Derivatives of 1-Methoxy-3-trimethylsilyloxy-1,3-butadiene for Diels–Alder Reactions

Samuel Danishefsky,*[1a] Cheng-Feng Yan,[1a] Rajendra K. Singh,[1a] Ronald B. Gammill,[1a] Patrick M. McCurry, Jr.,[1b] Nancy Fritsch,[1c] and Jon Clardy*[1c]

Contribution from the Departments of Chemistry, University of Pittsburgh, Pittsburgh, Pennsylvania 15260, Carnegie-Mellon University, Pittsburgh, Pennsylvania 15213, and Cornell University, Ithaca, New York 14853. *Received January 12, 1979*

Abstract: The preparation and Diels–Alder cycloadditions of the following highly functionalized dienes are described: (1) (*E*)-1-methoxy-2-methyl-3-trimethylsilyloxy-1,3-butadiene (**5**), (2) (*E,Z*)-1-methoxy-3-trimethylsilyloxy-4-methyl-1,3-butadiene (**6**), (3) (*E,Z*)-1-methoxy-2,4-dimethyl-3-trimethylsilyloxy-1,3-butadiene (**7**), (4) (*E,Z*)-1-methoxy-3-trimethylsilyloxy-1,3-butadiene (**25**), and (5) 1,1-dimethoxy-3-trimethylsilyloxy-1,3-butadiene (**46**). The use of these dienes in Diels–Alder reactions enables rapid access to diversely functionalized aromatics, cyclohexenones, cyclohexadienones, and 3-methoxycyclohexenones.

Introduction

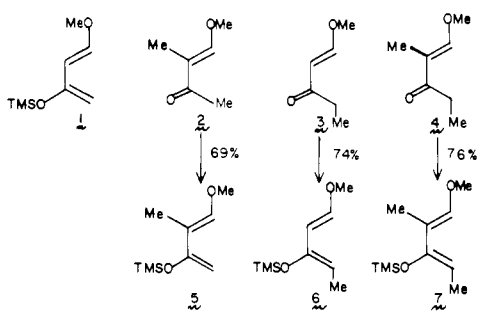
We have described the preparation[2a] and reactions[2b] of *trans*-1-methoxy-3-trimethylsilyloxy-1,3-butadiene (**1**). This compound is a powerful enophile for Diels–Alder reactions with electron-deficient dienophiles. It was of interest to investigate the feasibility of incorporating additional functionality into diene systems of the type **1**, thereby enhancing the scope of the method. In this study we focused on three types of substitutions. First we examined the effects of incorporating additional methyl substituents into the diene to provide aromatics and cyclohexenones with alkyl substituents in predictable positions.

We also studied the possibility of the incorporation of a phenylseleno function at the 4 position of compound **1**, with the goal of producing 4,4-disubstituted cyclohexadienones.

Finally, we examined the possibility of incorporating an additional alkoxy group at the 1 position of the diene **1**. During the course of our studies, the desired compound, 1,1-dimethoxy-3-trimethylsilyloxy-1,3-butadiene (**46**), was prepared in another laboratory and shown to be effective vis-à-vis naphthoquinones.[2c] Our results with this compound,[3] using a broad range of dienophiles, are related herein.

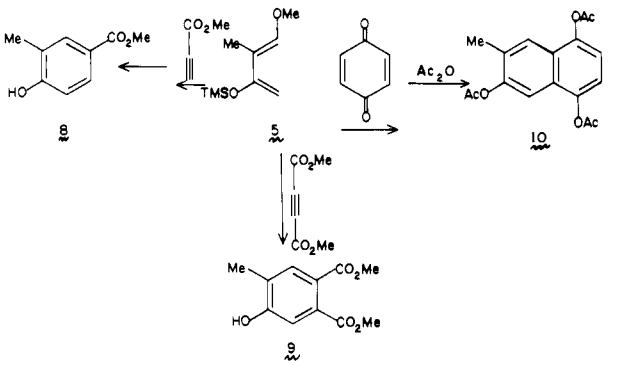
Results

(1) Methylated Derivatives of Compound 1. The desired dienes **5, 6,** and **7** were prepared in the indicated yield by the silylation of **2**,[4] **3**,[5] and **4**,[4] respectively, with trimethylchlorosilane using trimethylamine–zinc chloride.[2a]



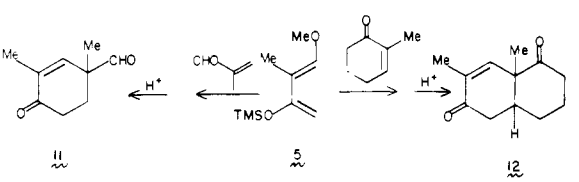
Compounds **6** and **7** could, in principle, be *Z* or *E* isomers about the silyl enol ether double bond. Their NMR spectra indicated them to be homogeneous. The proton at C_4 is seen, in each case, as a quartet, $J \simeq 7$ Hz, centered at δ 4.62 and 4.79 ppm, respectively. In view of the good yields of Diels–Alder products obtained from these dienes, it seemed reasonable[6] to formulate the methyl groups at *Z* (i.e., cis to the silyl enol ether) in the starting materials.

Cycloaddition of compound **5** with methyl propiolate in xylene under reflux is accompanied by elimination of methanol. Treatment with aqueous acid afforded an 83% yield of methyl 4-hydroxy-3-methylbenzoate (**8**). By a similar sequence, reaction of **5** with dimethyl acetylenedicarboxylate, in this case in benzene under reflux, followed by hydrolysis affords an 87% yield of dimethyl 4-hydroxy-5-methylphthalate (**9**).[7]



Another direct route from compound **5** to an aromatic system starts with its cycloaddition at ca. 25 °C with *p*-benzoquinone. The resultant adduct was treated with pyridine and acetic anhydride to afford a 77% yield of 7-methyl-1,4,6-triacetoxynaphthalene (**10**).

Compound **5** reacts with methacrolein in toluene under reflux. Treatment of the adduct with dilute HCl affords a 54% yield of 2,4-dimethyl-4-formylcyclohex-2-en-1-one (**11**). It will



be noted that the 2-methyl group of the diene is incorporated at the α carbon of the γ,γ-disubstituted enone. The introduction of a methyl group into this center, from a demethyl precursor, might represent a difficult synthetic problem, since the usual method of α-alkylation of an enone would be unavailable. Similarly, the cycloaddition of compound **5** with 2-methylcyclohex-2-en-1-one in xylene at 200 °C (sealed tube) followed by hydrolysis afforded a 42% yield of octalindione **12**.

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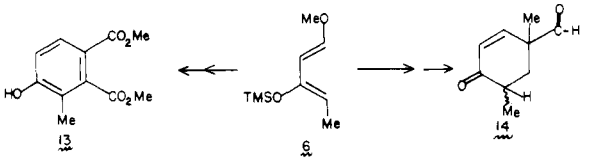
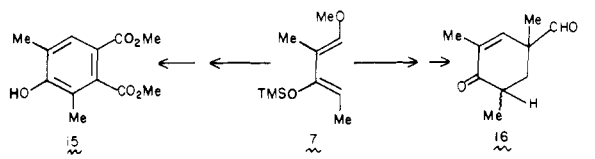
Compound **6** reacts with dimethyl acetylenedicarboxylate in benzene under reflux. Acidic hydrolysis provides a 66% yield of dimethyl-3-methyl-4-hydroxyphthalate (**13**). Cycloaddition of **6** with methacrolein followed by acidic unraveling[2b] and

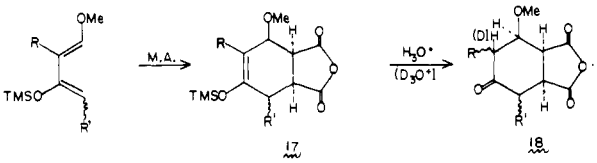


chromatography on silica gel affords a 56% yield of a 1:1 mixture of *cis*- and *trans*-4,6-dimethyl-4-formylcyclohex-2-en-1-one (**14**). The crude acidic hydrolysate was sufficiently complex such that we could not ascertain whether the epimeric mixture was a consequence of the cycloaddition–hydrolysis process or of the subsequent chromatographic purification.

In a similar way, diene **7** reacted with dimethyl acetylenedicarboxylate to afford, after hydrolysis, the hydroxyphthalate **15**[7] in 58% yield. Reaction with methacrolein affords, as above, an epimeric mixture of C_6 methyl compounds (**16**) in 34% yield.



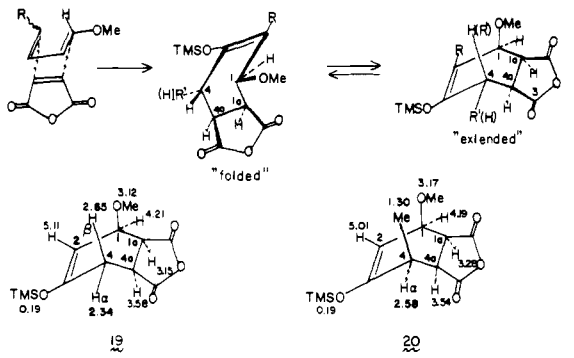
We now turn to the reactions of **5, 6,** and **7** with maleic anhydride. This study was directed toward establishing the geometry of the latter two dienes. As was seen in a previous study with compound **1**,[2a,b] acidic hydrolysis of the maleic anhydride adduct, of the type **17,** does not lead to the extrusion of methanol. Therefore, the maleic anhydride adducts **17** and their hydrolysates, **18,** provide maximum stereochemical information. It was deemed useful to analyze the stereochemical problem at the level of both **17** and **18.**



Examination of Drieding models of adduct system **17** indicates two possible conformations in which angle strain is minimized—both being of the boat type.[8] In the "extended" boat conformer, the anhydride and olefinic centers are anti with respect to the approximate plane comprising carbons 1, 1a, 4a, and 4. In the "*folded*" form, these centers are syn with respect to the same plane. It will be noted that the folded conformer corresponds to the consummation of the normally postulated endo transition state[6] for the Diels–Alder reaction. Clearly, the preference of the endo reaction mode in the cycloaddition process need not have any implications of conformational stability of the final product.

The proton chemical shifts (250 MHz, $CDCl_3$) of the previously reported adduct **19**[2a,b] are shown above. This spectral analysis suggested the arrangement of **19** to be a deformed version of the "extended" conformer, in which the α hydrogen at C_4 tends toward eclipsing the ring junction hydrogen at C_{4a}. The H_{4a} coupling constants of 10.70 and 5.10 Hz with the α and β hydrogens, respectively, at C_4 imply an almost coplanar relationship of H_{4a} with $H_{4\alpha}$ and a more gauche-like relationship of H_{4a} with $H_{4\beta}$.

The vinyl hydrogen at C_2 is seen as a doublet of doublets ($J_{1,2}$ = 6.35 and $J_{2,4\beta}$ = 2.60 Hz) centered at δ 5.11. The relatively large four-bond coupling ($J_{2,4\beta}$ = 2.60 Hz) is suggestive of an ideal relationship for allylic coupling[9] of H_2–C–C–C–$H_{4\beta}$



which is readily observed with the aid of models. The C_1 hydrogen, δ 4.21, gives rise to a doublet of doublets, $J_{1,2}$ = 6.35 and $J_{1,1a}$ = 4.15 Hz. The observed H_1, H_2 coupling indicates[9] near coplanarity. The H, H_{1a} coupling indicates a gauche rather than anti disposition of these bonds. Both relations for the C_1 hydrogen are satisfied only if it is α. The methoxy group is, accordingly, β. This is the expected result of endo addition, since the methoxy function in diene **1** is *E*.

As in the case of the parent compound, **1**, reaction of **6** with maleic anhydride occurs at room temperature (neat) and is complete in 5 min. Comparison of the NMR spectrum of the adduct, so produced, with that of **19** suggests that the configuration of the C_4 methyl group is β, and that its structure and conformation are as depicted in **20.** The 4α proton, δ 2.58, is now seen as a doublet of quartets ($J_{4\alpha\text{-}4a}$ = 9.50 and $J_{4\alpha\text{-Me}}$ = 7.40 Hz). In adduct **19** the corresponding proton was seen as a doublet of doublets *J* = 17.75 and 10.70 Hz. The proton at C_{4a}, δ 3.54, is now seen as a doublet of doublets, ($J_{4a,1a}$ = 10.80 and $J_{4a,4\alpha}$ = 9.50 Hz). The gauche coupling seen for the 4a proton in **19** is thus absent in **20.** Correspondingly, the vinylic (C_2) proton appears as a doublet, *J* = 6.10 Hz, thus lacking the long-range coupling seen in **19.** This is again consistent with the absence of a β hydrogen in **20** and thus supports the 4β-methyl assignment in this compound.

As in **19,** the methine hydrogen at C_1 in compound **20,** δ 4.19, is seen as a doublet of doublets ($J_{1,1a}$ = 4.70 and $J_{1,2}$ = 6.10 Hz). This is consistent only with a cis-gauche relationship of the C_{1a} and C_1 protons. Thus, the methoxy and methyl groups in **20** are cis. By the principle of suprafacial addition in Diels–Alder reactions, these groups must have the same relationship to the C_2–C_3 single bond in olefin **2**. Since the methoxy group in all the dienes is *E* (i.e., trans to C_3), the methyl group in **6** is demonstrated to be *Z* (i.e., trans to C_2). Thus, *the cycloadditions of both* **1** *and* **6** *with maleic anhydride have occurred through a folded (endo) transition state, giving rise to tetrahydrophthalic anhydride adducts, whose preferred conformation is of the extended type.*

As was reported[2a,b] for the conversion **1** → **19** → **21,** adduct **20** was transformed (dilute HCl) to a keto anhydride, mp 180–182 °C, in 67% overall yield. By conducting these hydrolyses in deuterated media, it was demonstrated that there was no exchange at C_4 under these reaction conditions. Hence, it is safe to relate the configuration of the ketone at C_4 to its silyl enol ether precursor **20.** Accordingly, the stereochemistry of the ketone is formulated as shown in **22.**

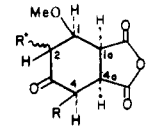
By conducting the unraveling experiment of **19** → **21** in the deuterated medium, and comparing the NMR spectrum thus produced with that of **21** itself, one sees that >95% of one of the diastereotopic protons at C_2 was missing while the other "survived". A similar result was obtained in the conversion **20** → **22.** In each case, the higher field resonance (δ 2.30, *J* with H_1 = 2.10 Hz, in the case of **21** and δ 2.55, *J* with H_1 = 1.80 Hz, in the case of **22**) is missing. In both compounds, the lower field proton (δ 2.91 in each case) which remains is the one which is slightly more coupled to H_1 (δ 3.50 in the case of **21** and δ 5.00 in the case of **22**) in the parent ketone. From con-

siderations of gauche hetero substituent shielding effects in cyclohexane rings,[10] it might thus be argued that the higher field resonance is, in each case, due to the β proton and hence that protonation has occurred from the β face, but a more precise knowledge of the conformation of these ketones would be necessary to make such an assignment rigorous.

In a similar way, compound **5** reacts with maleic anhydride to afford an adduct which, upon hydrolysis in the usual[11] way, gives **23,** mp 125–127 °C. In this case, a new chiral center is created at C_2 via the hydrolysis. Again apparently only a single product is obtained in 88% yield; thus the hydrolysis is stereospecific. The proton at C_2 in **23** now appears as a quartet of doublets at δ 2.33, J with H_t = 2.00 Hz. Comparison of this coupling constant with those of **21** and **22** in conjunction with monodeuterio-**21** and -**22** (vide supra) indicates that protonation has taken place from the same sense in the three cases.

Finally, cycloaddition of **7** with maleic anhydride followed by hydrolysis gave a 62% yield of **24,** mp 203–204 °C. The vicinal coupling constant between H_2 and H_1 in this compound is 1.75 Hz, again indicating (vide supra) the same, as yet unidentified, stereochemical sense of protonation. The vicinal H_{C_4}-(δ 2.77)-$H_{C_{4a}}$ (δ 3.67) coupling constant in this compound is 8.60 Hz. This compares very closely with the corresponding chemical shifts and couplings in ketone **22** [H_{C_4}-(δ 2.80)-$H_{C_{4a}}$-(δ 3.69) = 8.75 Hz], thus supporting the notion that the stereochemistry at C_4 in both compounds is the same. Accordingly, the geometry of diene **7** must correspond to that of **6**.

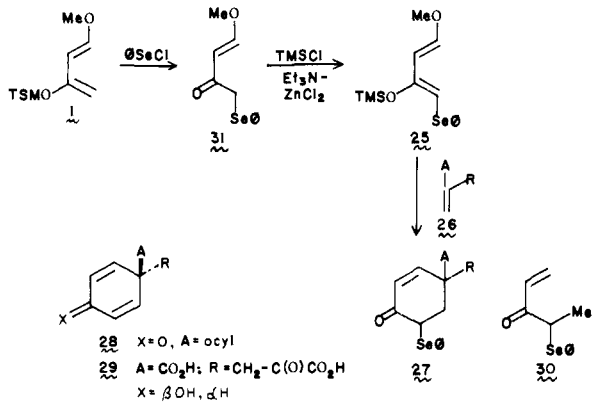
The C_4–C_{4a} coupling constants in **22** and **24,** so formulated, also correspond closely with that of **32** (vide infra) of known configuration.



1 → **21** R = R' = H
6 → **22** R = Me; R' = H
5 → **23** R = H; R' = Me
7 → **24** R = R' = Me

(2) Diels–Alder Reactions of (*E,Z*)-1-Methoxy-3-trimethylsilyloxy-4-phenylseleno-1,3-butadiene (25).[12] It was projected that cycloaddition of diene **25** with dienophile **26** would afford **27** which, on oxidation,[13a,b] would provide generic target system **28.**[14,15] Ultimately we envisioned the possibility of using such a sequence in a synthesis of prephenic acid (**29**).[16,17] While this hope was not realized in practice (vide infra), diene **25** did provide a route to systems such as **28.**

The preparation of **25** proved to be quite simple. It was anticipated that the previously described diene **1** (a vinylogous ketene acetal) would react with phenylselenyl chloride.[18-20] In the event, **31** was produced in 82% yield. Enol silylation of **31** afforded an 80% yield of the desired **25.** This diene resisted complete purification by either chromatography or distillation. It was invariably contaminated with ca. 10–15% of enone **1a** but this did not seriously compromise its use. The enol silylation of **31** produced apparently a single isomer (cf. enol silylations of **3** and **4**). That the stereochemistry is as shown was deduced by crystallographic analysis of its maleic anhydride adduct, vide infra.



28 X = O, A = acyl
29 A = CO_2H; R = CH_2-C(O)CO_2H
X = βOH, αH

Cycloaddition of diene **25** occurs quite smoothly with highly reactive dienophiles. Thus, with maleic anhydride, reactions occur at room temperature. Cleavage of the silyl enol ether is easily accomplished under acidic conditions to provide a 67% overall yield of methoxy ketone **32.** As in the case of Diels–Alder reaction of parent diene **1** and its methylated derivatives (vide supra), desilylation of the maleic anhydride adducts is not accompanied by loss of methanol.

In our initial communication,[12] the stereochemistry of this methoxy ketone was provisionally formulated as **33.** It was in this fashion that we reconciled the small coupling constant (2.5 Hz) between the hydrogen at C_t which bears the methoxyl function and its vicinal junction hydrogen at C_{ta}, as well as the substantial coupling (8 Hz) between the proton at C_4, which bears the phenylseleno group, and its nearest junction hydrogen at C_{4a}. Examination of Drieding models of the "folded" boat conformation in an apparently unstrained form, suggested this relationship, which is embraced in structure **33.** Accordingly, the structure of the diene was formulated to be **34.**[12]

What was not perceived in this crude analysis was revealed by crystallographic examination of the methoxy ketone, which can now be defined to be ***32.*** The hydrolyzed adduct crystallized in the monoclinic crystal system. Lattice constants, determined by a least-squares fit of 15 diffractometer-measured 2θ values between 35 and 45°, were a = 11.593 (9) Å, b = 5.595 (5) Å, c = 22.844 (9) Å, and β = 107.81 (7)°. An observed and calculated (Z = 4) density of 1.66 g/cm^3 indicated four molecules of $C_{15}H_{14}SeO_5$ in the unit cell. Systematic extinctions $h0l$ (missing if $h + l = 2n + 1$) and $0k0$ (missing if $k = 2n + 1$) uniquely required space group $P2_1/n$. All unique diffraction maxima with $2\theta \leq 114°$ were surveyed using a computer-controlled four-circle diffractometer with graphite monochromated Cu Kα (1.541 78 Å) radiation and a variable-speed ω-scan technique. All scans were 1° wide and a background of one-half the total scan time was measured 1° from the center of each scan. Of the 1782 reflections measured, 1386 (78%) were considered observed ($I \geq 3\sigma(I)$) after correction for Lorentz, polarization, and background effects.[21] The position of the Se was derived from a sharpened three-dimensional Patterson synthesis and the nonhydrogen atoms were located in subsequent electron density syntheses. Hydrogen atoms were located on difference electron density syntheses after partial refinement. Full-matrix least-squares refinements have currently converged to a standard crystallographic residual of 0.054 for the observed data. Tables of fractional coordinates and temperature factors, bond distances and angles, and observed and calculated structure factors are given in the supplementary material described at the end of this paper. There were no large maxima in a final difference electron density synthesis nor any unusually close intermolecular contacts.

While the computer-generated perspective drawing of **32** could crudely be described in terms of a chair conformation, examination of the relevant dihedral angles indicated considerable contortion in the direction of a boat. In particular, the C_1–C_{ta}–C_{4a}–C_4 dihedral angle is ca. 40° and the corresponding C_{ta}–C_{4a}–C_4–C_3 is ca. 34°. The more relevant (in terms of analysis of the NMR data) but less well known hydrogen dihedral angles are H–C_t–C_{ta}–H ~ 48°, H–C_{ta}–C_{4a}–H ~30°, and H–C_{4a}–C_4–H ~19°

While the precise degree of applicability of the crystallo-

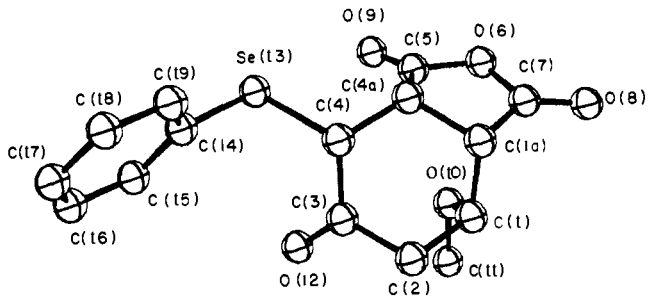


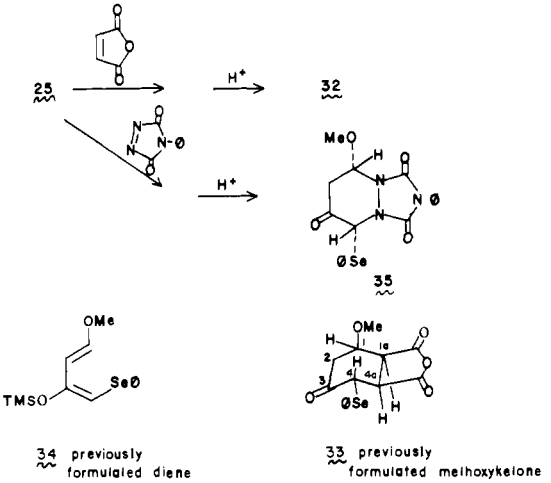
Figure 1. Computer-generated drawing of methoxy ketone **32**.[21]

graphic data to the solution phase remains open to conjecture, the general source of the erroneous NMR based conclusion is clear; i.e., the twisting of the six-membered ring can be such as to allow for a large (11 Hz) coupling between the junction hydrogens, 1a and 4a, and a large (8 Hz) coupling between the junction hydrogen at C_{4a} and its cis related vicinal hydrogen at C_4 which bears the phenylseleno group. The relationship between the hydrogens at C_t (bearing the methoxyl group) and its vicinal junction center at C_{ta} is cis, as previously[12] surmised. These findings serve to underline the hazards of deducing configurations in flexible cis-fused systems from coupling constants, in tandem with examination of Drieding or other models.

The absence of epimerization during the hydrolytic conversion of the maleic anhydride adduct of **25** to methoxy ketone **25** was established. Thus, when the hydrolysis was conducted in dilute DCl-D_2O, the proton at C_4 was not exchanged. Only one deuterium was introduced, in undetermined stereochemistry at C_2.

Accordingly, the definition of stereostructure **32** (Figure 1) to the methoxy ketone requires, from the suprafacial nature of [2 + 4] cycloadditions, that the diene itself be formulated at **25.** Thus, in the conversion **1a** → **25,** the trimethylsilyloxy has been introduced cis to the phenylseleno function. The striking similarity between the relevant couplings of **32** and those of ketones **23** and **24** from the methylated dienes **6** and **7** strongly supports the structures which were proposed above.

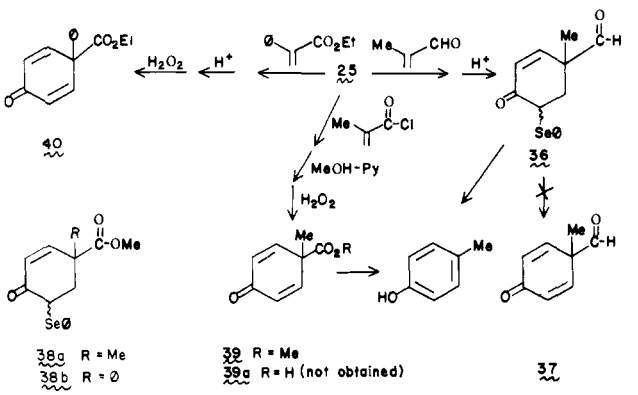
Similarly, cycloaddition of diene **25** with 4-phenyltriazoline-3,5-dione[22] occurs at room temperature. Acidic hydrolysis affords a methoxy ketone, mp 213–214 °C, which must now be reformulated as **35.**



More forcing conditions were required to realize cycloaddition of diene **25** with substituted acrylic types of dienophiles. Reaction of **25** with methacrolein in benzene under reflux for 40 h afforded an adduct, which upon acid hydrolysis gave a 38% yield of epimeric enones, **36.** Several attempts, using known methods,[13a,b] to achieve the oxidative deselenenylation of **36,** with a view to preparing **37,** were unsuccessful, leading in each case to *p*-cresol in high yield.

The synthesis of a target 4-acylcyclohexadienone by this methodology was achieved with a methacrylyl dienophile. Attempted cycloaddition of **25** with methyl methacrylate gave, after acidic hydrolysis, rather low yields (ca. 10%) of **38a.** A somewhat more satisfactory yield was achieved using the more reactive methacrylyl chloride as the dienophile. Compound **25** was heated with this acid chloride in benzene under reflux for 2 h. Treatment of the crude adduct with methanol–pyridine, followed by aqueous hydrogen peroxide, afforded a 29% yield of **39.** Treatment of **39** with KOH–methanol, in an attempt to prepare the corresponding acid **39a,** afforded, virtually instantaneously, *p*-cresol.

With a view toward the synthesis of mesembrenoid alkaloids,[23] we attempted to prepare 4-phenyl-4-carbethoxycyclohexadienone (**40**). Cycloaddition of **25** with ethyl 2-phen-



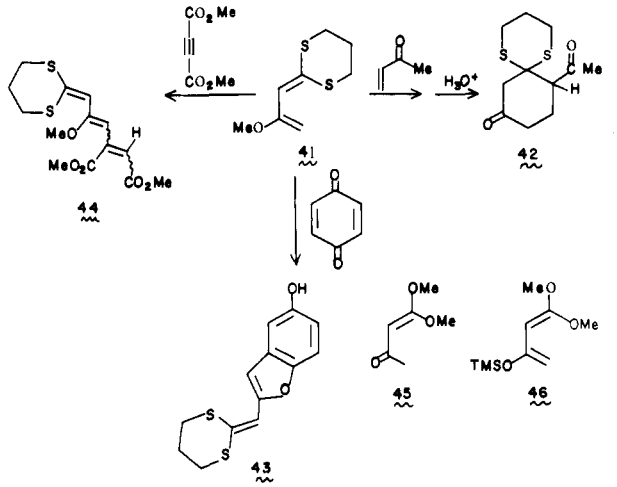
ylacrylate was conducted in benzene in a sealed tube at 115 °C for 24 h. Hydrolysis with dilute acid followed by oxidative deselenylation in the usual way afforded a 50% overall yield of **40.**

Thus, on balance, diene **25** does offer a route to the desired target systems **28.** However, the reactivity of this diene is sharply reduced relative to the parent system, **1.** An alternative Diels–Alder strategy to such systems was necessary and was, in fact, developed as described in the paper which follows.[24]

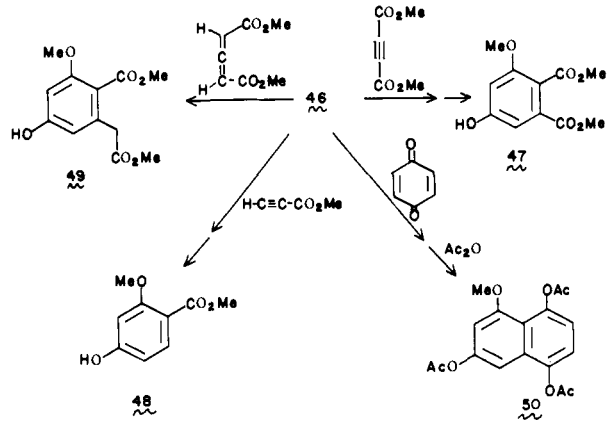
(3) Diels–Alder Reactions of 1,1-Dimethoxy-3-trimethylsilyloxy-1,3-butadiene. The final type of substitution on parent diene **1** which we describe here was addressed to an attempted Diels–Alder route to more oxygenated aromatic targets, and to six-membered rings containing β-dicarbonyl or equivalent functionality.[25] Our first attempt along these lines, which was recently described,[26] involved recourse to diene **41.** Indeed, this readily available diene did undergo cycloaddition with, for instance, dienophiles such as methyl vinyl ketone to afford, after hydrolysis, a 35% yield of ketodithiane **42.** In addition to this rather disappointing yield, a more general limitation in the utility of diene **41** became apparent. Thus, more electrophilic dienophiles such as *p*-benzoquinone and dimethyl acetylenedicarboxylate reacted with compound **41** to afford **43** and **44,** respectively. These are the apparent products of Michael addition and proton transfer. Similar findings were recently reported by Tsuji.[3]

While these studies were in progress, a Canadian group prepared diene **40**[2,27] from the known **45** and studied its cycloaddition with several quinones. There was no apparent complication from competing Michael reactions, such as were observed in the case of **41** with the parent *p*-benzoquinone. Accordingly, we investigated the cycloaddition of **46** with a variety of dienophiles.[25]

Cycloaddition of diene **46** with dimethyl acetylenedicarboxylate followed by hydrolysis with dilute acid afforded an

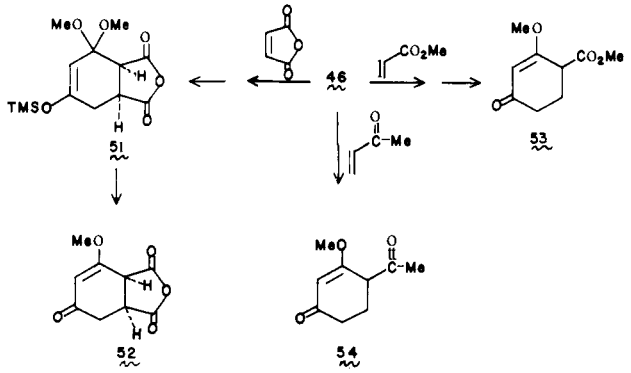


89% yield of the phthalic acid derivative, **47**. Other applications of **46** to the synthesis of oxygenated aromatic systems are shown below.



Cycloaddition of **46** with maleic anhydride occurs exothermically at 0 °C to afford a 95% yield of **52**. Presumably the cleavage occurs through the presence of adventitious acid contaminants (possibly in the maleic anhydride). It will also be noted that one of the two methoxy groups of the likely intermediate adduct **51** is lost much more readily than the single methoxy group of intermediates such as **17** which arise from **1**.

Cycloadditions of **46** with acrylyl dienophiles were also examined and the results are shown below. The use of this route to specific enol ethers of β-diketones in the total synthesis of griseofulvin will be described separately.[28]



In summary, considerable substituent variation is possible on the basic diene **1**, while still retaining the possibility of cycloaddition. The benefits of increased functionality[29,30] in the products may well compensate for some erosion in the quality of the Diels–Alder reaction.

Experimental Section[31]

Preparation of (*E*)-1-Methoxy-2-methyl-3-trimethylsilyloxy-1,3-butadiene (5). Anhydrous zinc chloride (1.5 g, 11 mmol) was added to triethylamine (85 g) and the system was stirred for 1 h at room temperature. To this was added a solution of methoxy enone **2** (41.22 g, 0.36 mol) in 85 mL of benzene. After this was added trimethylchlorosilane (78.12 g, 0.72 mol). The system was stirred vigorously and heated at 40 °C overnight.

After being cooled, the reaction mixture was poured into 1 L of ether and a white solid was filtered. The filtrate and combined washings were concentrated in vacuo to afford a brown residue. Distillation at 5 mmHg afforded 53.9 g of distillate from 45 to 49 °C. NMR analysis indicated this to be an 85:15 mixture of **5**:**2**. Compound **5** (69% yield) was used in this form in subsequent reactions. $\delta(CDCl_3)$: 0.20 (s, 9), 1.70 (s, 3), 3.67 (s, 3), 4.17 (s, 1), 4.28 (s, 1), 6.50 (br s, 1) ppm.

Formation of Methyl 3-Methyl-4-hydroxybenzoate (8). A solution of compound **5** (514 mg, 2.76 mmol) and methyl propiolate (504 mg, 6 mmol) in 2 mL of xylene was heated under reflux overnight. The cooled solution was treated with 5 mL of 0.1 N HCl–THF for 30 min. After dilution with ether and extraction with aqueous sodium bicarbonate, the organic phase was dried over anhydrous magnesium sulfate. Evaporation of the volatiles in vacuo afforded a residue which was chromatographed on 35 g of silica gel. Elution with 2% ether in benzene afforded 383 mg (83%) of compound **8**:[32] mp 124–125 °C; λ_{max} ($CHCl_3$) 3.05, 5.85, 6.21 μ; $\delta(CDCl_3)$ 2.30 (s, 3), 3.90 (s, 3), 5.85 (s, 1), 6.84 (d, J = 9 Hz, 1), 7.84 (d, J = 9 Hz, 1), 7.92 (s, 1) ppm.

Anal. Calcd for $C_9H_{10}O_3$: C, 65.50; H, 6.07. Found: C, 65.30; H, 5.98.

Formation of Dimethyl 4-Hydroxy-5-methylphthalate (9). A solution of compound **5** (372 mg 2 mmol) and dimethyl acetylenedicarboxylate (570 mg, 4 mmol) in 2 mL of benzene was heated under reflux overnight. Workup as above gave a residue which was chromatographed on 35 g of silica gel. Elution with 2% ether in benzene afforded 388 mg of **9**: mp 147–148 °C (lit.[7] 142–143 °C); λ_{max} ($CHCl_3$) 2.78, 2.94, 3.30, 5.80, 6.20 μ; $\delta(CD_3)_2CO$ 2.25 (s, 3), 3.80 (s, 6), 7.09 (s, 1), 7.60 (s, 1), 9.33 (br s, 1) ppm; *m/e* (P) 224.0687 (calcd, 224.0684).

Formation of 1,4,6-Triacetoxy-7-methylnaphthalene (10). A solution of compound **5** (2.44 g, 13 mmol) and *p*-benzoquinone (972 mg, 9 mmol) in 10 mL of ethanol was stirred at room temperature for 10 min. The color changed from orange-red to yellow. To this solution were added 20 mL of acetic anhydride and 1 drop of pyridine and the system was heated overnight under reflux. Methanol (10 mL) was added to the cooled solution. The total reaction mixture was poured into saturated brine and extracted with ether. The ether layer was successively extracted with 5% sodium bicarbonate, dilute HCl, and brine. The organic phase was dried over magnesium sulfate and the volatiles were evaporated in vacuo to afford 2.17 g (77%) of **10** as a white, crystalline residue: mp 131–132 °C (ether); λ_{max} ($CHCl_3$) 3.34, 5.70 μ; $\delta(CDCl_3)$ 2.34 (s, 6), 2.40 (s, 3), 2.45 (s, 3), 7.21 (s, 2), 7.56 (s, 1), 7.72 (s, 1) ppm.

Anal. Calcd for $C_{17}H_{16}O_6$: C, 64.55; H, 5.10. Found: C, 64.68; H, 4.91.

Formation of 2,4-Dimethyl-4-formylcyclohex-2-en-1-one (11). A solution of compound **5** (558 mg, 3 mmol) and methacrolein (420 mg, 6 mmol) in 3 mL of toluene was heated under reflux for 24 h. The cooled solution was treated with 5 mL of 0.1 N HCl–THF for 30 min at room temperature. Workup in the usual way left a residue which was chromatographed on 25 g of silica gel. Elution with 4% ether–benzene afforded 247 mg (54%) of **11**: λ_{max} ($CHCl_3$) 3.70, 5.79, 5.96 μ; $\delta(CDCl_3)$ 1.28 (s, 3), 1.80 (d, J = 2 Hz, 3), 1.9–2.6 (m, 4), 6.50 (s, 1), 9.52 (s, 1) ppm.

Calcd for $C_9H_{12}O_2$: *m/e* 152.083 73. Found: 152.082 95.

Formation of *cis*-7,8a-Dimethyl-1,6-dioxo-1,8a,2,3,4,4a,5,6-octahydronaphthalene (12). A solution of compound **5** (372 mg, 2 mmol) and 2-methylcyclohexenone (110 mg, 1 mmol) in 1 mL of xylene was heated in a sealed glass tube at 200 °C for 50 h. This solution was diluted with ether and treated with 3 mL of 0.005 N HCl saturated with ammonium chloride for 60 min at 0 °C. The organic phase was extracted with 10% sodium hydroxide and dried over magnesium sulfate. Evaporation left a residue which was chromatographed on 20 g of silica gel. Elution with 5% ethyl acetate–benzene afforded 80 mg (42%) of **12**: λ_{max} ($CHCl_3$) 3.30, 3.41, 5.80, 5.96 μ; $\delta(CDCl_3)$ 1.41 (s, 3), 1.80 (d, J = 2 Hz, 3), 6.40 (br s, 1).

Calcd for $C_{12}H_{16}O_2$: *m/e* 192.115 03. Found: 192.115 12.

Preparation of (*E*)-1-Methoxy-3-trimethylsilyloxypenta-1,3-diene

(6). The same procedure as was used for the preparation of **2** was followed here. Using 0.3 g (2.2 mmol) of zinc chloride, 16 g (0.158 mol) of triethylamine, 8.0 g (0.07 mol) of ketone **3**, and 15.12 g (0.14 mol) of trimethylchlorosilane there was obtained 9.57 g (74%) of diene **6** from 54 to 58 °C (3.25 mm): λ_{max} ($CHCl_3$) 3.32, 3.38, 6.02, 6.16, 6.28 μ; $\delta(CDCl_3)$ 0.20 (s, 9), 1.60 (d, J = 8 Hz, 3), 3.57 (s, 3), 4.62 (q, J = 8 Hz, 1), 5.38 (d, J = 13 Hz, 1), 6.68 (d, J = 13 Hz, 1) ppm.

Formation of Dimethyl 3-Methyl-4-hydroxyphthalate (13). The same procedure as was used for the formation of **9** was followed. From 186 mg (1 mmol) of **6** and 284 mg (2 mmol) of dimethyl acetylenedicarboxylate there was obtained, without chromatography, 148 mg (66% yield) of **13:** mp (Et_2O-$CHCl_3$) 148–150 °C; λ_{max} ($CHCl_3$) 3.0, 3.31, 3.38, 5.84, 6.29 μ; $\delta(CDCl_3)$ 2.18 (s, 3), 3.86 (s, 3), 4.00 (s, 3), 6.82 (d, J = 8 Hz, 1), 7.02 (br s, 1), 7.80 (d, J = 8 Hz, 1) ppm.

Anal. Calcd for $C_{11}H_{12}O_5$: C, 58.93; H, 5.39. Found: C, 59.13; H, 5.51.

Preparation of the Epimeric Mixture of 4,6-Dimethyl-4-formylcyclohex-2-en-1-one (14). The same procedure was used as for the preparation of **11.** From 1.86 g (10 mmol) of diene **6** and 1.05 g (15 mol) of methacrolein there was obtained, after silica gel (120 g) chromatography and elution with 6% ethyl acetate in hexane, 855 mg (56%) of **14** as 1:1 mixture of epimers: λ_{max} ($CHCl_3$) 3.70, 5.80, 5.95, 6.15 μ.

Calcd for $C_9H_{12}O_2$: *m/e* 152.083 73. Found: 152.083 09.

Preparation of (*E,Z*)-1-Methoxy-2-methyl-3-trimethylsilyloxy-1,3-pentadiene (7). The same procedure as was employed for the preparation of **5** and **6** was followed. From 0.4 g (3 mmol) of zinc chloride, 23 g (0.2 mol) of triethylamine, 21.7 g (0.2 mol) of trimethylchlorosilane, and 12.8 g (0.1 mol) of ketone **4** there was obtained 15.17 g of diene **7** from 44 to 46 °C (0.7 mm): λ_{max} ($CHCl_3$) 3.39, 6.04, 6.12 μ; $\delta(CDCl_3)$ 0.20 (s, 9), 1.62 (d, J = 7 Hz, 3), 1.68 (s, 3), 3.68 (s, 3), 4.79 (q, J = 7 Hz, 1), 6.38 (s, 1) ppm.

Formation of Dimethyl 3,5-Dimethyl-4-hydroxyphthalate (15). The same procedure employed in the preparation of **9** and **13** was followed. From 200 mg (1 mmol) of compound **7** and 284 mg (2 mmol) of dimethyl acetylenedicarboxylate, there was obtained, after chromatography on silica gel (25 g) and elution with 2% ether–benzene, 139 mg (58%) of **15:** mp 137–138 °C (lit.[7] 132 °C); $\delta(CDCl_3)$ 2.2 (br s, 6), 3.90 (s, 3), 3.98 (s, 3), 5.88 (s, 1), 7.66 (s, 1) ppm; *m/e* (P) 238.0845 (calcd, 238.0841).

Formation of the Epimeric Mixture of 2,4,6-Trimethyl-4-formylcyclohex-2-en-1-one (16). The same procedure as was used to obtain **14** was followed. For 600 mg (3 mmol) of diene **7** and 420 mg (6 mmol) of methacrolein there was obtained, after chromatography on silica gel (70 g) and elution with 3% ethyl acetate–hexane, 172 mg (34%) of epimer **16:** λ_{max} ($CHCl_3$) 3.69, 5.77, 5.95 μ; *m/e* 166.

Calcd for $C_{10}H_{14}O_2$: *m/e* 166.0994. Found: 166.0999.

Preparation of Methoxy Keto Anhydrides 22, 23, and 24. The same procedure was followed throughout for the preparation of **22, 23,** and **24** from **6, 5,** and **7,** respectively. Maleic anhydride (1 equiv) was added to the diene (1.5 equiv) without solvent. The system was stirred for 5 min at room temperature with 3 mL of 0.1 N HCl–THF. White crystals separated and were collected by filtration.

For **22** (mp 180–182 °C, 67% yield): λ_{max} ($CHCl_3$) 3.30, 5.59, 5.81 μ; $\delta(CDCl_3)$(see text).

Anal. Calcd for $C_{10}H_{12}O_5$: C, 56.60; H, 5.70. Found: C, 56.37; H, 5.56.

For **23** (mp 125–127 °C, 88% yield): λ_{max} ($CHCl_3$) 3.30, 5.59, 5.81 μ; $\delta(CDCl_3)$ (see text).

Calcd for $C_{10}H_{12}O_5$: *m/e* 212.068 47. Found: 212.068 53.

For **24** (mp 203–204 °C, 62% yield): λ_{max} ($CHCl_3$) 3.31, 5.61, 5.80 μ; $\delta(CDCl_3)$ (see text).

Anal. Calcd for $C_{11}H_{14}O_5$: C, 58.40; H, 6.24. Found: C, 58.19; H, 6.34.

Preparation of *trans*-1-Methoxy-4-phenylselenobut-1-en-3-one (31). To a solution of diene **1** (5.16 g, 30 mmol) in 50 mL of benzene was added a solution of phenylselenenyl chloride (6.0 g, 31 mmol) in 50 mL of benzene. The red color of the phenylselenenyl chloride solution disappeared almost immediately. Evaporation of the volatiles left a residue which was chromatographed on 1 kg of silica gel. Elution with 6% ethyl acetate in benzene afforded 6.23 g (82%) of **31** as an oil: λ_{max} ($CHCl_3$) 5.95, 6.10 μ; $\delta(CDCl_3)$ 3.62 (br s, 5), 5.64 (d, J = 13 Hz, 1), 7.1–7.8 (m, 6) ppm; *m/e* 256 (P).

Preparation of (*E,Z*)-*trans*-1-Methoxy-3-trimethylsilyloxy-4-phenylseleno-1,3-butadiene (25). Anhydrous zinc chloride (0.5 g, 3.7 mmol) was added to triethylamine (3 g) and the system was stirred for 1 h at room temperature. To this was added at 0 °C a solution of **31** (2.81 g, 11 mmol) in 25 mL of benzene. After this was added trimethylchlorosilane (2.39 g, 22 mmol). The system was stirred vigorously at room temperature overnight. The reaction mixture was then poured into 300 mL of ether and a white solid was filtered. The filtrate and combined washings were washed with 5% aqueous sodium bicarbonate and saturated aqueous sodium chloride solution. The organic phase was dried over anhydrous magnesium sulfate. Evaporation of the volatiles left a brown residue, 3.513 g (80%). NMR analysis indicated this to be compound **25** (ca. 82%) and starting **31** (ca. 18%): λ_{max} ($CHCl_3$) 3.31, 3.37, 6.10 μ; $\delta(CDCl_3)$ 0.30 (s, 9), 3.62 (s, 3), 5.52 (d, J = 13 Hz, 1), 5.60 (s, 1), 6.84 (d, J = 13 Hz, 1), 7.2–7.6 (m, 5); *m/e* 328 (P).

Preparation of Methoxy Anhydride 32. To compound **25** (164 mg, 0.5 mmol) was added maleic anhydride (60 mg, 0.6 mmol) slowly in neat form. The system was stirred for 10 min at room temperature and then treated with 2 mL of 4:1 0.1 N HCl–THF for 30 min at room temperature. The solution was then washed with 5% aqueous sodium bicarbonate and brine. The organic phase was dried over magnesium sulfate. Evaporation of the volatiles left a residue which was triturated with cold ether to afford pure white crystals (103 mg). The residue was chromatographed on 10 g of silica gel. Elution with 30% ether in *n*-hexane afforded another 15 mg of compound **32.** The total yield was 118 mg (67%): mp 136–137 °C (chloroform); λ_{max} ($CHCl_3$) 5.58, 5.85 μ; $\delta(CDCl_3)$ see text; *m/e* 354 (P).

Anal. Calcd for $C_{15}H_{14}SeO_5$: C, 51.00; H, 3.99. Found: C, 51.18; H, 4.02.

Preparation of Methoxyphenylseleno Ketone 35. To compound **25** (360 mg, 1.1 mmol) was added *N*-phenyl-1,2,4-triazoline-3,5-dione (175 mg, 1.0 mmol) slowly in neat form. The red color of dione disappeared in a few minutes. The system was stirred for an additional 5 min at room temperature and then treated with 3 mL of 4:1 0.1 N HCl–THF for 30 min at room temperature. The solution was then washed with 5% aqueous sodium bicarbonate and brine. The organic phase was dried over magnesium sulfate. Evaporation of the volatiles left a residue which was triturated with cold ether to afford 329 mg of essentially pure **35:** mp 213 °C (acetone); λ_{max} ($CHCl_3$) 5.61, 5.81 μ; $\delta((CD_3)_2CO)$ 3.42 (s, 3), 5.68 (dd, J_1 = 15, J_2 = 3.9 Hz, 1), 6.4 (s, 1), 7.3–7.9 (m, 10) ppm; *m/e* 431 (P).

Anal. Calcd for $C_{19}H_{17}N_3O_4Se$: C, 53.03; H, 3.98. Found: C, 52.93; H, 4.02.

Preparation of 4-Methyl-4-carbomethoxycyclohexa-2,5-dienone (39). A solution of compound **25** (164 mg, 0.5 mmol) and methacryloyl chloride (157 mg, 1.5 mmol) in 2 mL of benzene was heated under reflux for 2 h. The cooled solution was treated with a solution of 2 mL of methanol and 2 drops of pyridine in 5 mL of methylene chloride at 0 °C for 5 min. There was then added 1.0 mL of 15% hydrogen peroxide and stirring was continued for 10 min at 0 °C. The solution was poured into 10 mL of 5% aqueous sodium bicarbonate solution and extracted with 3 × 20 mL of methylene chloride. The organic phase was dried over anhydrous magnesium sulfate. Evaporation of the volatiles left a residue which was chromatographed on 5 g of silica gel. Elution with 30% ether in *n*-hexane afforded 29% of compound **39:** λ_{max} ($CHCl_3$) 5.79, 5.99, 6.12 μ; $\delta(CDCl_3)$ 1.56 (s, 3), 3.78 (s, 3), 6.32 (d, J = 10 Hz, 2), 7.10 (d, J = 10 Hz, 2) ppm; *m/e* 166 (P); *m/e* (P) 166.0609 (calcd, 166.0632).

Formation of 4-Methyl-4-formyl-6-phenylselenocyclohex-2-en-1-one Epimers (36). A solution of compound **25** (327 mg, 1 mmol) and methacrolein (350 mg, 5 mmol) in 5 mL of benzene was heated under reflux for 40 h. The cooled solution was treated with 2 mL of 4:1 0.1 N HCl–THF for 20 min at room temperature. After dilution with 30 mL of chloroform and extraction with 5% aqueous sodium bicarbonate, the organic phase was dried over anhydrous magnesium sulfate. Evaporation of the volatiles in vacuo afforded a residue which was chromatographed on 20 g of silica gel. Elution with 20% ethyl acetate in *n*-hexane afforded 113 mg (38%) of compound **36** as 1:1 mixture of epimers: λ_{max} ($CHCl_3$) 5.77, 5.95 μ; $\delta(CDCl_3)$ 1.28 and 1.32 (1:1 singlets, combined 3), 2.0–2.8 (m, 2), 4.2 (m, 1), 6.0–6.2 (two doublets, J = 10 Hz for each, combined 1), 6.76 (two doublets, J = 10 Hz, for each, combined 1), 7.2–7.8 (m, 5), 9.5 and 9.8 (1:1 singlets, combined 1) ppm.

Anal. Calcd for $C_{14}H_{14}SeO$: C, 57.35; H, 4.81. Found: C, 57.19; H, 4.88.

Preparation of 4-Phenyl-4-carbethoxycyclohex-2-en-1-one (40). A solution of compound **25** (592 mg, 1.81 mmol) and ethyl α-phenylacrylate (528 mg, 3.0 mmol) in 2 mL of benzene was heated in a

scaled glass tube at 115 °C for 24 h. The cooled solution was treated with 10 mL of 0.005 N HCl solution, saturated with ammonium chloride at room temperature for 2 h. After dilution with 50 mL of chloroform and extraction with 5% aqueous sodium bicarbonate, the organic phase was dried over anhydrous magnesium sulfate. Evaporation of the volatiles in vacuo afforded a residue which was chromatographed on 120 g of silica gel. Elution with 10% ethyl acetate in *n*-hexane afforded 252 mg (35%) of enone **38b** and 118 mg (15%) of 4-phenyl-4-carbethoxyl-5-methoxycyclohex-2-en-1-one. The latter was converted quantitatively to enone **38b** by treatment of sodium ethoxide (1 equiv, 25 min at room temperature) to give a 50% overall yield of crude 4-phenyl-4-carbethoxy-6-phenylselenocyclohex-2-en-1-one. To this compound (80 mg, 0.2 mmol) in 2 mL of methylene chloride containing 0.04 mL of pyridine at 0 °C was added 0.40 mL of 15% aqueous hydrogen peroxide. Stirring was continued for 20 min at 0 °C and 15 min at room temperature. The solution was diluted with 20 mL of methylene chloride and was washed with a 5% aqueous bicarbonate, 10% cold aqueous HCl, and brine. The organic phase was dried over anhydrous magnesium sulfate. Evaporation of the volatiles afforded 48.0 mg (50% overall) of essentially pure **40:** λ_{max} ($CHCl_3$) 5.79, 6.0, 6.14 μ; δ($CDCl_3$) 1.30 (t, J = 7 Hz, 3), 4.3 (q, J = 7 Hz, 2), 6.39 (d, J = 10 Hz, 2), 7.1–7.6 (m, 7) ppm.

Preparation of Dimethyl 4-Hydroxy-6-methoxyphthalate (47). Dimethyl acetylenedicarboxylate (355 mg, 25 mmol) was added dropwise to diene **46**[2] (505 mg, 2.5 mol). Exothermicity was noted. The reaction mixture was stirred at room temperature for 15 min at 0 °C, then diluted with 5 mL of a solution of THF, containing 5 drops of 3% HCl. This was stirred at room temperature for 10 min. The volatiles were removed in vacuo. The residue was dissolved in ether and chromatographed on 420 g of silica gel. Elution with ether gave 456 mg (76%) of diester **47**, mp 141–142 °C.

An 89% yield of **47** was realized by conducting the reaction in benzene (1 mL/100 mg of **46**) under reflux for 30 min: λ_{max} ($CHCl_3$) 2.7–3.3, 5.83, 6.25 μ; δ($CDCl_3$) 3.70 (s, 3), 3.80 (s, 3), 3.88 (s, 3), 6.78 (d, J = 2 Hz, 1), 7.00 (d, J = 2 Hz, 1) ppm.

Anal. Calcd for $C_{11}H_{12}O_6$: C, 55.04; H, 5.04. Found: C, 55.19; H, 5.00.

Preparation of Methyl 2-Carbomethoxymethyl-4-hydroxy-6-methoxybenzoate (49). A solution of diene **46** (802 mg, 3.92 mmol) and dimethyl allene-1,3-dicarboxylate (620 mg, 3.36 mmol) in 5 mL of benzene was heated under reflux for 1 h. The volatiles were evaporated in vacuo and the resulting residue was dissolved in 10 mL of THF containing 7 drops of 3% aqueous HCl. This solution was stirred at room temperature for 15 min. Evaporation of the volatiles in vacuo left a residue which was dissolved in ether. The ether solution was dried and the volatiles were evaporated in vacuo. Chromatography on silica gel afforded 720 mg (72%) of **49:** mp 70–72 °C; λ_{max} ($CHCl_3$) 3.0, 5.8–5.9 (br), 6.20 μ; *m/e* 254 (P); δ($CDCl_3$) 3.83 (s, 2), 3.66 (s, 6), 3.82 (s, 3), 6.45 (br s, 2) ppm.

Preparation of Methyl 2-Methoxy-4-hydrophthalate (48). A solution of diene **46** (303 mg, 1.5 mmol) and methyl propiolate (84 mg, 1 mmol) in 2 mL of benzene was heated under reflux for 16 h. Workup in the usual way followed by chromatography on silica gel and elution with 1:1 hexane–ethyl acetate afforded 135 mg (74%) of **48:** mp 150–151 °C (lit.[33] 152–153 °C); λ_{max} ($CHCl_3$) 2.7–3.2, 5.86, 6.26 μ; δ($CDCl_3$) 3.83 (s, 3), 3.95 (s, 3), 6.6–7.0 (m, 2), 7.2–7.4 (m, 2) ppm.

Preparation of 1,4,6-Triacetoxy-8-methoxynaphthalene (50). To a solution of diene **46** (363 mg, 1.8 mmol) in 3 mL of benzene was added *p*-benzoquinone (108 mg, 1 mmol). The color of the reaction mixture turned from brown to light yellow. Evaporation of the volatiles left a residue which was dissolved in 4 mL of acetic anhydride. Pyridine (5 drops) was added and the solution was heated under reflux for 12 h. Evaporation of the volatiles left a residue which was chromatographed on 25 g of silica gel. Elution with 7:3 hexane–ethyl acetate afforded 260 mg (78%) of **50:** mp 172–173 °C; λ_{max} ($CHCl_3$) 5.69, 6.14, 6.21, 6.30 μ; δ($CDCl_3$) 2.33 (s, 6), 2.40 (s, 3), 3.90 (s, 3), 6.65 (d, J = 2 Hz, 1), 7.10 (d, J = 8 Hz, 1), 7.2–7.4 (2 doublets, J = 8, 2 Hz, combined 2) ppm.

Preparation of *cis*-3-Methoxycyclohex-3-en-5-one-2,3-dicarboxylic Acid Anhydride (52). Maleic anhydride (980 mg, 10 mmol) was added portionwise, over 15 min, with stirring, to diene **46** (1.89 g, 11 mmol). The reaction mixture was diluted with chloroform and extracted with water. Evaporation of the chloroform afforded a residue which crystallized on contact with ether, giving 1.55 g (95%) of **52:** mp 152–153 °C; λ_{max} ($CHCl_3$) 5.60, 5.84, 6.10, 6.22 μ; δ($CDCl_3$) 2.77 (dd, J_1 = 18, J_2 = 8 Hz, 1), 2.96 (dd, J_1 = 18, J_2 = 4 Hz, 1), 3.80–3.85 (m, 1), 3.92 (s, 3), 4.18 (d, J = 10 Hz, 1), 5.82 (s, 1) ppm.

Anal. Calcd for $C_9H_8O_5$: C, 55.11; H, 4.11. Found: C, 55.16; H, 4.10.

Preparation of Methyl 2-Methoxycyclohex-2-en-4-one-1-carboxylate (53). A solution of diene **46** (1.01 g, 5 mmol) and methyl acrylate (860 mg, 10 mmol) in 6 mL of benzene was heated under reflux for 24 h. The residue left upon evaporation of the volatiles was treated with 5 mL of 4:1 THF–aqueous 1% HCl. Workup in the usual way gave a residue of 800 mg which was chromatographed on 25 g of silica gel. Elution with 4:1 hexane–ethyl acetate afforded 514 mg (56%) of ester **53** as an oil: λ_{max} ($CHCl_3$) 5.75, 6.05, 6.20 μ; *m/e* 184 (P); δ($CDCl_3$) 2.2–2.4 (m, 4), 3.43 (t, J = 5 Hz, 1), 3.70 (s, 3), 3.73 (s, 3), 5.43 (s, 1) ppm.

Anal. Calcd for $C_9H_{12}O_4$: C, 58.69; H, 6.57. Found: C, 58.51; H, 6.69.

Preparation of 3-Methoxy-4-acetylcyclohex-2-en-1-one (54). Diene **46** (2.02 g, 10 mmol) and methyl vinyl ketone (350 mg, 5 mmol) were heated neat at 45–50 °C for 7 h. Acid hydrolysis and workup in the usual way followed by chromatography on 25 g of silica gel and elution with ether afforded 378 mg of **54** as an oil: *m/e* 168 (P); δ($CDCl_3$) 2.2–2.5 (m, 7 containing s, ca. 3 at 2.20), 3.42 (t, J = 5 Hz, 1), 3.65 (s, 3), 5.40 (s, 3) ppm.

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Supplementary Material Available: Tables of fractional coordinates, structure factors, bond distances, and angles for compound **32** (7 pages). Ordering information is given on any current masthead page.

References and Notes

(1) (a) University of Pittsburgh. (b) Carnegie-Mellon University. (c) Cornell University.
(2) (a) Danishefsky, S.; Kitahara, T. *J. Am. Chem. Soc.* **1974**, *96*, 7807. (b) Danishefsky, S.; Kitahara, T.; Yan, C. F.; Morris, J. *J. Am. Chem. Soc.* **1979**, *101*, 6996. (c) Banville, J.; Brassard, P. *J. Am. Chem. Soc., Perkin Trans 1* **1976**, 1852.
(3) For a related study see: Yamamoto, K.; Suzuki, S.; Tsuji, T. *Chem. Lett.* **1978**, 649.
(4) Sugasawa, S.; Yamada, S. I.; Harahashi, M. *J. Pharm. Soc. Jpn.* **1951**, *71*, 1345.
(5) Hitts, P. R.; McQuittin, F. J. *J. Chem. Soc.* **1953**, 4060.
(6) Onischenko, A. "Diene Synthesis"; Israel Program of Scientific Translations, Daniel Davy and Co.: New York, 1964. For a recent example of effective cycloaddition of a 1,1-dialkylated diene see: Kropf, H.; Schroder, R.; Fotsing, R. *Synthesis* **1977**, 894.
(7) Vogel, P.; Wilthelm, B.; Prinzback, H. *Helv. Chim. Acta* **1969**, *52*, 584.
(8) Galeeva, R. I.; Odinikov, V. N. *Khim. Vyoskomol. Soedin. Neftekhim.* **1973**, *41. Chem. Abstr.* **1974**, *80*, 132650.
(9) Garbisch, E. W. *J. Am. Chem. Soc.* **1964**, *86*, 5563.
(10) Tori, K.; Komeno, T. *Tetrahedron* **1965**, *21*, 309.
(11) Cf. ref 1a,b and Ibuka, T.; Mori, Y.; Aoyami, T.; Inubushi, Y. *Synth. Commun.* **1977**, *7*, 131. In all cases of 1-monooxygenated 3-sitoxybutadienes hydrolysis of the sityl enot ether leads to retention of the 1-oxygen function. In the case of the 1,1-dimethoxy system, compound **46** (vide infra), one of the methoxy groups is lost; see compound **51**.
(12) For a preliminary account of this work see: Danishefsky, S.; Yan, C. F.; McCurry, P. M. *J. Org. Chem.* **1977**, *42*, 1821.
(13) (a) Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc.* **1975**, *97*, 5434. (b) Sharpless, K. B.; Lauer, R. F.; Teranishi, A. Y. *Ibid.* **1973**, *95*, 6137.
(14) For a general review see: Waring, A. J. "Advances in Aliycyclic Chemistry", Hart, H., Karabatsos, G., Eds.; Academic Press: New York, 1966.
(15) Marx, J. N.; Argyle, J. C.; Norman, L. R. *J. Am. Chem. Soc.* **1974**, *94*, 2121. Marx, J. N.; Bombach, E. J. *Tetrahedron Lett.* **1977**, 2391.
(16) Ptieninger, H. *Angew. Chem., Int. Ed. Engl.* **1962**, *1*, 7.
(17) Ptieninger, H.; Arnold, L.; Fischer, R.; Hoffmann, W. *Chem. Ber.* **1965**, *98*, 1774. Gramtich, W.; Ptieninger, H. *Tetrahedron Lett.* **1978**, 475. Gramtich, W.; Ptieninger, H. *Chem. Ber.* **1978**, 1944.
(18) Mura, S.; Kuroki, J.; Hasegawa, K.; Tsutsumi, S. *J. Chem. Soc., Chem. Commun.* **1972**, 946.
(19) Danishefsky, S.; Yan, C. F. *Synth. Commun.* **1978**, *8*, 211.
(20) Subsequent to our communication,[12] this reaction was reported: Ryu, I.; Murai, S.; Nuva, I.; Sonoda, N. *Synthesis* **1977**, 874.
(21) All crystallographic calculations were done on a Prime 400 computer operated by the Materials Science Center and the Department of Chemistry, Cornell University. The principal programs used were REDUCE and UNIQUE, data reduction programs, M. E. Leonowicz, Cornell University, 1978; BLS, block diagonal least-squares refinement, K. Hirotsu, Cornell University, 1978; ORFLS (modified), full matrix least squares, W. R. Busing, K. O. Martin, and H. S. Levy, Oak Ridge, ORNL-TM-305; ORTEP, crystallographic illustration program, C. Johnson, Oak Ridge, ORNL-3794; BOND, structural parameters and errors, K. Hirotsu, Cornell University, 1978; MULTAN-76, direct methods and fast Fourier transform, G. Germain, P. Main, and M. Woolfson, University of York.

(22) Cookson, R. C.; Gitani, S. S. H.; Stevens, I. D. R. *Tetrahedron Lett.* **1962**, 615.
(23) For a review of this field see: Stevens, R. V. In "The Total Synthesis of Natural Products", Vol. III; ApSimon, J., Ed.; Wiley-Interscience: New York, 1977.
(24) Danishefsky, S.; Harayama, T.; Singh, R. K. *J. Am. Chem. Soc.* **1979**, *101*, 7008.
(25) For a preliminary communication of these results see: Danishefsky, S.; Singh, R. K.; Gammill, R. B. *J. Org. Chem.* **1978**, *43*, 379.
(26) Danishefsky, S.; McKee, R.; Singh, R. K. *J. Org. Chem.* **1976**, *41*, 2934. The Experimental Section associated with this paper is contained in the microfilm edition of that journal and in the Ph.D. Thesis of R. McKee, University of Pittsburgh, 1978.
(27) For inclusion of still another oxygen function on a diene see: Grandmaison, J. L.; Brassard, P. *J. Org. Chem.* **1978**, *43*, 1435.
(28) Danishefsky, S.; Walker, F. *J. Am. Chem. Soc.* **1979**, *101*, 7018.
(29) Harayama, T.; Cho, H.; Inubushi, Y. *Tetrahedron Lett.* **1977**, 3273.
(30) Ketty, T. R. *Tetrahedron Lett.* **1978**, 1387.
(31) Melting points are uncorrected. Combustion analyses were performed by Galbraith Associates. Infrared spectra were measured on a Perkin-Elmer 137 or 247 spectrometer. Low-resolution mass spectra were measured on an LKB 9000 system by direct insertion. High-resolution mass spectra were measured on a Varian Associates CH-5 system. Unless otherwise indicated, NMR spectra were measured at 60 MHz in $CDCl_3$ solution, containing tetramethylsilane as an internal standard. Chemical shifts are reported in parts per million (δ) from the Me_4Si resonance.
(32) The corresponding acid was reported: King, L. C.; McWhirter, M.; Barton, D. M. *J. Am. Chem. Soc.* **1945**, *67*, 2089.
(33) Cresp, T. M.; Sargent, M. V.; Felix, J. A.; Murphy, D. P. H. *J. Chem. Soc., Perkin Trans. 1* **1973**, 340.

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

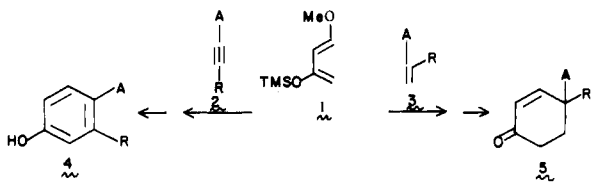
S. Danishefsky,* T. Harayama, and R. K. Singh

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

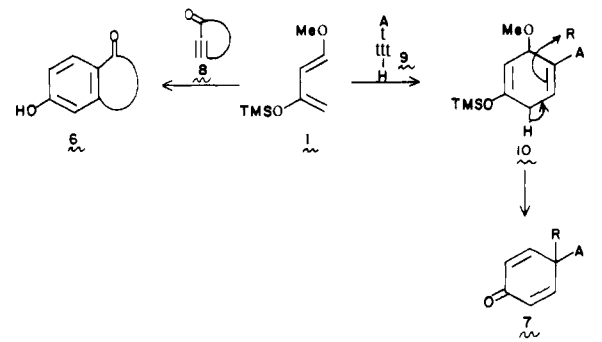
Abstract: The use of β-phenylsulfinyl-α,β-unsaturated carbonyl dienophiles as synthetic equivalents of α,β-ethynyl carbonyl systems has been demonstrated. The sulfoxides were prepared by oxidation of the sulfides, which in turn were obtained from the β-dicarbonyl systems by standard methods. A key feature 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.

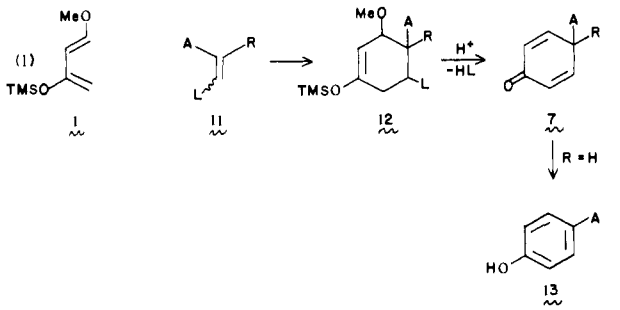


In this paper we describe the results of research directed to a Diels–Alder-based synthesis of phenols of the type **6** and cyclohexadienones[2] such as **7**.[2a,b] For the synthesis of **6**, by the cycloaddition logic above, there would be required cycloalkynones such as **8**, which are in the case 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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