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On the Use of β-Phenylsulfinyl-α,β-Unsaturated Carbonyl Dienophiles in Diels–Alder Reactions

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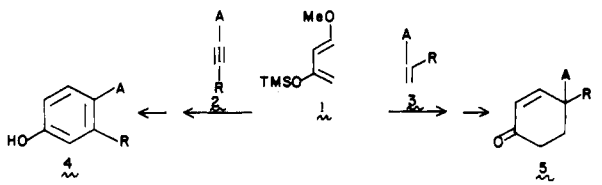
Contribution from the Department of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260. *Received January 12, 1979*

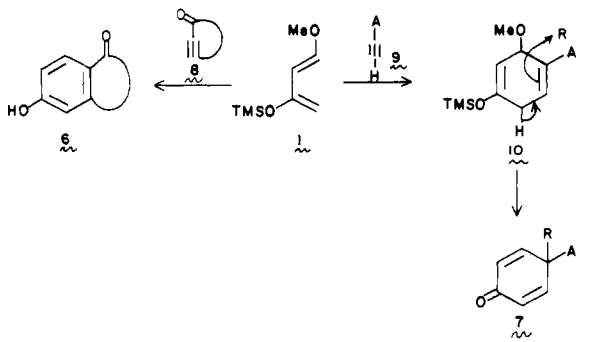
Abstract: The use of β-phenylsulfinyl-α,β-unsaturated carbonyl dienophiles as synthetic equivalents of α,β-ethynyl carbonyl systems has been demonstrated. The sulfoxides were prepared by oxidation of the sulfides, which in turn were obtained from the β-dicarbonyl systems by standard methods. A key feature of the scheme is that the phenylsulfinyl group does not compete with the carbonyl function in determining the regiochemistry of cycloaddition with the highly nucleophilic *trans*-1-methoxy-3-trimethylsilyloxy-1,3-butadiene. Application of the methodology to the synthesis of the disodium prephenate dimethyl acetals is described.

Background

In a preceding paper[1a] we have shown that cycloaddition of **1**, with dienophiles such as **2** and **3**, leads to *p*-acylphenols and 4-acylcyclohex-2-en-1-one systems such as **4** and **5**, respectively.



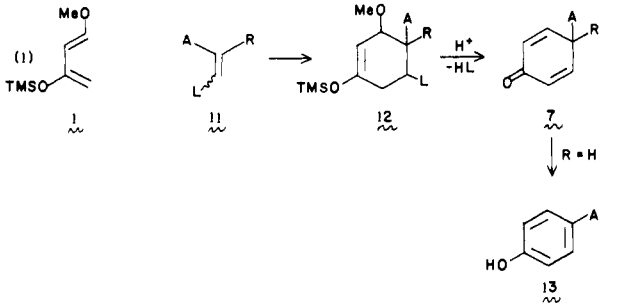
In this paper we describe the results of research directed to a Diels–Alder-based synthesis of phenols of the type **6** and cyclohexadienones[2] such as **7**.[2a,b] For the synthesis of **6**, by the



cycloaddition logic above, there would be required cycloalkynones such as **8**, which are in the case of five-, six-, and seven-membered rings, in fact, inaccessible. Implementation of the aforedescribed design for reaching **7** using a feasible dienophile such as **9** would require a subsequent introduction (base-catalyzed alkylation,[3] etc.) of the "R" group onto the normal Diels–Alder adduct, **10**, or a derivative thereof. In view of the virtually certain aromatization of systems such as **10**, this scheme would be improbable of general success.

In the preceding paper[1b] we described an approach to systems such as **7**, using a 4-phenylseleno derivative of **1**. Unfortunately, the quality of the Diels–Alder cycloaddition step, with several dienophiles, left much to be desired. Accordingly, we investigated the possibility of an alternative strategy which is set forth herein.

The plan was to modify the dienophile with a function, L, such that, after cycloaddition, elimination of "HL" would provide a route to **7**. In the case of R = H, the aromatization



of **7** to phenol type **13** would be expected, thus embracing the special case of **1** → **6** discussed above.

The conditions for the reduction of this scheme to practice are several. Thus, the synthesis of the generalized dienophile **11** must be straightforward. Furthermore, the quality of the cycloaddition step of **1** with what must minimally be a trisubstituted olefin must not be undermined. *Moreover, the leaving group function, L, which provides the access to the additional unit of unsaturation must not, in itself, compete*

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with the A function for control of the regiochemistry of the cycloaddition step.[4a] Finally, the elimination of HL must be facile, and must allow for the survival of the very sensitive target system, **7**. A variety of possible L groups were investigated. Eventually it was found that the arrangement L = PhS(O) nicely optimized the various requirements.[4b,c]

Results

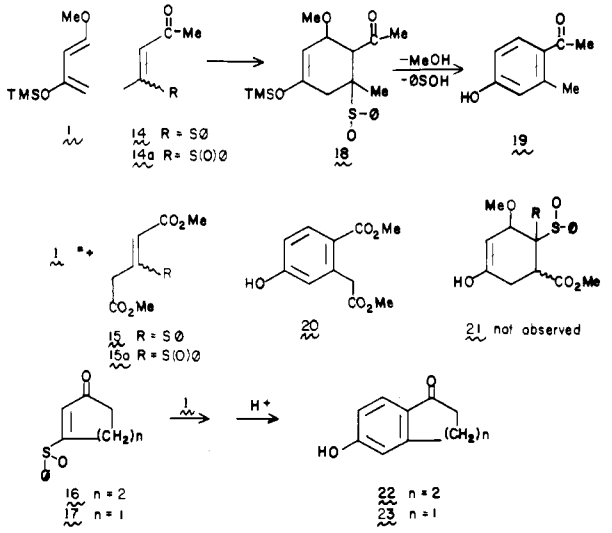
(1) A Synthesis of *p*-Acylphenols. The required sulfoxides were prepared in each case by controlled oxidation of the sulfides. The latter were prepared by standard methods, relying heavily on chemistry developed by Ireland and Marshall,[4d] as described in the Experimental Section.

Cycloaddition of **14a** with excess **1** was carried out in toluene under reflux for 67 h. The precise status of the adduct at this stage was difficult to surmise by NMR analysis, owing to the large excess of diene and decomposition products therefrom. Acidic hydrolysis followed by silica gel chromatography afforded a 75% yield of phenol **19**. In a similar way, cycloaddition of the β-phenylsulfinyl derivative **15a**, derived from **15**, afforded phenol **20**, though only in 42% yield.

In neither of these cases was there any indication of products which might have arisen from adducts of the type **21**. Of course, the yields of phenols were far from quantitative. Since the ultimate fate of adducts such as **21**, were they produced, is hardly clear, one cannot rule out the possibility that such adducts were produced in the reaction.

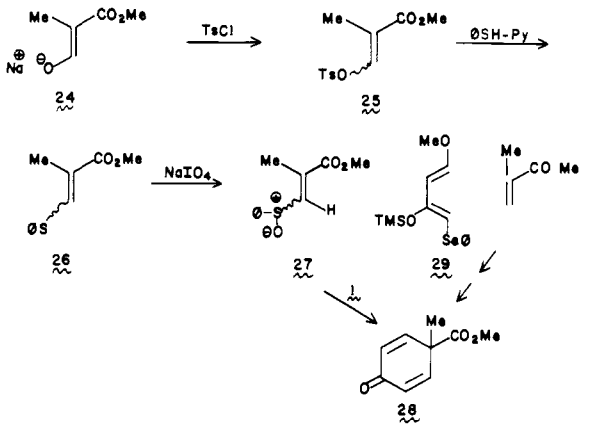
Substantial competition from the cycloaddition mode leading to **21** would have been unlikely in the light of results of preliminary model studies of the comparably hindered dienophiles, methyl vinyl ketone and phenyl vinyl sulfoxide.[5] As described previously,[1a] methyl vinyl ketone reacts with diene **1** at ca. 75–80 °C. On the other hand, the cycloaddition of **1** with phenyl vinyl sulfoxide required temperatures of ca. 135–150 °C.[6] *Thus, at least toward parent diene, **1**, it is clear that a carbonyl group constitutes a more potent dienophile activator than a sulfoxide.*

In this connection, it was of interest to examine the cycloaddition of dienophiles **16** and **17** with diene **1**. In these cases, the steric factor would favor control by the sulfoxide. In the event, cycloaddition of **16** with **1** (xylene, reflux, 24 h)



afforded, after suitable treatment, a 90% yield of tetralone **22**.[7] Similarly cycloaddition of **17** with **1** afforded indanone **23**[8] in 68% yield. While these particular phenols were well known via other syntheses, it would appear that the Diels–Alder route described here might provide a versatile entry to such systems with otherwise difficultly accessible substitutions on the aromatic ring, and would allow for modification of ring size and substituents on the reduced B ring. In practice, these possibilities were not explored.

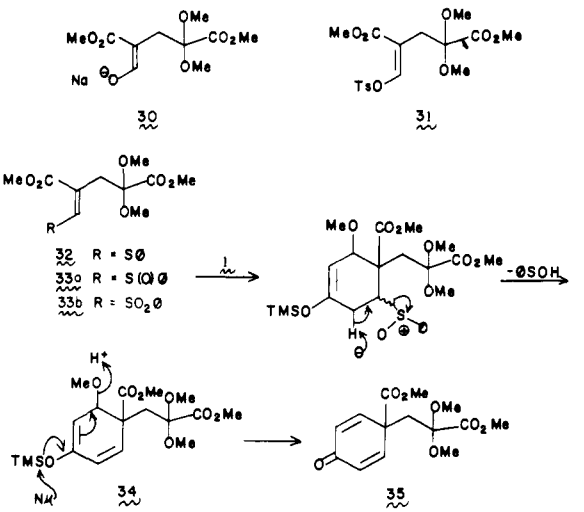
(2) A Diels–Alder Entry to the Prephenate Series. We next investigated the cycloaddition of diene **1** with dienophile **27**. The latter was obtained in poor yield in three steps from the sodium salt (**24**) of the hydroxymethylene derivative of methyl



propionate,[2b] in the manner shown. The weakest step in the synthesis of **28** was in the displacement of enol tosylate **25** to afford vinyl sulfide **26**. At this stage we were only concerned with the feasibility of the Diels–Alder route to cyclohexadienones and did not attempt to optimize the synthesis of the dienophile. Reaction of diene **1** with dienophile **27** was carried out in toluene under reflux for 50 h. The crude product, whose nature was difficult to define at this stage owing to the large excess of **1** which was employed, was treated in the usual way **1a** with aqueous HCl–THF. There was thus obtained, after silica gel chromatography, an 83% yield of **28**. This compound had previously been obtained in our laboratory by a sequence starting with the cycloaddition of modified diene **29**[1b] with methyl methacrylate. The yield via **27** was far superior and it was on the β-phenylsulfinyl substituted dienophiles that we placed our reliance to reach prephenic acid.[9a,b]

The route we hoped to follow is shown below. Our target system was dienone **35**, which was to be assembled by a Diels–Alder reaction between diene **1** and dienophile **33a**. It was hoped that methods might be developed wherein **35** could be converted to prephenic acid.

The dienophile **33a** was synthesized along the same lines which we had used for **27**, though in much improved yield. Enol tosylate **31** was obtained in 71% yield from sodium salt **30**.[9b]

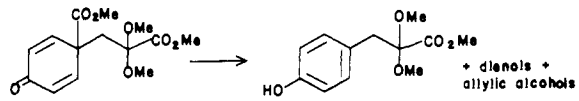


Compound **31** was converted to the thiophenoxy derivative **32** in 85% yield. Oxidation of **32** with sodium metaperiodate afforded **33a** (in ca. 80% yield). There were also isolated traces

of sulfone **33b**. Cycloaddition of **33a** with **1** was carried out in toluene under reflux for 72 h. The materal which resulted was complex, but our presumption, on the basis of NMR analysis, was that it was best represented by structure **34**, wherein the elements of phenylsulfenic acid had been eliminated under the conditions of the Diels–Alder reaction. The presumed **34** was treated with dilute acid. Silica gel chromatography of the material afforded a 58% yield of the desired dienone **35**, mp 73–75 °C. The diethyl ester diethyl acetal version of **35** had previously been prepared by Plieninger by dehydrogenation of an enone precursor.[9a,b,10]

The reduction of the dienone system of **35** to the corresponding dienol was first attempted with sodium borohydride. In our hands,[11] this reduction gives rise to a serious mixture of products. In addition to epimeric dienols, there could be detected by NMR and mass spectral analysis epimeric tetrahydro (i.e., singly allylic alcohols) products. The major isolated product, ca. 40% yield, was the phenol **36**. Whether this actually arose from prior delivery of "hydride" to the ester or whether it arose from adventitious nonreductive nucleophile (for instance, hydroxide) was not clarified.

It was hoped that one might suppress this deacylation-aromatization by using the more selective and hindered reducing agent, lithium tri-*tert*-butoxyaluminum hydride. In the event, reaction of **35** with this reagent afforded **36** as the major product.



35 **36**

Progress was realized when dienone **35** was subjected to the action of 9-BBN[12] in THF at room temperature. This reduction afforded the dienols **37** (mp 96–98 °C; R_f 5% MeOH–$CHCl_3$ 0.65) and **38** (oil, R_f 5% MeOH–$CHCl_3$ 0.50) in 26 and 35% isolated yields, respectively.

The stereochemical assignment of these stereoisomers was secured by correlation with a crystalline compound of unambiguous configuration which did, *in fact*, lead to prephenic acid.[13c] Thus, the structures of **37** and **38** are known with certainty.

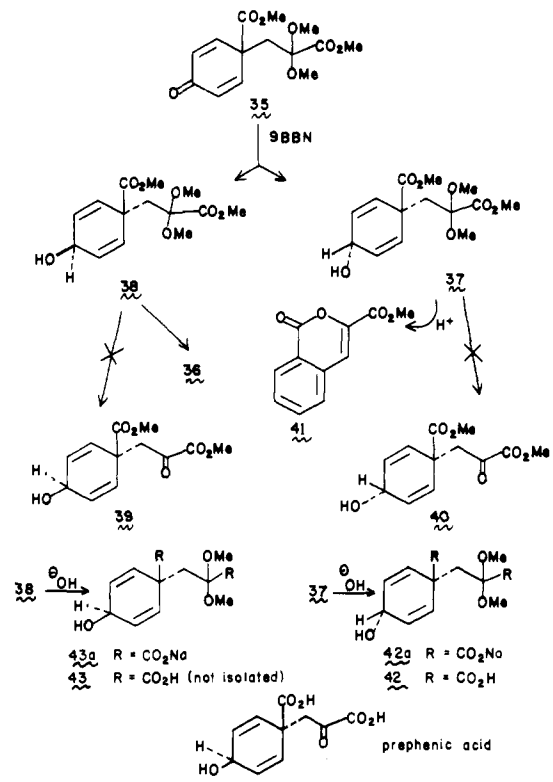
It was our intention to cleave the acetal linkage of **38** to afford prephenic acid dimethyl ester (**39**), an unknown substance. Unfortunately, all efforts to produce **39** by treatment of **38** with various acids were unsuccessful. Similar difficulties were encountered in attempts to obtain what would have been dimethyl epiprephenate (**40**) from **37**. Among the products which could be recognized from such treatments were phenol **36** and benzopyrone **41**. Similar difficulties undermined various attempts to achieve deketalization at the stage of **35**.

Compounds **37** and **38** could be saponified with 2 equiv of sodium hydroxide in aqueous THF. The disodium salts **42a** and **43a** could be obtained in hand. Their NMR spectra measured in D_2O solution (see Experimental Section) were completely supportive of their proposed structure.

All attempts to isolate either free prephenic acid dimethyl acetal (**43**) or epiprephenic acid dimethyl acetal (**42**) from sodium salts **43a** and **42a**, respectively, were fruitless. Even at pH 3.5, each salt was rapidly converted to phenol **36**.

Our closest approach in this regard was to treat **43a** with an Amberlite resin at −60 °C, *followed immediately* by treatment with excess diazomethane. There was thus regenerated the ketal diester **38**, suggesting that the free diacid acetal **43** does have a finite viability.

In summary, the general chemical objectives stated at the outset were achieved. However, the desired synthesis of prephenic acid was unsuccessful. The total synthesis of prephenic acid in a manner which took cognizance of the lessons accumulated during these studies is described in the next paper of this series.[13c] Another application of these dienophiles to the total synthesis of griseofulvin will be described.[13d]



Experimental Section[14]

Preparation of 4-Phenylthiopent-3-en-2-one (14). A solution of 4-chloropent-3-en-2-one (3.6 g, 0.030 mol) and thiophenol (7.00 g, 0.063 mol) in 10 mL of pyridine was heated at 100 °C overnight. Evaporation of the volatiles afforded a residue which was diluted with water. This mixture was extracted with chloroform. Evaporation of the dried ($MgSO_4$) chloroform extracts afforded a residue which was chromatographed on 200 g of silica gel. Elution with 4:1 hexane–ether provided 1.30 g (23%) of **14**: mp (hexane) 68–69 °C; λ_{max} ($CHCl_3$) 6.02, 6.47 μ; $\delta(CDCl_3)$ 1.83 (s, 3), 2.29 (s, 3), 6.36 (s, 1), 7.2–7.7 (m, 5) ppm.

Anal. Calcd for $C_{11}H_{12}OS$: C, 68.71; H, 6.29. Found: C, 68.86; H, 6.32.

Preparation of 4-Phenylsulfinylpent-3-en-2-one (14a). The thioether **14** (1.150 g, 6 mmol) and sodium metaperiodate (14 g, 0.06 mol) in 20 mL of methanol and 5 mL of water was stirred for 5 days at room temperature. After separation of the insolubles by filtration, the filtrate was diluted with water and extracted with chloroform. The volatiles from the combined, dried ($MgSO_4$) organic phases were evaporated in vacuo and the residue was chromatographed on 100 g of silica gel. Elution with ether gave first 283 mg of recovered **14**. A small fraction (30 mg, 2%) of 4-phenylsulfonylpent-3-en-2-one was next obtained. Finally, there was isolated 811 mg (62%) of sulfoxide **14a** as pale yellow crystals: mp 72–74 °C (hexane–ether); λ_{max} ($CHCl_3$) 5.92, 6.23 μ; $\delta(CDCl_3)$ 2.00 (d, J = 2 Hz, 3), 2.33 (s, 3), 6.60 (q, J = 2 Hz, 1), 7.4–7.7 (m, 3), 7.8–8.0 (m, 2) ppm.

Anal. Calcd for $C_{11}H_{12}O_2S$: C, 63.43; H, 5.81. Found: C, 63.60; H, 5.92.

Preparation of 3-Methyl-4-acetylphenol (19). The sulfoxide **14a** (750 mg, 3.6 mmol) and diene **1** (5.8 g, 35.8 mmol) in 15 mL of toluene was heated under reflux for 67 h. The volatiles were removed in vacuo and the residue was stirred in a solution prepared from 10 mL of 1% aqueous HCl and 40 mL of THF at room temperature for 1 h. The mixture was diluted with water and extracted with chloroform. Evaporation of the volatiles from the dried organic phase afforded a residue which was chromatographed on 150 g of silica gel. Elution with 2:3 ether–hexane afforded 340 mg of phenol **19** as colorless prisms, mp 134–135 °C (lit.[15] 128 °C).

Preparation of Dimethyl 3-Phenylthioglutaconate (15). A solution of dimethyl acetone-1,3-dicarboxylate (6.96 g, 0.004 mol), thiophenol

(8.88 g, 0.08 mol), and *p*-toluenesulfonic acid (0.2 g) in 200 mL of toluene was heated under reflux (with azeotropic removal of water) for 45 h. The reaction mixture was diluted with ether and washed successively with 5% aqueous sodium bicarbonate solution and aqueous brine. Evaporation of the volatiles from the dried organic phase afforded a crude residue of 11.2 g which was chromatographed on 160 g of silica gel. Elution with 20:1 hexane-ethyl acetate afforded 970 mg of a residue which was methyl 3-phenylthiocrotonate. Continued elution with 9:1 hexane-ethyl acetate afforded 5.1 g (81%) of **15:** λ_{max} ($CHCl_3$) 5.72, 5.85, 6.12, 6.22 μ; δ($CDCl_3$) 3.60 (s, 3), 3.72 (s, 3), 3.82 (s, 2), 5.42 (s, 1), 7.2–7.7 (m, 5) ppm.

Preparation of Dimethyl 3-Phenylsulfinylglutaconate (15a). To a solution of **15** (5.66, g, 0.02 mol) in 240 mL of methanol and 60 mL of water was added sodium metaperiodate (44.8 g, 0.21 mol). The reaction mixture was stirred for 96 h and diluted with ether. After separation of the precipitate by filtration through Celite, most of the ether and methanol was evaporated from the filtrate at the water pump. The system was diluted with ether and washed with aqueous brine. Evaporation of the volatiles from the dried ($MgSO_4$) organic phase afforded a residue which was chromatographed on 180 g of silica gel. Elution with 7:3 hexane-ethyl acetate gave 3.72 g (63%) of sulfoxide **15a:** δ($CDCl_3$) 3.53 (s, 3), 3.76 (s, 3), 3.4–3.9 (m, 2), 6.9 (s, 1), 7.4–7.8 (m, 5) ppm.

Preparation of 3-Carbomethoxymethyl-4-carbomethoxyphenol (20). A solution of the sulfoxide **15a** (564 mg, 2 mmol) and diene **1** (2.064 g, 12 mmol) in 8 mL of toluene was heated under reflux for 36 h. There was then added an additional quantity (688 mg, 4 mmol) of diene **1** and heating was continued for an additional 24 h. Evaporation of the volatiles in vacuo left a residue which was treated at room temperature for 30 min with a solution prepared from 2 mL of 1% aqueous HCl and 8 mL of THF. Workup in the usual way afforded a residue which was chromatographed on 25 g of silica gel. Elution with 4:1 hexane-ethyl acetate gave 188 mg (42%) of **20:** mp 111–113 °C; λ_{max} ($CHCl_3$) 2.85, 5.75, 5.85, 6.20, 6.32 μ; δ($CDCl_3$) 3.75, (s, 3), 3.83 (s, 3), 3.95 (s, 2), 6.6–6.8 (m, 2), 7.9 (d, J = 10 Hz, 1) ppm.

Preparation of 3-Phenylsulfinylcyclohex-2-en-1-one (16). A mixture of cyclohexane-1,3-dione (6.72 g, 0.06 mol) and thiophenol (13.2 g, 0.12 mol) in 250 mL of benzene containing 0.2 g of *p*-toluenesulfonic acid was heated under reflux for 5 h with azeotropic removal of water. The reaction mixture was diluted with ether and washed with 5% aqueous sodium bicarbonate, water, and brine. Evaporation of the volatiles from the dried ($MgSO_4$) organic phase gave a residue which was chromatographed on 270 g of silica gel. Elution with 9:1 hexane-ethyl acetate afforded 9.11 g of crude 3-phenylthiocyclohex-2-en-1-one. To a solution of this material (7.36 g, 0.04 mol) in 240 mL of methanol and 60 mL of water was added sodium metaperiodate (85.2 g, 0.4 mol). The reaction mixture was stirred at room temperature for 72 h. Workup in the usual way afforded a residue which was chromatographed on 180 g of silica gel. Elution with 7:3 hexane-ethyl acetate afforded 1.50 g (21%) of 3-phenylsulfonylcyclohex-2-en-1-one. Further elution with 1:1 hexane-ethyl acetate gave 5.05 g (65%) of sulfoxide **16:** δ($CDCl_3$) 1.8–2.6 (m, 6), 6.90 (br s, 1), 7.65 (m, 5) ppm.

Preparation of 6-Hydroxy-1-tetralone (22). The sulfoxide **16** (220 mg, 1 mmol) and diene **1** (1.032 g, 6 mmol) in 4 mL of xylene was heated under reflux for 24 h. An additional 344 mg (2 mmol) of diene **1** was added and heating was continued for an additional 24 h. Workup in the usual way afforded a residue of 565 mg. Chromatography on 50 g of silica gel afforded 147 mg (90%) of the known **22:** mp 150–152 °C (lit.[7] 150–152 °C); λ_{max} ($CHCl_3$) 2.75, 6.00, 6.23, 6.35 μ.

Preparation of 3-Phenylsulfinylcyclopent-2-en-1-one (17). This was prepared in a manner analogous to that used for **16.** From 3.00 g of cyclopentane-1,3-dione, 6.6 g of thiophenol, and 40 mg of *p*-TsOH, in 200 mL of benzene, heated under reflux for 48 h, there was obtained after chromatography on 60 g of silica gel and elution with 4:1 hexane-ethyl acetate 2.73 g (48%) of 3-phenylthiocyclopent-2-en-1-one: λ_{max} ($CHCl_3$) 5.92, 6.45 μ; δ($CDCl_3$) 2.3–2.9 (m, 4), 5.60 (br s, 1), 7.3–7.6 (m, 5) ppm.

Oxidation of 1.21 g of this material in 75 mL of methanol and 75 mL of water with 13.56 g of sodium metaperiodate afforded a crude product which was chromatographed on 40 g of silica gel. Elution with 4:1 hexane-ethyl acetate afforded 444 mg of 3-phenylsulfonylcyclohex-2-en-1-one. Further elution with 7:3 hexane-ethyl acetate gave 419 mg of **17:** λ_{max} ($CHCl_3$) 5.82, 6.30 μ; δ($CDCl_3$) 2.53 (br s, m), 6.73 (br s, 1), 7.4–7.8 (m, 5) ppm

Preparation of 5-Hydroxy-1-indanone (23). The reaction was carried out in the same way as described for **22.** From 206 mg (1 mmol) of **17** and 1.376 g (8 mmol) of diene **1** there was obtained a residue which after chromatography on 25 g of silica gel and elution with 9:1 hexane-ethyl acetate gave 100 mg (68%) of the known **23:** mp 183–185 °C (lit.[8] 182 °C; λ_{max} (KBr) 2.95, 6.00, 6.20, 6.30 μ; δ(CD_3)$_2$C=O 2.4–2.9 (m, 5), 6.7–7.00 (m, 2), 7.50 (d, J = 8 Hz, 1) ppm.

Preparation of Methyl 2-Phenylthiomethylenepropionate (26). A mixture of sodium salt **24** (5.52 g, 40 mmol) and triethylamine (12.12 g, 0.12 mol) in 200 mL of ether was cooled to 0 °C. To this was added in increments over 30 min *p*-toluenesulfonyl chloride (11.43 g, 60 mmol). The reaction mixture was stirred at room temperature for 24 h. It was poured into 100 mL of ice-water and extracted with ether. The ether layer was washed with aqueous brine and dried over $MgSO_4$. Evaporation of the volatiles afforded the crude tosylate **25,** which was used directly.

A solution of crude **25** and thiophenol (8.8 g, 0.08 mol) in 150 mL of pyridine was heated at 100 °C for 12 h. The reaction mixture was poured into 150 mL of water and extracted with ether. The ether layer was washed with 5% aqueous HCl, water, and brine. Evaporation of the volatiles from the dried organic phase afforded 4.2 g of residue which was chromatographed on 70 g of silica gel. Elution with 9:1 hexane-ethyl acetate afforded 780 mg (9%) of **26:** λ_{max} ($CHCl_3$) 5.87, 6.21 μ; δ($CDCl_3$) 2.0 (s, 3), 3.72 (s, 3), 7.2–7.5 (m, 5), 7.65 (br s, 1) ppm.

Preparation of Methyl 2-Phenylsulfinylmethylenepropionate (27). To a solution prepared from the thioether **26** (780 mg, 375 mmol) in 40 mL of methanol and 10 mL of water was added 7.98 g (37.5 mmol) of sodium metaperiodate. The reaction mixture was stirred for 84 h at room temperature. After dilution with ether and filtration through Celite, most of the methanol was evaporated in vacuo. The aqueous system was extracted with ether and the ether solution was washed with aqueous brine. Evaporation of the volatiles from the dried organic phase gave 816 mg of crude product. Chromatography on 45 g of silica gel and elution with 7:3 hexane-ethyl acetate afforded 669 mg (80%) of pure **27:** λ_{max} ($CHCl_3$) 5.85, 6.18 μ; δ($CDCl_3$) 2.34 (d, J = 2 Hz, 1), 3.80 (s, 3), 7.20 (m, 2), 7.4–8.0 (m, 5) ppm.

Preparation of 4-Methyl-4-carbomethoxycyclohexadienone (28). A solution of the sulfoxide **27** (244 mg, 1 mmol) and diene **1** (1.032 g, 6 mmol) in 4 mL of toluene was heated under reflux for 24 h. More diene (344 mg, 2 mmol) was added and heating was continued for an additional 26 h. Evaporation of the volatiles in vacuo left a residue which was treated for 30 min at room temperature with a solution prepared from 1 mL of 1% aqueous HCl and 4 mL of THF. Evaporation of the volatiles afforded a residue which was dissolved in 100 mL of ether. The ether layer was washed with aqueous brine and dried over $MgSO_4$. Evaporation of the volatiles afforded a residue which was chromatographed on 25 g of silica gel. Elution with 9:1 hexane-ethyl acetate afforded 137 mg (83%) of **28:**[2b] λ_{max} ($CHCl_3$) 5.78, 6.00, 6.15 μ; δ($CDCl_3$) 1.6 (s, 3), 3.76 (s, 3), 6.30 (d, J = 10 Hz, 2), 7.08 (d, J = 10 Hz, 2) ppm.

Preparation of Dimethyl 2-Tosyloxymethylene-4,4-dimethoxyglutarate (31). A mixture of sodium salts **30**[9a] (9.95 g, 0.037 mol), tosyl chloride (9.50 g, 0.498 mol), and triethylamine (10 g, 0.1 mol) in 100 mL of anhydrous ether was stirred for 41 h from 0 °C to room temperature. The reaction mixture was diluted with water and extracted with ether. The ether layer was dried over $MgSO_4$. Evaporation of the volatiles afforded a residue which was chromatographed on 600 g of silica gel. Elution with ether gave 10.55 g (71%) of **31:** mp 72–74 °C (ether-hexane); λ_{max} ($CHCl_3$) 5.70, 5.80, 6.01, 6.42 μ; δ($CDCl_3$) (250 MHz) 2.50 (s, 3), 2.89 (s, 2), 3.24 (s, 6), 3.73 (s, 3), 3.76 (s, 3), 7.42 (d, J = 8 Hz, 2), 7.73 (s, 1), 7.88 (d, J = 8 Hz, 2) ppm.

Anal. Calcd for $C_{17}H_{22}O_9S$: C, 50.72; H, 5.51. Found: C, 50.97; H, 5.73.

Preparation of Dimethyl 2-Thiophenylmethylene-4,4-dimethoxyglutarate (32). A solution of tosylate **31** (10.55 g, 0.026 mol) and thiophenol (10 g, 0.091 mol) in 50 mL of pyridine was heated at 100 °C for 17 h. The volatiles were evaporated in vacuo and the residue was taken up in chloroform. The chloroform solution was dried over magnesium sulfate. Evaporation of the volatiles in vacuo afforded a residue which was chromatographed on 700 g of silica gel. Elution with 1:1 hexane-ether gave 7.60 g (85%) of thioether **32:** λ_{max} ($CHCl_3$) 5.68, 5.72, 6.27 μ; δ($CDCl_3$) 3.08 (s, 2), 3.36 (s, 6), 3.70 (s, 3), 3.77 (s, 3), 7.4 (m, 5), 7.73 (s, 1) ppm; *m/e* 340 (P).

Preparation of Dimethyl 2-Phenylsulfinylmethylene-4,4-dimethoxyglutarate (33a). The thioether **32** (7.60 g, (0.022 mol) and sodium metaperiodate (53.4 g, 0.23 mol) in methanol (160 mL) and

water (40 mL) was stirred for 5 days at room temperature. The precipitate was separated by filtration. The filtrate was diluted with 500 mL of water and the aqueous system was extracted with 3 × 400 mL of chloroform. The residue obtained upon evaporation of the combined dried organic extracts was chromatographed on 500 g of silica gel. Elution with ether afforded first 339 mg of starting **32.** There was next obtained 295 mg (4%) of sulfone **33b,** mp 115–117 °C. The major fraction (6.85 g, 87%) was sulfoxide **33a,** mp 85–87 °C (ether–acetone).

For **33b:** λ_{max} ($CHCl_3$) 5.70, 5.78, 6.12 μ; δ($CDCl_3$) 3.33 (s, 6), 3.66 (s, 2), 3.73 (s, 3), 3.77 (s, 3), 7.03 (s, 1), 7.5–7.8 (m, 3), 7.9–8.1 (m, 2) ppm.

Anal. Calcd for $C_{16}H_{20}O_8S$: C, 51.60; H, 5.41. Found: C, 51.85; H, 5.60.

For **33a:** λ_{max} ($CHCl_3$) 5.71, 5.77 μ; δ($CDCl_3$) 3.27 (s, 3), 3.43 (s, 3), 3.73 (s, 3), 3.77 (s, 3), 7.03 (s, 1), 7.4–8.0 (m, 1) ppm.

Anal. Calcd for $C_{18}H_{20}O_7S$: C, 53.92; H, 5.66. Found: C, 53.91; H, 5.83.

Preparation of 4-Carbomethoxy-4-(2,2-dimethoxy-2-carbomethoxy)ethylcyclohexadienone (35). A solution of the sulfoxide **33a** (7.85 g, 0.031 mol) and diene **1** (31 g, 0.187 mol) in 100 mL of toluene was heated under reflux for 3 days. The volatiles were removed in vacuo. The residue was treated with a solution prepared from 20 mL of 0.1 N aqueous THF and 80 mL of water for 1 h. Dilution with 500 mL of water was followed by extraction with 3 × 300 mL of chloroform. Evaporation of the volatiles from the combined dried organic extracts afforded a residue which was chromatographed on 800 g of silica gel. Elution with ether afforded 3.8 g (58%) of **35:** mp (ether–hexane) 73–75 °C; λ_{max} ($CHCl_3$) 5.71, 5.98, 6.11 μ; δ($CDCl_3$) 2.57 (s, 2), 3.30 (s, 6), 3.75 (s, 6), 6.33 (d, J = 10 Hz, 2), 7.50 (d, J = 10 Hz, 2) ppm.

Anal. Calcd for $C_{14}H_{18}O_7$: C, 56.37; H, 6.08. Found: C, 56.89; H, 6.27.

Formation of Dienols 37 and 38. To a solution of dienone **35** (3.55 g, 0.0119 mol) in 70 mL of THF was added, at room temperature, a solution of 9-BBN (4.9 g, 0.0218 mol) in 70 mL of THF. The resultant solution was stirred for 1 h at room temperature. Excess reagent was decomposed with 20 mL of methanol, followed by 20 mL of water. The mixture was diluted with 600 mL of water and extracted with 3 × 500 mL of chloroform. The volatiles from the dried combined organic extracts were evaporated in vacuo to afford a residue which was chromatographed on 400 g of silica gel. Elution with ether provided (after discarding early boron-containing fractions) 2.8 g of combined alcohols **39** and **40.** This was rechromatographed on 250 g of silica. Elution with 1% methanol–chloroform afforded 830 mg (23%) of dienol **37,** mp (ether–hexane) 96–98 °C. Continued elution by the same solvent system provided 1.366 g (38%) of dienol **38** as an oil.

For **38:** λ_{max} ($CHCl_3$) 2.70, 2.90 (br), 5.70, 5.81 μ; δ($CDCl_3$) (250 MHz) 2.38 (s, 2), 3.24 (s, 6), 3.68 (s, 3), 3.74 (s, 3), 4.45 (m, $W_{1/2}$ = 12.1 Hz, 1), 5.99 (s, 4) ppm.

For **39:** λ_{max} ($CHCl_3$) 2.83, 5.75, 5.80 μ; δ($CDCl_3$) (250 MHz) 2.54 (s, 2), 3.28 (s, 6), 3.68 (s, 3), 3.74 (s, 3), 4.34 (m, $W_{1/2}$ = 17.4 Hz, 1), 5.86 (d, J = 10.4 Hz, 1), 6.04 (dd, J_1 = 10.4, J_2 = 4.1 Hz, 2) ppm.

Anal. Calcd for $C_{14}H_{20}O_7$: C, 55.99; H, 6.71. Found: C, 56.04; H, 6.90.

Disodium Prephenate Dimethyl Acetal (43a). The dienol **38** (200 mg, 0.67 mmol) in a solution prepared from 4 mL of methanol and 1 mL of water containing 65 mg of sodium hydroxide was stirred at room temperature for 5 days. The volatiles were concentrated in vacuo. The residue was triturated with methanol. Disodium salt **43a** was obtained by filtration (75 mg, 36%): λ_{max} (KBr) 6.09, 6.31 μ; δ (D_2O,DSS) (250 MHz)[16] 2.29 (s, 2), 3.11 (s, 6), 4.51 (m, J_1 = 3.0, J_2 = 1.3 Hz, 1), 5.80 (dd, J_1 = 10.2, J_2 = 3.0 Hz, 2), 5.94 (dd, J_1 = 10.2, J_2 = 1.3 Hz, 2) ppm.

Disodium Epiprephenate Dimethyl Acetal (42a). A solution of dienol **37** (200 mg, 0.67 mmol) in 4 mL of methanol was stirred at room temperature for 5 days. Evaporation to dryness afforded a residue which was triturated with methanol to give, after filtration, disodium salt **42a** (165 mg, 78%): λ_{max} (KBr) 6.16, 6.34 μ; δ(D_2O,DSS) (250 MHz)[16] 2.33 (s, 2), 3.14 (s, 6), 4.38 (m, J_1 = 3.4, J_2 = 0.8 Hz, 1), 5.82 (dd, J_1 = 10.1, J_2 = 3.4 Hz, 2), 5.96 (dd, J_1 = 10.1, J_2 = 0.8 Hz, 2) ppm.

Acknowledgments. This research was supported by Public Health Service Grant CA-12107-13 and then by AI-13939-01. Auxiliary support from the Merck Co. and Ciba-Geigy Co. are gratefully acknowledged. The 250-MHz spectra were measured on facilities supported by RR-00297-08. We also wish to thank Mr. Glen Herman for mass spectral determination.

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