme VII). Furthermore, *trans*-**23** could be readily crystallized from the mixture, thus facilitating the purification. The stereochemistry of the trans compound was established also by chemical transformation to the known compound **32** according to Scheme VIII.[16]

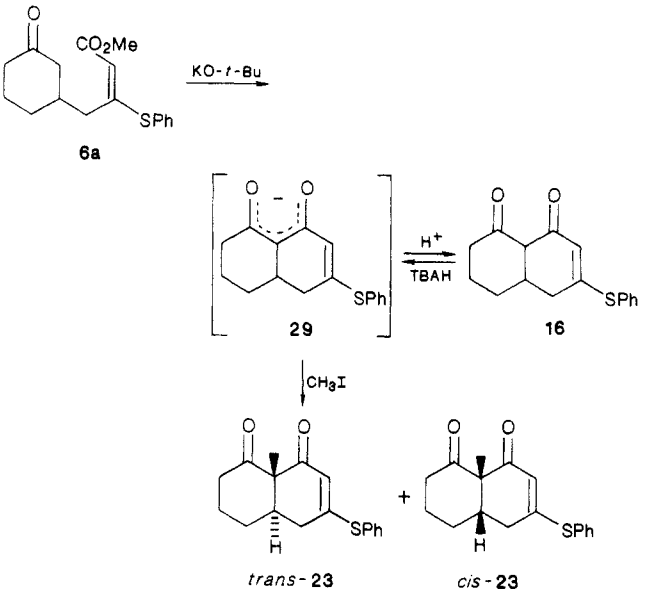
Scheme V



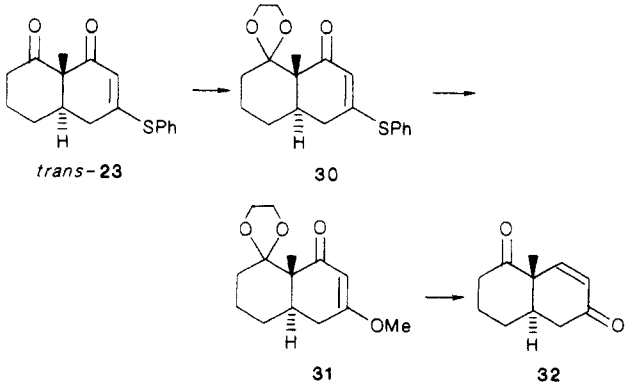
Scheme VI



Scheme VII



Scheme VIII

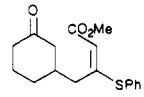
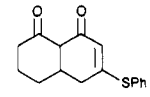
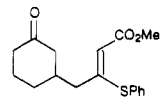
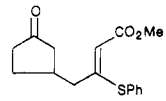
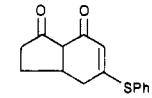
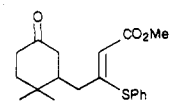
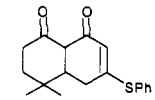
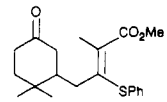


Alternatively, alkylation product **23** can be obtained from **16** under phase-transfer conditions using tetrabutylammonium hydroxide (TBAH) and methyl iodide. The yield was improved to 89% with the ratio of trans/cis remaining at 9:4. There is no significant difference between phase-transfer conditions and in situ alkylation of the anion during cyclization.

(15) Danishefsky, S.; Kitahara, T.; Yan, C. F.; Morris, J. *J. Am. Chem. Soc.* **1979**, *101*, 6996.

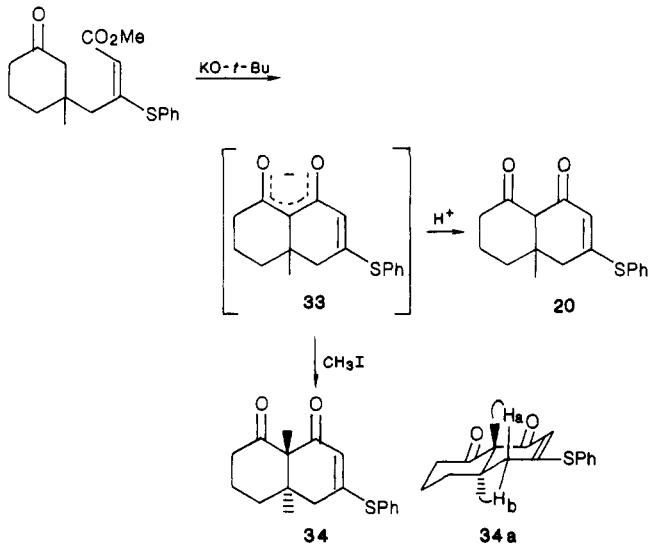
(16) (a) Grieco, P. A.; Ferrino, S.; Oguri, T. *J. Org. Chem.* **1979**, *44*, 2593. (b) Gopalakrishnan, G.; Jayaraman, S.; Rajagopalan, K.; Swaminathan, S. *Synthesis* **1983**, *10*, 797.

Table IV. Thiophenoxide-Induced Cyclization of Michael Adducts

entry	Michael adduct	product	yield, %
1		 16	93
2		16	93
3		 18	69
4		 21	91
5		*a*	

[a] None of the expected bicyclic compound was isolated.

Finally, alkylation of the anion **33** derived from the cyclization of **11** with methyl iodide gave stereoselectivity the trans compound **34**. The stereochemistry of **34** was established by NOE experiments. Irradiation of the ring-junction methyl groups selectively enhances either H_a or H_b as indicated in **34a**. This can only be possible with a ring junction of trans stereochemistry.



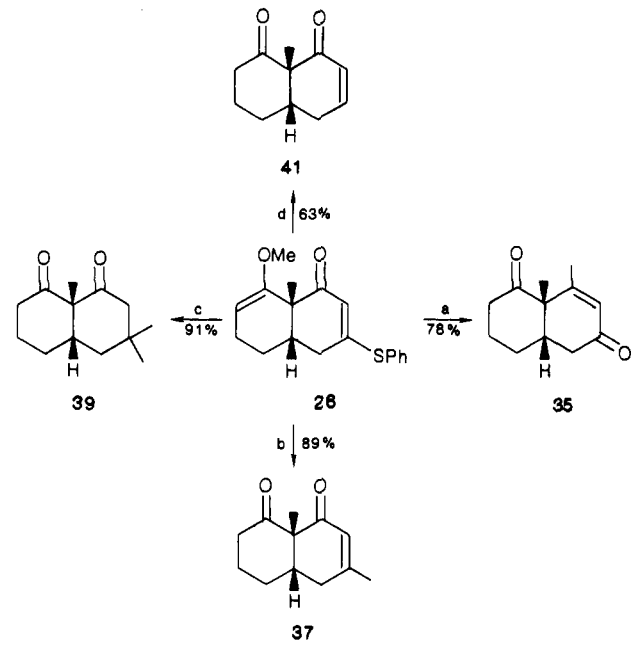
5. Functional Group Transformation of the Decalin System. The annelation sequence involving the tandem Michael–Claisen condensation allows the conversion of cyclohexenone to a decalin system. Furthermore, in the case where there is a methyl group at the 9 position, a reasonable degree of stereocontrol is possible to give either the cis or trans stereoisomers. Since many natural products, including steroids and terpenoids, are based on the decalin structure, the annelation reaction offers the potential as an entry to the synthesis of many of these compounds.

Compound **23** contains three carbonyl groups, with one of them masked in the form of an enol thio ether. In order to use them effectively in organic synthesis, the three carbonyl groups should be differentiated with relative ease. The selective protection of carbonyl at C(8) can be done readily. When *cis*-**23** was treated with trimethyl orthoformate and a catalytic amount of *p*-toluenesulfonic acid in CH_3OH, the monomethyl enol ether **26** was isolated in 87% yield (Scheme VI). Similarly *trans*-**23** was protected at the C(8) position by using ethylene glycol and a catalytic amount of *p*-toluenesulfonic acid in benzene to give the acetal **30** in 83% yield (Scheme VIII). It is noteworthy that during either of these conditions, none of the other functional groups in the decalin system were affected. Furthermore, 1,2-ethanedithiol also can be used instead of ethylene glycol with compound **23**.

In addition to the conversion of **26** or **31** to the corresponding enedione compounds **27** and **32**, other transformations are possible.

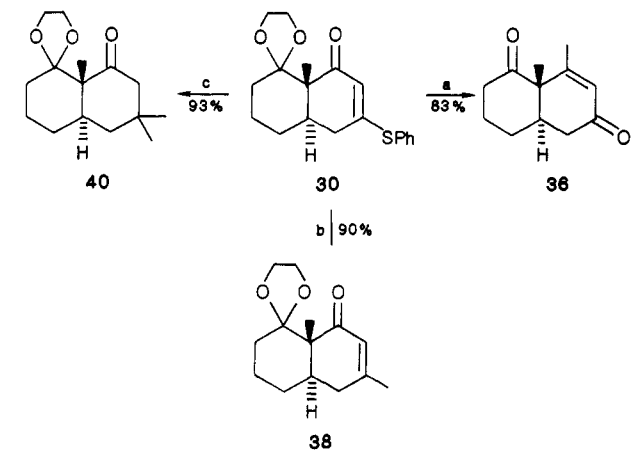
For example, compounds **26** and **30** reacted smoothly with methyllithium to give the corresponding tertiary alcohols, which were hydrolyzed in mineral acid to give the methyl-substituted enediones **35** and **36**, respectively, in good yields (Schemes IX and X). On the other hand,

Scheme IX[a]



[a] (a) CH_3Li, H^+; (b) $(CH_3)_2CuLi$, −78 °C, H^+; (c) $(CH_3)_2CuLi$, 0 °C, H^+; (d) Raney Ni.

Scheme X[a]



[a] (a) CH_3Li, H^+; (b) $(CH_3)_2CuLi$, −78 °C, H^+; (c) $(CH_3)_2CuLi$, 0 °C, H^+.

compounds **26** and **30** when treated with lithium dimethylcuprate at −78 °C followed by quenching with aqueous saturated ammonium chloride at −78 °C gave conjugative addition products. Thus, compound **26** gave the β-alkylated enedione **37**, whereas compound **30** gave the β-alkylated enone **38** in excellent yields. β,β-Dialkylated compounds were obtained with lithium dimethylcuprate, but at room temperature. Thus, compound **26** gave the β,β-dialkylated dione **39** after acid hydrolysis, whereas compound **30** gave **40** in excellent yields (Schemes IX and X).

Finally we demonstrated that the sulfur moiety of **26** can be removed by hydrogenolysis with Raney Ni. The reaction went smoothly to give the enedione **41** in 63% yield (Scheme IX).

Conclusion

Based on the propensity of 3-(phenylthio)-1-(trimethylsiloxy)-1-methoxy-1,3-butadiene (**1**) to undergo Michael reaction with α,β-unsaturated ketones under Lewis acid conditions, we have developed an annelation reaction using the tandem Michael–Claisen condensation. In the 9-methyl-substituted system, the annelation reaction can be controlled to give stereoselectively the trans- or cis-fused compounds. Chemoselective transformations of the three carbonyl groups can be effected. It seems reasonable to expect that this annelation reaction can be used for the synthesis of a number of natural products. Efforts in this direction are currently being explored.[17]

Experimental Section

Melting and boiling points are uncorrected. Infrared spectra were obtained from films on NaCl plates for liquids and from solutions in 0.1-mm cells or as a KBr pellet for solids on a Perkin-Elmer 297 spectrophotometer. The ^{1}H NMR spectra were recorded on Varian XL-200, T-60, and T-60A instruments and are reported in δ units with Me_4Si as internal standard; the abbreviations s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, and br = broad are used throughout. Mass spectra were obtained on a Dupont 492B machine operating at 70 eV. Column chromatography was performed on silica gel 60 (Merck). Et_3N and i-Pr_2NH were dried by distillation from CaH_2. THF was distilled under nitrogen from sodium–benzophenone directly into the reaction vessel. Other solvents were purified by using standard procedures. Microanalyses were performed at Guelph Chemical Laboratories Ltd.

1-(Trimethylsiloxy)-1-methoxy-3-(phenylthio)buta-1,3-diene (1) was prepared according to the literature procedure.[5]

Methyl 3-(Phenylthio)-7-oxooct-2-enoate (5). To a well-stirred mixture of methyl vinyl ketone (0.33 mL, 4 mmol) and aluminum chloride (536 mg, 4 mmol) in 20 mL of CH_2Cl_2 under nitrogen at 0 °C was added **1** (1.12 g, 4 mmol). After 6 h, the orange mixture was added to aqueous $NaHCO_3$ and extracted with ether. The extract was dried ($MgSO_4$) and evaporated to give an oil that was column chromatographed (eluant, 20% ethyl acetate–hexane) to give *E* (viscous oil) and *Z* (viscous oil) isomers of methyl 3-(phenylthio)-7-oxooct-2-enoate in the ratio of 1.1:1, respectively, with 52% yield.

(*E*)-5a: IR (neat) 2948, 1710, 1596 cm^{-1}; ^{1}H NMR ($CDCl_3$) 7.42 (s, 5 H), 5.18 (s, 1 H), 3.58 (s, 3 H), 2.15 (s, 3 H), 3.02–1.48 (m, 6 H); MS, *m/z* (relative intensity) 278 (M^+, 38), 246 (64), 189 (52), 169 (69), 137 (90), 109 (89), 43 (100); exact mass calcd for $C_{15}H_{18}O_3S$ 278.098, obsd 278.099.

(*Z*)-5b: IR (neat) 2956, 1705, 1580 cm^{-1}; ^{1}H NMR ($CDCl_3$) 7.57 (m, 5 H), 5.8 (s, 1 H), 3.73 (s, 3 H), 2.0 (s, 3 H), 2.43–1.23 (m, 6 H); MS, *m/z* (relative intensity) 278 (M^+, 29), 246 (44), 189 (58), 169 (45), 110 (100), 43 (93); exact mass calcd for $C_{15}H_{18}O_3S$ 278.098, obsd 278.096.

(17) Prasad, C. V. C.; Chan, T. H., *J. Org. Chem.*, following paper in this issue.

Methyl 3-(Phenylthio)-4-(3-oxocyclohexyl)but-2-enoate (6). To a well-stirred mixture of titanium tetrachloride (0.44 mL, 4 mmol) and titanium isopropoxide (0.95 mL, 3.2 mmol) in 20 mL of CH_2Cl_2 under nitrogen at −78 °C was added a mixture of **1** (1.12 g, 4 mmol) and 2-cyclohexen-1-one (0.39 mL, 4 mmol) in 5 mL of CH_2Cl_2. After 4 h, the dark red mixture was added to aqueous $NaHCO_3$ and extracted with ether. The extract was dried ($MgSO_4$) and evaporated to give an oil that was column chromatographed (eluant, 20% ethyl acetate–hexane) to give *E* (mp 89–91 °C) and *Z* (mp 88–90 °C) isomers of methyl 3-(phenylthio)-4-(3-oxocyclohexyl)but-2-enoate in the ratio of 1.4:1, respectively, in 79% yield.

(*E*)-6a: IR (KBr) 2980, 2930, 1710, 1605 cm^{-1}; ^{1}H NMR ($CDCl_3$) 7.38 (s, 5 H), 5.2 (s, 1 H), 3.55 (s, 3 H), 3.05–1.38 (m, 11 H); MS, *m/z* (relative intensity) 304 (M^+, 57), 273 (37), 208 (43), 195 (22), 176 (48), 163 (39), 134 (70), 28 (100); exact mass calcd for $C_{17}H_{20}O_3S$ 304.113, obsd 304.120.

(*Z*)-6b: IR (KBr) 2942, 1705, 1690, 1680 cm^{-1}; ^{1}H NMR ($CDCl_3$) 7.6–7.2 (m, 5 H), 5.78 (s, 1 H), 3.7 (s, 3 H), 2.53–1.03 (m, 11 H); MS, *m/z* (relative intensity) 304 (M^+, 36), 273 (32), 208 (36), 195 (23), 163 (46), 134 (64), 110 (72), 41 (100); exact mass calcd for $C_{17}H_{20}O_3S$ 304.113, obsd 304.115.

Methyl 3-(Phenylthio)-4-(3-oxocyclopentyl)but-2-enoate (9). The reaction was performed as above with 2-cyclopenten-1-one (0.34 mL, 4 mmol) and the oil was column chromatographed (eluant, 20% ethyl acetate–hexane) to give *E* (viscous oil) and *Z* (viscous oil) isomers of methyl 3-(phenylthio)-4-(3-oxocyclopentyl)but-2-enoate in the ratio of 1.1:1, respectively, with 55% yield. (The yield was calculated on the basis that 20% of unreacted 2-cyclopenten-1-one was also recovered.)

(*E*)-9a: IR (film) 2952, 1742, 1710, 1600 cm^{-1}; ^{1}H NMR ($CDCl_3$) 7.5 (s, 5 H), 5.27 (s, 1 H), 3.63 (s, 3 H), 3.23–1.6 (m, 9 H); MS, *m/z* (relative intensity) 290 (M^+, 75), 259 (47), 208 (61), 181 (36), 149 (86), 134 (64), 110 (96), 28 (100); exact mass calcd for $C_{16}H_{18}O_3S$ 290.098, obsd 290.091.

(*Z*)-9b: IR (KBr) 2950, 1735, 1695 cm^{-1}; ^{1}H NMR ($CDCl_3$) 7.65–7.27 (m, 5 H), 5.9 (s, 1 H), 3.78 (s, 3 H), 2.5–1.33 (m, 9 H); MS, *m/z* (relative intensity) 290 (M^+, 40), 208 (23), 176 (10), 147 (30), 135 (39), 110 (60), 86 (100); exact mass calcd for $C_{16}H_{18}O_3S$ 290.098, obsd 290.100.

Methyl 3-(Phenylthio)-4-(3-oxo-2-methylcyclohexyl)but-2-enoate (10). The reaction was performed as above with 2-methyl-2-cyclohexen-1-one (0.44 g, 4 mmol) and the oil was column chromatographed (eluant, 20% ethyl acetate–hexane) to give *E* (viscous oil) and *Z* (viscous oil) isomers of methyl 3-(phenylthio)-4-(3-oxo-2-methylcyclohexyl)but-2-enoate in the ratio of 1:1, respectively, with 86% yield.

(*E*)-10a: IR (film) 2940, 1705, 1595 cm^{-1}; MS, *m/z* (relative intensity) 318 (M^+, 16), 208 (43), 176 (26), 149 (34), 134 (55), 111 (52), 31 (100); exact mass calcd for $C_{18}H_{22}O_3S$ 318.129, obsd 318.126; ^{1}H NMR ($CDCl_3$) 7.4 (s, 5 H), 5.33 (s, 1 H), 5.23 (s, 1 H), 3.6 (s, 3 H), 3.57 (s, 3 H), 3.2–1.6 (m, 10 H), 1.13 (d, J = 7 Hz, 3 H), 1.09 (d, J = 7 Hz, 3 H).

(*Z*)-10b: IR (KBr) 2950, 1702, 1685 cm^{-1}; MS, *m/z* (relative intensity) 318 (M^+, 8), 208 (51), 192 (44), 177 (33), 150 (65), 135 (70), 110 (63), 28 (100); exact mass calcd for $C_{18}H_{22}O_3S$ 318.129, obsd 318.132; ^{1}H NMR ($CDCl_3$) 7.67–7.23 (m, 5 H), 5.9 (s, 1 H), 5.83 (s, 1 H), 3.83 (s, 3 H), 3.75 (s, 3 H), 3.1–0.93 (m, 10 H), 0.48 (d, J = 7 Hz, 3 H), 0.43 (d, J = 7 Hz, 3 H).

Methyl 3-(Phenylthio)-4-(3-oxo-3-methylcyclohexyl)but-2-enoate (11). To a well-stirred mixture of titanium tetrachloride (0.44 mL, 4 mmol) and titanium isopropoxide (0.95 mL, 3.2 mmol) in 2 mL of CH_2Cl_2 under nitrogen at −78 °C was added a mixture of **1** (1.12 g, 4 mmol) and 3-methyl-2-cyclohexen-1-one (0.44 g, 4 mmol) in 3 mL of CH_2Cl_2. After 4 h, the dark red mixture was added to aqueous $NaHCO_3$ and extracted with ether. The extract was dried ($MgSO_4$) and evaporated to give an oil that was column chromatographed (eluant, 20% ethyl acetate–hexane) to give **11** (viscous oil) in 23% yield. (The formation of the *Z* isomer of **11** cannot be ruled out, but we could isolate only the *E* isomer in pure form.)

(*E*)-11a: IR (film) 2960, 1715, 1602 cm^{-1}; ^{1}H NMR ($CDCl_3$) 7.4 (s, 5 H), 5.27 (s, 1 H), 3.57 (s, 3 H), 3.17–1.67 (m, 10 H), 1.1 (s, 3 H); MS, *m/z* (relative intensity) 318 (M^+, 24), 208 (34), 177 (21), 149 (42), 134 (31), 111 (52), 55 (100); exact mass calcd for $C_{18}H_{22}O_3S$ 318.129, obsd 318.127.

Methyl 3-(Phenylthio)-4-(3-oxo-6,6-dimethylcyclohexyl)but-2-enoate (12). To a well-stirred mixture of **1** (1.12 g, 4 mmol) and 4,4-dimethyl-2-cyclohexen-1-one (0.53 mL, 4 mmol) in 20 mL of CH_2Cl_2 under nitrogen at −78 °C was added titanium tetrachloride (0.44 mL, 4 mmol). After 5 h, the dark red mixture was added to aqueous $NaHCO_3$ and extracted with ether. The extract was dried ($MgSO_4$) and evaporated to give an oil that was column chromatographed (eluant, 20% ethyl acetate–hexane) to give *E* (mp 146–148 °C) and *Z* (mp 134–136 °C) isomers of methyl 3-(phenylthio)-4-(3-oxo-6,6-dimethylcyclohexyl)but-2-enoate in the ratio of 3:1, respectively, with 68% yield. In several runs the *E* and *Z* isomers of **12** were also obtained in pure form from the crude reaction mixture by crystallization from 10% ethyl acetate–hexane.

(*E*)-12a: IR (KBr) 2930, 1690, 1590 cm^{-1}; ^1H NMR ($CDCl_3$) 7.42 (s, 5 H), 5.28 (s, 1 H), 3.58 (s, 3 H), 3.42–1.48 (m, 9 H), 1.12 (s, 3 H), 1.08 (s, 3 H); MS, *m/z* (relative intensity) 332 (M^+, 39), 301 (16), 219 (26), 176 (29), 134 (29), 55 (100); exact mass calcd for $C_{19}H_{24}O_3S$ 332.145, obsd 332.148.

(*Z*)-12b: IR (KBr) 2940, 1690, 1678 cm^{-1}; ^1H NMR ($CDCl_3$) 7.67–7.1 (m, 5 H), 5.82 (s, 1 H), 3.77 (s, 3 H), 2.87–1.23 (m, 9 H), 0.73 (s, 3 H), 0.4 (s, 3 H); MS, *m/z* (relative intensity) 332 (M^+, 56), 300 (16), 258 (39), 223 (41), 205 (60), 149 (49), 110 (60), 28 (100); exact mass calcd for $C_{19}H_{24}O_3S$ 332.145, obsd 332.141.

Ethyl 3-(Phenylthio)-2-methyl-4-(3-oxo-6,6-dimethylcyclohexyl)but-2-enoate (13). The reaction was performed as above with 3-(phenylthio)-2-methyl-1-(trimethylsiloxy)-1-ethoxy-1,3-butadiene (1.18 g, 4 mmol) and the oil was column chromatographed (eluant, 20% ethyl acetate–hexane) to give *E* (viscous oil) and *Z* (viscous oil) isomers of ethyl 3-(phenylthio)-2-methyl-4-(3-oxo-6,6-dimethylcyclohexyl)but-2-enoate in the ratio of 1:2.9, respectively, with 35% yield.

(*E*)-13a: IR (film) 2950, 1708, 1582 cm^{-1}; ^1H NMR ($CDCl_3$) 7.25 (s, 5 H), 4.18 (q, J = 7 Hz, 2 H), 3.03–0.8 (m, 9 H), 2.17 (s, 3 H), 1.32 (t, J = 7 Hz, 3 H), 0.88 (s, 3 H), 0.5 (s, 3 H); MS, *m/z* (relative intensity) 360 (M^+, 6), 277 (28), 205 (21), 190 (38), 149 (22), 125 (37), 28 (100).

(*Z*)-13b: IR (film) 2950, 1710, 1582 cm^{-1}; ^1H NMR ($CDCl_3$) 7.47–7.13 (m, 5 H), 4.24 (q, J = 7 Hz, 2 H), 2.57–1.47 (m, 9 H), 2.00 (s, 3 H), 1.32 (t, J = 7 Hz, 3 H), 0.9 (s, 3 H), 0.7 (s, 3 H); MS, *m/z* (relative intensity) 360 (M^+, 8), 315 (5), 205 (32), 149 (22), 110 (44), 28 (100).

3-(Phenylthio)-2-methyl-1-(trimethylsiloxy)-1-ethoxy-1,3-butadiene (1a). To a solution of 1.7 mL of diisopropylamine (12 mmol) in 30 mL of dry THF under nitrogen was added 8.0 mL of 1.5 M *n*-butyllithium in hexane after cooling to 0 °C. The reaction mixture was cooled to −78 °C. A quantity of 2.0 mL of chlorotrimethylsilane (16 mmol) was added, and the solution was stirred for 5 min. Then a quantity of 2.36 g (10 mmol) of ethyl 3-(phenylthio)-2-methylbut-2-enoate (contains mixture of *E* and *Z* isomers) in 5 mL of THF was added and the solution stirred for 10 min. Then, the solvent was removed under reduced pressure and the residue was washed and filtered with cold dry hexane. The hexane was removed from the filtrate in vacuo to yield **1a** in quantitative yield: IR (film) 2986, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) 7.5–7.07 (m, 5 H), 5.17 (s, 1 H), 5.00 (s, 1 H), 3.7 (q, J = 7 Hz, 2 H), 1.7 (s, 3 H), 1.1 (t, J = 7 Hz, 3 H), 0.2 (s, 9 H); ^{29}Si NMR ($CDCl_3$) 20.52 (s).

3-(Phenylthio)-5,6,4a,8a-tetrahydronaphthalene-1,8-(4*H*,7*H*)-dione (16). To a well-stirred solution of methyl 3-(phenylthio)-4-(3-oxocyclohexyl)but-2-enoate (1.22 g, 4 mmol) in 20 mL of THF under nitrogen at room temperature was added potassium *tert*-butoxide (470 mg, 4 mmol). After 2 h, the solvent was removed under vacuum and the crude viscous mass was treated with 5 mL of saturated aqueous NH_4Cl solution followed by extraction with ether. The extract was dried (Na_2SO_4) and the solvent was removed. The yellow solid was crystallized from hexane to give **16** as yellow prisms (mp 129–131 °C) in 89% yield: IR (KBr) 2940, 1595, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) 7.4 (s, 5 H), 5.45 (d, J = 1.8 Hz, 1 H), 3.00–1.17 (m, 9 H), 15.07 (s, 1 H); MS, *m/z* (relative intensity) 272 (M^+, 88), 244 (62), 242 (40), 163 (65), 149 (35), 135 (88), 28 (100); exact mass calcd for $C_{16}H_{16}O_2S$ 272.087, obsd 272.080. Anal. Calcd for $C_{16}H_{16}O_2S$: C, 70.59; H, 5.88; S, 11.77. Found: C, 70.36; H, 6.28; S, 12.09.

5-(Phenylthio)-2,3,3a,7a-tetrahydro-1*H*-indene-1,7(4*H*)-dione (18). The reaction was performed as above with methyl 3-(phenylthio)-4-(3-oxocyclopentyl)but-2-enoate (1.16 g, 4 mmol) except that CH_2Cl_2 was used for extraction instead of ether, and the crude product was column chromatographed (eluant, 50% ethyl acetate–hexane) to give **18** (mp 135–137 °C) in 72% yield: IR (KBr) 2930, 1722, 1615, 1555 cm^{-1}; ^1H NMR (CD_3OD) 7.02 (s, 5 H), 4.92 (br, 1 H), 2.73–1.4 (m, 8 H); MS, *m/z* (relative intensity) 258 (M^+, 100), 230 (34), 213 (36), 202 (43), 176 (33), 149 (50), 109 (76); exact mass calcd for $C_{15}H_{14}O_2S$ 258.071, obsd 258.068.

7-Methyl-4-(phenylthio)bicyclo[4.2.2]dec-3-ene-2,8-dione (19). To a well-stirred solution of **10a** (1.27 g, 4 mmol, contains mixture of isomers) in 20 mL of THF under nitrogen was added potassium *tert*-butoxide (470 mg, 4 mmol), and the solution was refluxed for 3 h. The solvent was then removed under vacuum and the crude product was treated with 5 mL of saturated aqueous NH_4Cl solution followed by extraction with ether. The ether extract was dried (Na_2SO_4) and the solvent removed. The crude product was column chromatographed (eluant, 30% ethyl acetate–hexane) to give **19** (viscous oil) in 63% yield: IR (film) 2975, 1715, 1660, 1442 cm^{-1}; ^1H NMR ($CDCl_3$) 7.6 (m, 5 H), 5.57 (s, 1 H), 3.53 (d, J = 5 Hz, 1 H), 2.78–1.67 (m, 8 H), 1.11 (d, J = 6 Hz, 3 H); ^{13}C NMR ($CDCl_3$) 206.7, 196.6, 161.6, 135.4, 130.3, 130.1, 121.9, 55.9, 45.5, 41.9, 40.9, 27.1, 22.6; MS, *m/z* (relative intensity) 286 (M^+, 72.3), 258 (34), 231 (39), 209 (32), 203 (61), 176 (44), 131 (49), 28 (100); exact mass calcd for $C_{17}H_{18}O_2S$ 286.103, obsd 286.102.

3-(Phenylthio)-5,6,4a,8a-tetrahydro-4a-methylnaphthalene-1,8(4*H*,7*H*)-dione (20). To a well-stirred solution of **11a** (1.27 g, 4 mmol) in 20 mL of THF under nitrogen at room temperature was added potassium *tert*-butoxide (470 mg, 4 mmol). After 2 h, the solvent was removed under vacuum and the crude viscous mass was treated with 5 mL of saturated aqueous NH_4Cl solution followed by extraction with ether. The extract was dried (Na_2SO_4) and the solvent removed. The yellow mass was column chromatographed (eluant, 10% ethyl acetate–hexane) to give **20** (mp 76–78 °C) in 83% yield: IR (KBr) 2940, 1595 cm^{-1}; ^1H NMR ($CDCl_3$) 7.4 (s, 5 H), 5.47 (d, J = 2 Hz, 1 H), 2.77–1.53 (m, 8 H), 1.2 (s, 3 H), 15.3 (s, 1 H); MS, *m/z* (relative intensity) 286 (M^+, 32), 271 (100), 244 (10), 218 (21), 193 (34), 176 (37), 162 (54), 135 (58), 105 (60); exact mass calcd for $C_{17}H_{18}O_2S$ 286.103, obsd 286.098.

3-(Phenylthio)-5,6,4a,8a-tetrahydro-5,5-dimethylnaphthalene-1,8(4*H*,7*H*)-dione (21). The reaction was performed as above with **12a** (1.33 g, 4 mmol) and the yellow solid was crystallized from hexane to give **21** (mp 124–126 °C) in 86% yield: IR (KBr) 2934, 1565, 1270 cm^{-1}; ^1H NMR ($CDCl_3$) 7.5–7.4 (m, 5 H), 5.41 (s, 1 H), 2.73–2.13 (m, 5 H), 1.65–1.47 (m, 2 H), 1.04 (s, 3 H), 0.88 (s, 3 H), 15.15 (s, 1 H); MS, *m/z* (relative intensity) 300 (M^+, 78), 298 (100), 283 (38), 255 (36), 244 (59), 191 (50), 135 (96), 110 (52), 28 (97); exact mass calcd for $C_{18}H_{20}O_2S$ 300.118, obsd 300.121.

3-(Phenylthio)-5,6,4a,8a-tetrahydro-2,5,5-trimethylnaphthalene-1,8(4*H*,7*H*)-dione (22). The reaction was performed as above with **13a** (1.44 g, 4 mmol) and the yellow mass was column chromatographed (eluant, 10% ethyl acetate–hexane) to give **22** (mp 115–117 °C) in 79% yield: IR (KBr) 2936, 1568 cm^{-1}; ^1H NMR ($CDCl_3$) 7.37 (s, 5 H), 2.97–1.23 (m, 7 H), 2.03 (d, 3 H), 0.73 (s, 3 H), 0.7 (s, 3 H); MS, *m/z* (relative intensity) 314 (M^+, 32), 258 (31), 236 (22), 218 (28), 205 (34), 140 (56), 135 (34), 84 (100); exact mass calcd for $C_{19}H_{22}O_2S$ 314.134, obsd 314.137.

General Method for the Cyclization of Michael Adducts with Lithium Thiophenoxide. To a well-stirred solution of thiophenol (1.54 mL, 15 mmol) in 20 mL of THF at 0 °C under nitrogen was added 6 mL of 2.5 M *n*-BuLi (15 mmol) followed by **12b** (498 mg, 1.5 mmol) in 5 mL of THF, and then the solution was refluxed for 20 h. The solvent was removed and the crude yellow crystalline mass was dissolved in ether and washed twice with 8% aqueous sodium hydroxide. The ether extracts were dried (Na_2SO_4) and the solvent was removed. The yellow crude mass was crystallized from hexane to give **21** in 91% yield and was identical in all respects with the one prepared by the potassium *tert*-butoxide method.

Methyl 3-(Phenylthio)-4-(3-(trimethylsiloxy)-2-methyl-2-cyclohexenyl)but-2-enoate (24). To a well-stirred solution of **10a** (750 mg, 2.36 mmol) in 20 mL of CH_2Cl_2 under nitrogen at −23 °C was added hexamethyldisilazane (0.6 mL, 2.83 mmol) and

iodotrimethylsilane (0.4 mL, 2.83 mmol). The reaction mixture is stirred at −23 °C for 30 min and then 2 h at room temperature. The solvent was removed under vacuum and 200 mL of dry hexane was added. The liberated salts were filtered off and the hexane was removed under vacuum to give **24** in quantitative yield: IR (film) 2950, 1690, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) 7.33 (s, 5 H), 5.2 (s, 1 H), 3.57 (s, 3 H), 3.1–0.8 (m, 9 H), 1.67 (br, 3 H), 0.22 (s, 9 H); MS, *m/z* (relative intensity) 390 (M^+, 2), 282 (7), 183 (100), 109 (7), 73 (41); exact mass calcd for $C_{21}H_{30}O_3SSi$ 390.169, obsd 390.167.

***cis*-3-(Phenylthio)-5,6,4a,8a-tetrahydro-8a-methylnaphthalene-1,8(4*H*,7*H*)-dione (*cis*-23).** To a well-stirred solution of **24** (390 mg, 1 mmol) in 3 mL of THF under nitrogen at room temperature was added potassium *tert*-butoxide (118 mg, 1.05 mmol). After 20 min, 5 mL of dry DMF was added and stirring continued for another 20 h. The solvent was removed under vacuum, and the crude product was treated with 2 mL of saturated NH_4Cl solution and extracted with ether. The ether extract was washed twice with 15 mL of saturated aqueous NaCl solution to remove any traces of DMF. The ether extract was dried (Na_2SO_4) and the solvent was evaporated. The crude product was column chromatographed (eluant, 20% ethyl acetate–hexane) to give **23** (mp 109–111 °C) in 63% yield: IR (KBr) 2960, 1715, 1665, 1394, 1321 cm^{-1}; ^1H NMR ($CDCl_3$) 7.5–7.43 (m, 5 H), 5.36 (d, J = 2 Hz, 1 H), 2.92 (ddd, J = 2.2 Hz, 5.2 Hz, 18.2 Hz, 1 H), 2.34 (dd, J = 2.5 Hz, 18.2 Hz, 1 H), 2.38–1.5 (m, 7 H), 1.24 (s, 3 H); ^{13}C NMR ($CDCl_3$) 208.4, 195.7, 163.8, 135.5, 130.4, 130.0, 127.5, 118.2, 60.3, 45.3, 39.9, 33.3, 28.2, 25.5, 18.3; MS, *m/z* (relative intensity) 286 (M^+, 62), 176 (100), 148 (50), 91 (20), 85 (20), 67 (93); exact mass calcd for $C_{17}H_{18}O_2S$ 286.103, obsd 286.104. Anal. Calcd for $C_{17}H_{18}O_2S$: C, 71.33; H, 6.29; S, 11.19. Found: C, 70.99; H, 6.52; S, 10.98.

***trans*-3-(Phenylthio)-5,6,4a,8a-tetrahydro-8a-methylnaphthalene-1,8(4*H*,7*H*)-dione (*trans*-23).** To a well-stirred solution of **16** (2.6 g, 9.56 mmol) in 25 mL of benzene was added a 10% aqueous solution of tetrabutylammonium hydroxide (2.73 g in 27.3 mL of water, 10.52 mmol) followed by iodomethane (2.98 mL, 47.8 mmol), and the solution was stirred for 20 h. Then, the solvent benzene was removed and the crude product was extracted with ether. At this stage any crystallized tetrabutylammonium iodide was filtered off and the organic phase was dried (Na_2SO_4) and column chromatographed to give *trans*-**23** (mp 115–119 °C) and *cis*-**23** in a 9:4 ratio with 89% yield. In several runs *trans*-**23** was also obtained in pure form from the crude reaction mixture by crystallization from 25% ethyl acetate–hexane.

***trans*-23**: IR (KBr) 3320, 2950, 1660, 1150 cm^{-1}; ^1H NMR ($CDCl_3$) 7.50–7.40 (m, 5 H), 5.40 (d, J = 0.8 Hz, 1 H), 2.75–1.60 (m, 9 H), 1.37 (s, 3 H); MS, *m/z* (relative intensity) 286 (M^+, 36), 176 (60), 148 (39), 109 (21), 85 (35), 67 (73), 28 (100); exact mass calcd for $C_{17}H_{18}O_2S$ 286.103, obsd 286.099.

***trans*-3-(Phenylthio)-5,6,4a,8a-tetrahydro-4a,8a-dimethylnaphthalene-1,8(4*H*,7*H*)-dione (34).** To a well-stirred solution of methyl 3-(phenylthio)-4-(3-oxo-1-methylcyclohexyl)-but-2-enoate (159 mg, 0.5 mmol) in 10 mL of THF under nitrogen at room temperature was added potassium *tert*-butoxide (59 mg, 0.53 mmol). After 1 h, iodomethane (0.16 mL, 2.5 mmol) was added and stirring continued for another 3 h. The solvent was removed under reduced pressure and the crude product was extracted with ether. The ether extract was washed with 10% aqueous NH_4Cl solution. The organic phase was dried (Na_2SO_4) and the solvent was removed. The crude product was column chromatographed (eluant, 50% ethyl acetate–hexane) to give **34** in 65% yield. Compound **34** was crystallized from ethyl acetate–hexane as a white crystallization solid (mp 183–185 °C): IR (KBr) 2960, 1714, 1648, 1582 cm^{-1}; ^1H NMR ($CDCl_3$) 7.45–7.42 (m, 5 H), 5.24 (d, J = 2.2 Hz, 1 H), 2.79–2.61 (m, 1 H), 2.74 (ddd, J = 17.8 Hz, 2.2 Hz, 0.8 Hz, H_a), 2.12 (d, J = 17.8 Hz, H_b), 2.16–1.85 (m, 5 H), 1.41 (s, 3 H), 1.02 (d, J = 0.8 Hz, 3 H); MS, *m/z* (relative intensity) 300 (M^+, 61), 176 (94), 147 (43), 110 (27), 85 (37), 67 (100); exact mass calcd for $C_{18}H_{20}O_2S$ 300.118, obsd 300.115. Anal. Calcd for $C_{18}H_{20}O_2S$: C, 72.00; H, 6.67; S, 10.67. Found: C, 71.66; H, 6.71; S, 10.88.

***cis*-3-(Phenylthio)-8-methoxy-4a,5,6,8a-tetrahydro-8a-methylnaphthalen-1(1*H*)-one (26).** To a well-stirred solution of *cis*-**23** (1.14 g, 4 mmol) in 30 mL of dry CH_3OH at room temperature was added a catalytic amount of *p*-toluenesulfonic acid and trimethyl orthoformate (2.19 mL, 20 mmol). After 20 h, the solvent was removed under vacuum and the crude product was dissolved in ether. The ether extract was washed with 10 mL of saturated aqueous $NaHCO_3$ and the extracts were dried (Na_2SO_4). The crude viscous mass was column chromatographed (eluant, 15% ethyl acetate–hexane) to give **26** in 87% yield: IR (film) 2936, 1660, 1598 cm^{-1}; ^1H NMR ($CDCl_3$) 7.43 (s, 5 H), 5.45 (br, 1 H), 4.63 (t, J = 4 Hz, 1 H), 3.5 (s, 3 H), 2.73–1.53 (m, 7 H), 1.4 (s, 3 H); MS, *m/z* (relative intensity) 300 (M^+, 14), 273 (3), 191 (5), 176 (3), 153 (19), 124 (40), 109 (35), 43 (100); exact mass calcd for $C_{18}H_{20}O_2S$ 300.118, obsd 300.118.

***cis*-3,4,4a,8a-Tetrahydro-8a-methylnaphthalene-1,6-(2*H*,5*H*)-dione (27).** To a well-stirred solution of **26** (150 mg, 0.5 mmol) in 15 mL of dry ether under nitrogen was added lithium aluminum hydride (5.7 mg, 0.6 mmol). After 30 min, once again lithium aluminum hydride (5.7 mg, 0.6 mmol) was added and refluxed for 60 min. The unreacted lithium aluminum hydride was destroyed by adding 5 mL of ethyl acetate. The reaction mixture was washed with 5 mL of 10% aqueous HCl and the ether layer was dried (Na_2SO_4). The solvent was removed under vacuum and the crude product was treated with 20% HCl in THF and stirred for 24 h. Then the solvent was removed and the crude product was extracted with ether. The ether extracts were dried (Na_2SO_4) and the solvent was removed. The crude product was column chromatographed (eluant, 20% ethyl acetate–hexane) to give **27** in 71% yield: IR (KBr) 2960, 1708, 1670 cm^{-1}; ^1H NMR ($CDCl_3$) 6.05 (d, J = 10 Hz, 1 H), 6.65 (d, J = 10 Hz, 1 H), 1.47 (s, 3 H), 1.6–2.2 (m, 4 H), 2.2–2.6 (m, 5 H); MS, *m/z* (relative intensity) 178 (M^+, 24), 150 (86), 135 (75), 121 (97), 109 (100); exact mass calcd for $C_{11}H_{14}O_2$ 178.099, obsd 178.099.

***trans*-3′,4′,4a′,8a′-Tetrahydro-8a′-methyl-6′-(phenylthio)-spiro[1,3-dioxolane-2,1′(2′*H*)-naphthalen]-8′(5′*H*)-one (30).** To a well-stirred solution of trans-**23** (1.14 g, 4 mmol) in 50 mL of benzene were added a catalytic amount of *p*-toluenesulfonic acid and ethylene glycol (0.37 g, 6 mmol). The reaction mixture was refluxed on a Dean–Stark apparatus. After 4 h, once again ethylene glycol (0.12 g, 2 mmol) was added and reflux continued for 2 h more. The solvent was removed and the residue was column chromatographed (eluant, 25% ethyl acetate–hexane) to give **30** (mp 128–130 °C) in 83% yield: IR (KBr) 2948, 1660, 1580 cm^{-1}; ^1H NMR ($CDCl_3$) 7.33 (s, 5 H), 5.27 (br, 1 H), 4.4–3.7 (m, 4 H), 2.6–2.0 (m, 3 H), 2.7–1.9 (m, 6 H), 1.2 (s, 3 H); MS, *m/z* (relative intensity) 330 (M^+, 50), 262 (9), 220 (49), 176 (20), 139 (41), 111 (88), 28 (100); exact mass calcd for $C_{19}H_{22}O_3S$ 330.129, obsd 330.132.

***trans*-3′,4,4a′,8a′-Tetrahydro-8a′-methyl-6′-methoxy-spiro[1,3-dioxolane-2,1′(2′*H*)-naphthalen]-8′(5′*H*)-one (31).** To a well-stirred solution of **30** (1.32 g, 4 mmol) in 15 mL of dry CH_3OH was added sodium methoxide (0.87 g, 16 mmol), and the solution was refluxed for 20 h. The solvent was removed under vacuum, treated with 10 mL of saturated aqueous $NaHCO_3$ solution, and extracted with ether. The ether extracts were dried (Na_2SO_4) and the solvent was removed. The crude product was column chromatographed (eluant, 30% ethyl acetate–hexane) to give **31** in 96% yield: IR (KBr) 2956, 1664, 1618 cm^{-1}; ^1H NMR ($CDCl_3$) 5.15 (s, 1 H), 4.47–3.87 (m, 4 H), 3.65 (s, 3 H), 2.47–2.03 (m, 3 H), 1.83–1.30 (m, 6 H), 1.22 (s, 3 H); MS, *m/z* (relative intensity) 252 (M^+, 40), 237 (16), 209 (27), 164 (17), 140 (24), 113 (41), 86 (100); exact mass calcd for $C_{14}H_{20}O_4$ 252.136, obsd 253.138.

***trans*-3,4,4a,8a-Tetrahydro-8a-methylnaphthalene-1,6-(2*H*,5*H*)-dione (32).** To a well-stirred solution of **31** (165 mg, 0.5 mmol) in 15 mL of dry ether under nitrogen was added lithium aluminum hydride (5.7 mg, 0.6 mmol). After 30 min, once again lithium aluminum hydride (5.7 mg, 0.6 mmol) was added, and the solution was refluxed for 1 h. Then, the excess lithium aluminum hydride was destroyed by adding 5 mL of ethyl acetate. The reaction mixture was washed with 10% aqueous HCl and the organic layer was dried (Na_2SO_4). The solvent was removed under vacuum, the crude product was treated with 20% HCl–THF, and the solution was stirred for 20 h. Then, the solvent was removed and the crude product was extracted with ether. The ether extracts were dried (Na_2SO_4) and the solvent was removed. The crude product was column chromatographed (eluant, 30% ethyl acetate–hexane) to give **32** (mp 65–67 °C) in 74% yield: IR (KBr) 2950, 1705, 1680 cm^{-1}; ^1H NMR ($CDCl_3$) 5.88 (d, J = 10 Hz, 1 H), 7.5 (d, J = 10 Hz, 1 H), 2.9–1.47 (m, 9 H), 1.33 (s, 3 H);

MS, m/z (relative intensity) 178 (M^+, 32), 150 (64), 134 (92), 121 (76), 109 (64), 28 (100); exact mass calcd for $C_{11}H_{14}O_2$ 178.099, obsd 178.100.

***cis*-8-Methyl-3,4,4a,8a-tetrahydro-8a-methylnaphthalene-1,6(2*H*,5*H*)-dione (35).** To a well-stirred mixture of **26** (150 mg, 0.5 mmol) in 20 mL of ether under nitrogen at 0 °C was added 0.43 mL of 1.4 M CH_3Li (0.6 mmol). After 2 h, the reaction mixture was washed with 5 mL of 10% aqueous NH_4Cl solution. The ether extracts were dried (Na_2SO_4) and the solvent was removed under vacuum. The crude product was stirred in 20 mL of 10% HCl–THF for 16 h. The solvent was removed under reduced pressure and the crude product was extracted with ether. The ether extracts were dried (Na_2SO_4) and the solvent was removed. The crude product was column chromatographed (eluant, 30% ethyl acetate–hexane) to give **35** (mp 96–98 °C) in 78% yield: IR (KBr) 2960, 1710, 1664, 1620 cm^{-1}; ^1H NMR ($CDCl_3$) 5.88 (q, J = 2 Hz, 1 H), 2.62–1.55 (m, 9 H), 1.77 (d, J = 2 Hz, 3 H), 1.4 (s, 3 H); MS, m/z (relative intensity) 192 (M^+, 5), 164 (79), 149 (43), 135 (40), 123 (100); exact mass calcd for $C_{12}H_{16}O_2$ 192.115, obsd 192.113.

***trans*-3,4,4a,8a-Tetrahydro-8,8a-dimethylnaphthalene-1,6(2*H*,5*H*)-dione (36).** To a well-stirred solution of **30** (165 mg, 0.5 mmol) in 20 mL of ether under nitrogen at 0 °C was added 0.43 mL of CH_3Li (0.6 mmol). After 2 h, the reaction was washed with 5 mL of 10% aqueous NH_4Cl solution. The ether extracts were dried (Na_2SO_4) and the solvent was removed under vacuum. The crude product was stirred in 10% HCl–THF for 16 h. The solvent was removed and the crude product was extracted with ether. The ether extracts were dried (Na_2SO_4) and the solvent was removed. The crude product was purified by column chromatography (eluant, 30% ethyl acetate–hexane) to give **36** in 83% yield: IR (film) 2948, 1706, 1660, 1615 cm^{-1}; ^1H NMR ($CDCl_3$) 5.83 (q, J = 2 Hz, 1 H), 3.18–1.8 (m, 9 H), 2.17 (d, J = 2 Hz, 3 H), 1.33 (s, 3 H); MS, m/z (relative intensity) 192 (M^+, 34), 164 (57), 149 (33), 135 (36), 123 (43), 112 (84), 28 (100); exact mass calcd for $C_{12}H_{16}O_2$ 192.115, obsd 192.116.

***cis*-5,6,4a,8a-Tetrahydro-3,8a-dimethylnaphthalene-1,8-(4*H*,7*H*)-dione (37).** To a well-stirred mixture of CuI (110 mg, 0.58 mmol) in 30 mL of dry ether under nitrogen at −78 °C was added 1.4 M CH_3Li (0.79 mL, 1.1 mmol). After 5 min, **26** (0.159 mg, 0.5 mmol) was added and stirring was continued for another 1 h. The reaction mixture was quenched at −78 °C with 5 mL of saturated aqueous NH_4Cl solution and then brought to room temperature. The aqueous phase was separated and washed with ether, and the washings were added to the organic phase. The organic phase was dried (Na_2SO_4) and the solvent was removed under vacuum. The crude product was stirred in 10% HCl–THF solution for 2 h. Then the THF was removed under vacuum and extracted with ether. The ether extracts were dried (Na_2SO_4) and the solvent was removed under vacuum. The crude product was column chromatographed (eluant, 30% ethyl acetate–hexane) to give **37** (mp 85–87 °C) in 89% yield: IR (KBr) 2940, 1712, 1645, 1630 cm^{-1}; ^1H NMR ($CDCl_3$) 5.83 (q, 1 H), 3.00–1.53 (m, 9 H), 1.98 (d, 3 H); MS, m/z (relative intensity) 192 (M^+, 37), 164 (21), 135 (11), 123 (27), 107 (19), 82 (100); exact mass calcd for $C_{12}H_{16}O_2$ 192.115, obsd 192.114.

***cis*-3,4,5,6,4a,8a-Hexahydro-3,3,8a-trimethylnaphthalene-1,8(2*H*,7*H*)-dione (39).** The reaction was carried out as above except that the reaction mixture was quenched at room temperature. The crude product was column chromatographed (eluant, 25% ethyl acetate–hexane) to give **39** (mp 56–58 °C) in 91% yield: IR (KBr) 2970, 1705, 1690, 1240 cm^{-1}; ^1H NMR ($CDCl_3$) 2.77–1.13 (m, 11 H), 1.4 (s, 3 H), 0.83 (s, 3 H), 1.03 (s, 3 H); MS, m/z (relative intensity) 208 (M^+, 53), 193 (56), 175 (30), 165 (38), 152 (96), 139 (41), 124 (81), 28 (100); exact mass calcd for $C_{13}H_{20}O_2$ 208.146, obsd 208.143.

***trans*-3′,4′,4a′,8a′-Tetrahydro-8a′,6′-dimethylspiro[1,3-dioxolane-2,1′(2′*H*)-naphthalen]-8′(5′*H*)-one (38).** To a well-stirred solution of CuI (110 mg, 0.58 mmol) in dry ether under nitrogen at −78 °C was added 1.4 M CH_3Li (0.79 mL, 1.1 mmol). After 5 min, **30** (165 mg, 0.5 mmol) was added and stirring continued for another 1 h. The reaction mixture was quenched at −78 °C with 5 mL of saturated NH_4Cl solution and then brought to room temperature. The aqueous phase was separated and washed with ether, and the washings were added to the organic phase. The organic phase was dried (Na_2SO_4) and the solvent was removed under vacuum. The crude product was column chromatographed (eluant, 25% ethyl acetate–hexane) to give **38** (oil) in 90% yield: IR (film) 2940, 1670, 1640 cm^{-1}; ^1H NMR ($CDCl_3$) 5.68–5.55 (br, 1 H), 4.4–3.85 (m, 4 H), 2.45–1.28 (m, 9 H), 1.87 (d, J = 2 Hz, 3 H), 1.17 (s, 3 H); MS, m/z 236 (relative intensity) (M^+, 21), 221 (14), 193 (19), 148 (27), 113 (25), 86 (100); exact mass calcd for $C_{14}H_{20}O_3$ 236.141, obsd 236.139.

***trans*-3′,4′,6′,6′,4a′,8a′-Hexahydro-6′,6′,8a′-trimethylspiro-[1,3-dioxolane-2,1′(2′*H*)-naphthalen]-8′(5′*H*)-one (40).** The reaction was carried out as above except that the reaction was quenched at room temperature. The crude product was column chromatographed (eluant, 10% ethyl acetate–hexane) to give **40** (oil) in 93% yield: IR (neat) 2956, 1712, 1170 cm^{-1}; ^1H NMR ($CDCl_3$) 4.33–3.73 (m, 4 H), 2.6–1.07 (m, 11 H), 1.23 (s, 3 H), 0.98 (s, 6 H); MS, m/z (relative intensity) 252 (M^+, 19), 209 (16), 151 (19), 112 (98), 99 (79), 86 (93), 28 (100); exact mass calcd for $C_{15}H_{24}O_3$ 252.173, obsd 252.172.

***cis*-5,6,4a,8a-Tetrahydro-8a-methylnaphthalene-1,8-(4*H*,7*H*)-dione (41).** To a well-stirred solution of **26** (150 mg, 0.5 mmol) in 20 mL of absolute ethanol was added 1.0 g of Raney nickel. After 3 h, the catalyst was filtered followed by removal of solvent. The crude product was extracted with ether and washed with 10 mL of water. The ether extracts were dried (Na_2SO_4) and the solvent was removed. The crude product was treated with 10% HCl–THF and stirred for 2 h. Then the solvent was removed and extracted with ether. The ether extracts were dried (Na_2SO_4) and the solvent was removed under vacuum. The crude product was column chromatographed to give **41** in 63% yield: IR (KBr) 2910, 1692, 1642 cm^{-1}; ^1H NMR ($CDCl_3$) 6.92–6.83 (m, 1 H), 6.01 (ddd, J = 1.3 Hz, 3.0 Hz, 10.2 Hz, 1 H), 2.85–2.55 (m, 1 H), 2.48–1.50 (m, 8 H), 1.34 (s, 3 H); MS, m/z (relative intensity) 17, (M^+, 52), 150 (25), 134 (11), 122 (20), 82 (19), 68 (100); exact mass calcd for $C_{11}H_{14}O_2$ 178.099, obsd 178.100.

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Registry No. 1, 102736-25-4; (*E*)-**1a**, 53700-03-1; (*Z*)-**1a**, 53700-05-3; **5a**, 105090-01-5; **5b**, 105090-02-6; **6a**, 105090-03-7; **6b**, 105090-04-8; **9a**, 105090-05-9; **9b**, 105090-06-0; **10a**, 105090-07-1; **11a**, 105090-08-2; **12a**, 105090-09-3; **12b**, 105090-10-6; **13a**, 105090-12-8; **13b**, 105090-13-9; **16**, 105090-14-0; **18**, 105090-15-1; **19**, 105090-16-2; **20**, 105090-17-3; **21**, 105090-18-4; **22**, 105090-19-5; *cis*-**23**, 105090-21-9; *trans*-**23**, 105090-22-0; **24**, 105090-20-8; **26**, 105090-24-2; **27**, 54584-41-7; **30**, 105090-25-3; **31**, 105090-26-4; **32**, 71099-14-4; **34**, 105090-23-1; **35**, 105090-27-5; **36**, 105090-28-6; **37**, 105090-29-7; **38**, 105090-31-1; **39**, 105090-30-0; **40**, 105090-32-2; **41**, 105090-33-3; 2-cyclopenten-1-one, 930-30-3; 3-methyl-2-cyclohexen-1-one, 1193-18-6; 3-(phenylthio)-2-methyl-1-(trimethylsiloxy)-1-ethoxy-1,3-butadiene, 105090-11-7; *cis*-2,3,4a,8a-tetrahydro-8a-methyl-6-(phenylthio)naphthalene-1,8-(4*H*,7*H*)-dione, 105090-21-9; methyl vinyl ketone, 78-94-4; 2-cyclohexen-1-one, 930-68-7; 2-methyl-2-cyclohexen-1-one, 1121-18-2; 4,4-dimethyl-2-cyclohexen-1-one, 1073-13-8.