$$(CH_3)_3CCH_2C(CH_3)_2CH_2C(CH_3)=CH_2 \xrightarrow{H^+ClO_4^-} (CH_3)_3CCH_2C(CH_3)_2CH_2(CH_3)_3C^+ \longrightarrow$$

$$(CH_3)_3CCH_2C(CH_3)=CH_2 + t\text{-}Bu^+ \xrightarrow{PhSH} t\text{-}BuSPH + t\text{-}BuCH_2C(CH_3)_2SPh$$

For analogous processes, see, e.g., D. Bethell and V.Gold, "Carbonium Ions an Introduction", Academic Press, London, 1967, p 200.
(7) J. F. Garst, in "Free Radicals", J. K. Kochi, Ed., Wiley, New York, 1973, p 503.
(8) G. D. Sargent and G. A. Lux, *J. Am. Chem. Soc.*, **90**, 7160 (1968).
(9) C. G. Screttas, *Chem. Commun.*, 752 (1972).
(10) The yellow coloration of the solution could be due to a complex of lithium thiophenoxide and alkyllithium, analogous to the metal alkoxide–RLi complexes: T. L. Brown, J. A. Ladd, and G. N. Newman, *J. Organomet. Chem.*, **3**, 1 (1965); K. Huml, *Czech. J. Phys.*, **15**, 699 (1965).
(11) M. Micha-Screttas and C. G. Screttas, *J. Org. Chem.*, **42**, 1462 (1977).
(12) J. F. Biellmann and J. B. Ducep, *Tetrahedron Lett.*, 5629 (1968); S.-Z. Song, M. Shiono, and T. Mukaiyama, *Chem. Lett.*, 1161 (1974).
(13) P. Beak and J. W. Worley, *J. Am. Chem. Soc.*, **94**, 597 (1972).
(14) This is probably due to the destabilizing effect of the substituent on the intermediate secondary benzylic radical, thus rendering it reactive enough to couple with $C_{10}H_8^{-}\cdot$ and form the $Ar(R)CHC_{10}H_8^{-}$ species. For substituent effects on benzylic radical stability, see W. A. Pryor, W. H. Davis, Jr., and J. R. Stanley, *J. Am. Chem. Soc.*, **95**, 4754 (1973).
(15) See ref 4, footnote 14.
(16) See, e.g., R. Waack and M. A. Doran, *J. Am. Chem. Soc.*, **91**, 2456 (1969).
(17) A. J. Birch, *J. Chem. Soc.*, 809 (1945).
(18) E. J. Corey and D. Seebach, *J. Org. Chem.*, **31**, 4097 (1966).
(19) M. J. Brienne, C. Quannes, and J. Jacques, *Bull. Soc. Chim. Fr.*, 613 (1967).
(20) "Dictionary of Organic Compounds", Vol. 3, Eyre and Spottiswood Publishers Ltd., London, 1965, p 1293.
(21) Details of the synthesis of the ether acid will be given in a separate publication.
(22) E. J. Corey and J. Casanova, Jr., *J. Am. Chem. Soc.*, **85**, 165 (1963).

Carbonyl Transposition Studies

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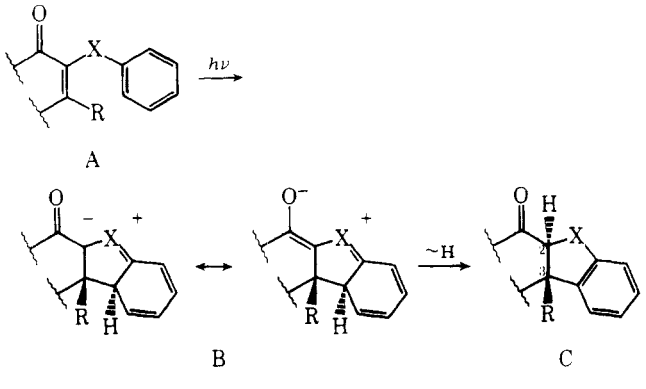
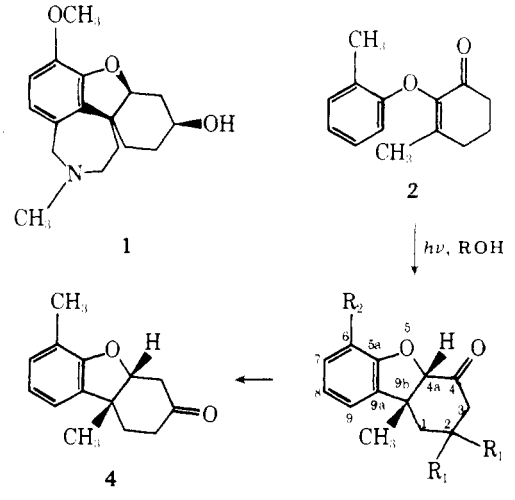
In a program directed toward the total synthesis of the *Amaryllidaceae* alkaloid lycoramine **1**, the model photoconversion **2** → **3** and the 1,2-carbonyl transposition **3** → **4** were studied in detail. Various methods for carbonyl transposition based on a favorable direction of enolization and kinetic enolate formation in **3** were explored. The most effective method in this system, as well as in the actual synthesis of *dl*-lycoramine, involves bissulfenylation of the kinetic enolate of **3** with phenyl phenylthiosulfonate to give thioketal ketone **17**, reduction of **17** to hydroxy thioketal **18a**, conversion of **18a** to thioketal mesylate **18c**, thioketal hydrolysis to give keto mesylate **14c**, and finally reductive cleavage of **14c** with chromous chloride in aqueous acetone at 25 °C to give **4** in 58% overall yield from **3**. Alternatively, hydroxy thioketal **18a** gives ketol **14b** (as a single tautomer), which is converted to keto mesylate **14c** and thence to **4** in 66% isolated yield from **3**.

We have demonstrated that photocyclization–rearrangement (heteroarom directed photoarylation) of aryl vinyl heteroatom systems is an extremely flexible method for carbon–carbon bond formation to an aromatic nucleus (e.g., A → B → C).[1] The heteroatoms oxygen, sulfur, selenium, and nitrogen can be employed and a wide variety of functional groups are compatible with the conditions for photocyclization. Furthermore, a high degree of stereochemical control is possible (e.g., at C(2) and C(3) in C),[2] and an important application of the photoreaction is the bonding of an aromatic ring to an angular carbon atom located at a ring junction.[3]

Early in our studies, we discovered that while simple aryl vinyl ethers undergo inefficient photocyclization, excellent chemical and photochemical cyclization yields are obtained with 2-aryloxyenones (A, X = oxygen). The carbonyl group in A establishes a chromophore (enone), with which relatively low energy Pyrex-filtered light may be employed and at the same time presumably provides for stabilization of the intermediate ylide B as shown.

As a result of an intended application of heteroatom directed photoarylation to a total synthesis of the *Amaryllidaceae* alkaloid lycoramine **1**, we became interested in the model photoconversion **2** → **3** and the 1,2-carbonyl transposition **3** → **4**. In this paper, we present a detailed study of carbonyl transposition in **3**. This report should be of general synthetic interest, because for the first time, a variety of





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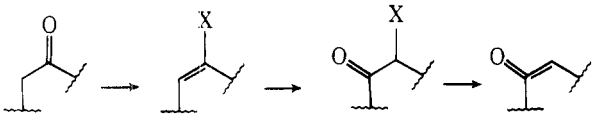
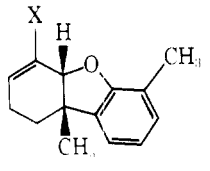
methods for carbonyl transposition in a complex molecule are compared. With an efficient method for carbonyl transposition in this type of benzodihydrofuran, we also extend the synthetic potential of heteroatom directed photoarylation.

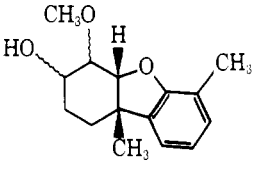
Our initial plan for carbonyl transposition centered on an exploitation of the thermodynamically most favorable direction of enolization in **3**. Thus, conversion of **3** to a vinyl derivative was expected to occur away from the dihydrofuran ring junction and directed hydroboration of the carbon–carbon double bond followed by oxidation of the intermediate organoborane was to provide a transposed α-substituted ketone. Reductive cleavage of the α substituent would complete the sequence.



Brown has demonstrated that hydroboration of an enol ether occurs rapidly, with boron adding exclusively to the β position.[4] Ketone **3** was converted to the enol methyl ether **5a** in essentially quantitative yield and hydroboration of **5a** with diborane in tetrahydrofuran (THF) followed by oxidation with basic hydrogen peroxide gave methoxy alcohol **6** as a



5a, X = OCH_3
b, X = SC_6H_5
c, X = pyrrolidinyl
d, X = piperidinyl
e, X = $OSi(CH_3)_3$
f, X = $OSi(CH_3)_2C(CH_3)_3$



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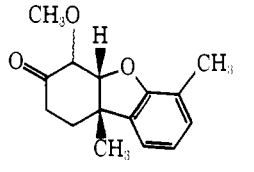


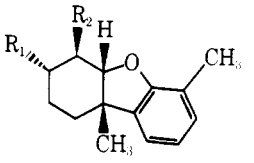
7

mixture of two diastereoisomers. Collins oxidation of **6** gave methoxy ketone **7** in 62% overall yield from **3**.

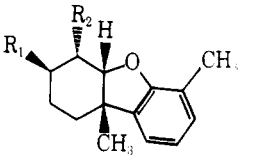
Although the reductive cleavage of a simple α-alkoxy ketone does not seem to have been reported,[5] we explored conditions that are useful with α-acyloxy or α-hydroxy ketones. Reductive cleavage of the methoxy substituent in **7** was unsuccessful under a variety of conditions. For example, treatment of **7** with zinc in refluxing acetic acid[6] or calcium in liquid ammonia[7] resulted in recovery of some **7** and complex mixtures of products. House has noted that chromium(II) salts seem to be more efficient reducing agents than zinc or calcium for cyclohexanone derivatives with α substituents constrained to occupy an equatorial conformation.[8] Under the most favorable conditions, reaction of **7** with chromous chloride in acetone gave a small amount of transposed ketone **4** (12%), but a good deal of polymer as well.

For efficient reductive cleavage in **7**, we reasoned that a leaving group better than methoxy was required. To this end, vinyl sulfide **5b** was prepared; however, attempted hydroboration of **5b** with diborane in THF solution gave a complex mixture of reaction products,[9] while with 9-borabicyclo[3.3.1]nonane (9-BBN) in refluxing THF solution **5b** was recovered unchanged.

The hydroboration of enamines derived from cyclohexanone, followed by oxidation of the intermediate β-amino alkylborane to give *trans*-β-aminocylcohexanols, has been reported by Borowitz and Williams.[10] The pyrrolidine enamine **5c** was prepared, but hydroboration with diborane in THF followed by oxidation of the intermediate organoborane at elevated temperature with alkaline hydrogen peroxide as described by Borowitz and Williams gave amine **8c** as the major reaction product and a small amount of the desired diastereoisomeric amino alcohols **8a** and **9a**. Under these



8a, R_1 = OH; R_2 = pyrrolidinyl
b, R_1 = OH; R_2 = piperidinyl
c, R_1 = H; R_2 = pyrrolidinyl
d, R_1 = OH; R_2 = *N*-oxypyrrolidinyl
e, R_1 = OH; R_2 = *N*-oxypiperidinyl
f, R_1 = OH; R_2 = $OSi(CH_3)_2C(CH_3)_3$

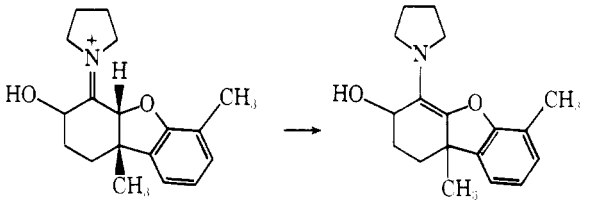


9a, R_1 = OH; R_2 = pyrrolidinyl
b, R_1 = OH; R_2 = piperidinyl
c, R_1 = OH; R_2 = *N*-oxypyrrolidinyl
d, R_1 = OH; R_2 = *N*-oxypiperidinyl

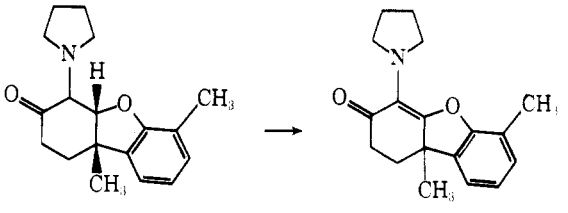
vigorous conditions, protonolysis rather than oxidation of the intermediate β-pyrrolidinyl alkylborane apparently predominates.[11]

On the other hand, room-temperature oxidation with hydrogen peroxide in aqueous sodium acetate followed by preparative chromatography gave amino alcohols **8a** (48% yield) and **9a** (22%). Finally, hydroboration with 9-BBN followed by the mild oxidation procedure gave a single amino alcohol **9a** in 90% isolated yield.

Oxidation of a mixture of **8a** and **9a** with Jones reagent, pyridinium chlorochromate,[12] or chromium trioxide–pyridine under a variety of conditions (0–25 °C) resulted in either little reaction or extensive polymerization. Treatment of **9a** with trifluoroacetic anhydride in dimethyl sulfoxide[13] did give a ketonic product in 79% yield; however, the structure was found to correspond to keto enamine **13**. Apparently initial oxidation of **9a** occurs at nitrogen to give iminium ion **10**, which suffers deprotonation as shown to give amino ketone **11** and (or)



10 **12**



11 **13**

enamine **12**. Both **11** and **12** presumably would undergo further oxidation to give **13**.

A carbonyl transposition based on enamine hydroboration has been described by Gore and co-workers.[14] The key to the process involves oxidation of an intermediate amino alcohol to the *N*-oxide and Cope elimination of the *N*-oxide to give the transposed ketone. The direction of Cope elimination is dependent on availability of hydrogen atoms and may result in production in an allylic alcohol as well as the transposed ketone. Concerted Cope elimination of the *N*-oxide derived from **9a**, however, would produce only transposed ketone **4**. Thus, both **8a** and **9a** were converted to their respective *N*-oxides **8d** and **9c** with *m*-chloroperbenzoic acid.

Attempted pyrolysis of **8d** or **9c** using the conditions described by Gore (neat, degassed, 160 °C at (10 mmHg)) resulted in polymerization. Employing benzene or xylene solvent at reflux also gave polymer. Cram has noted that elimination of *N*-oxides may be effected at lower temperature in polar solvents;[15] however, extended reaction of **8d** or **9c** in THF at 25 °C (or at reflux) again resulted in polymerization.

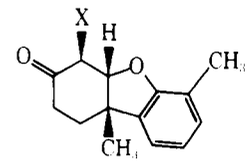
A complicating side reaction possibly encountered in elimination studies with **8d** and **9c** is pyrrolidine ring cleavage to give a homoallylic hydroxylamine. In fact, this kind of ring cleavage has been reported to occur with certain pyrrolidine *N*-oxides;[16] on the other hand, piperidine *N*-oxides seem to be somewhat more resistant to internal elimination. Piperidine *N*-oxides **8e** and **9d** were prepared (see Experimental Section), and indeed, under the most favorable reaction conditions (**9d** in refluxing chlorobenzene solution), the desired transposed ketone **4** was produced in 24% isolated yield; the major reaction product, however, was amino alcohol **9b** (40%). Apparently Cope elimination in this relatively rigid fused ring system proceeds with difficulty and disproportionation of the *N*-oxide occurs on extended heating.

The next vinyl derivative of **3** to be considered was the enol silyl ether **5e**. Selective preparation of **5e** must depend on kinetic selectivity of enolate generation in **3**. Sequential addition of (1) a THF solution of **3** and (2) excess chlorotrimethylsilane to 1 equiv of lithium diisopropylamide (LDA) in THF at −78 °C followed by warming to room temperature and anhydrous workup gave **5e** in >95% yield.

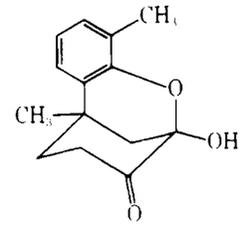
Hydroboration of the enol trimethylsilyl ether of cyclohexanone followed by oxidation with alkaline hydrogen peroxide has been reported to give *trans*-1,2-cyclohexandiol in 70% yield.[17] Although this literature result was encouraging, carbonyl transposition requires that there be some means of differentiation between the two alcohol functions; consequently, we felt that a milder procedure for oxidation of the intermediate organoborane perhaps would allow isolation of a trimethylsilyloxy alcohol. Hydroboration of **5e** followed by oxidation with hydrogen peroxide in aqueous sodium acetate gave a reaction product which had experienced trimethylsilyl ether cleavage. On the other hand, hydroboration–oxidation of the more stable[18] enol *tert*-butyldimethylsilyl ether **5f** gave the hydroxy *tert*-butyldimethylsilyl ether **8f** and oxidation of **8f** with chromium trioxide–pyridine in methylene chloride produced the crystalline α-*tert*-butyldimethylsilyloxy ketone **14a** in 75% overall yield.

In parallel with the reactivity of methoxy ketone **7**, we found that reductive cleavage of the silyloxy group in **14a** was not effective. However, we now seemed to have the option of converting **14a** to the keto mesylate **14c** via ketol **14b**. Attempted desilylation of **14a** using acetic acid–water–THF (3:1:1) at 55 °C resulted in extensive decomposition, whereas tetra-*n*-butylammonium fluoride in THF triggered β-elimination of the phenolic residue in **14a** (or **14b**; vide infra, **18a** → **15**) to give the internal hemiketal **15**.

At this juncture, we abandoned the concept of a high-yield carbonyl transposition via a vinyl derivative of **3** and turned our attention to methodology which incorporates the high regioselectivity of kinetic enolate generation with **3** (cf., **3** →

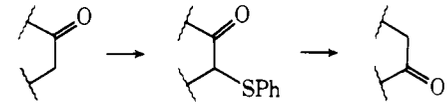


14a, X = $OSi(CH_3)_2C(CH_3)_3$
b, X = OH
c, X = OMs
d, X = $OCOCH_3$



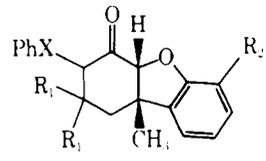
15

5e). Recently, Trost and co-workers have described a 1,2-carbonyl transposition based on the sulfenylation of a ketone

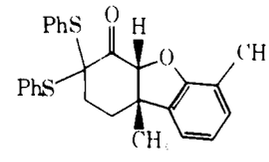


enolate with a disulfide to give an α-sulfenylated ketone.[20] Regioselectivity in enolate reaction and hence ketone carbonyl transposition was indicated in subsequent studies;[21] α-sulfenylation of 2-methylcyclohexanone with the reactive phenyl phenylthiosulfonate demonstrates that a product distribution corresponding to the kinetic selectivity of enolate generation[22] could be obtained with simple unsymmetrical ketones.

Formation of the kinetic enolate of **3** with LDA followed by addition of a THF solution of diphenyl disulfide or phenyl phenylthiosulfonate,[23] with or without added hexamethylphosphoramide (HMPA), gave unreacted **3** and variable amounts of the bissulfenylated ketone **17**. Most of the sulfenylation reagent was consumed in conversion to *N*,*N*-diisopropylbenzenesulfonamide and we could not detect the presence of the desired monosulfenylated ketone **16a**. To account for the observed product distribution, we presume that proton exchange between **3** and **16a** is faster than sulfenylation of **3** and diisopropylamine is sufficiently nucleophilic to react with the sulfenylation reagent (or possibly **16a**).



16a, X = S; R_1 = H; R_2 = CH_3
b, X = Se; R_1 = CH_3; R_2 = H



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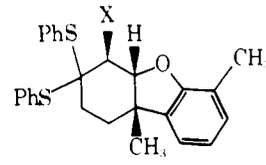
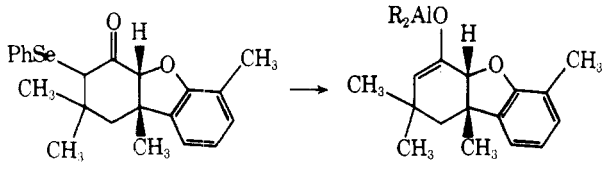


18a, X = OH
b, X = $OCOCH_3$
c, X = OMs

Indeed, with the lithium enolate of **3** generated by use of the relatively less nucleophilic amine tetramethylpiperidine[24] (1 equiv) and phenyl phenylthiosulfonate (1 equiv) in THF–HMPA solution, an ~1:1 mixture of **3** and **17** was obtained.

Frustrated in attempts to prepare **16a**, we turned our attention to the α-phenylseleno ketone **16b**. In contrast to the sulfur analogue, the α-phenylseleno group may be introduced by acid-catalyzed reaction of a ketone with phenyl selenyl chloride in ethyl acetate solution.[25] Thus prepared, **16b** was reacted with a variety of reducing reagents, but in all cases only ketone **3a** was isolated in high yield. Interestingly, treatment of **16b** with diisobutylaluminum hydride in THF followed by addition of chlorotrimethylsilane gave the enol

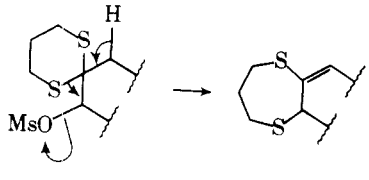


trimethylsilyl ether of ketone **3a** in moderate yield. Presumably, diisobutylaluminum hydride reacts with the α-phenylseleno ketone to give the aluminum enolate of ketone **3a** as shown.[26]

A high-yield carbonyl transposition which makes use of the conversion of a ketone to a propanedithiol derived thioketal ketone has been reported by Marshall and Roebke.[27] Thioketal formation required initial conversion of the ketone to a hydroxymethylene derivative and subsequent reaction with 1,3-propanedithiol di-*p*-toluenesulfonate. A potentially more direct route to a thioketal ketone seemed at hand in the conversion **3** → **17**; consequently, experimental conditions which produced **17** in a satisfactory yield were developed.

Generation of the lithium enolate of **3** with 1.1 equiv of lithium tetramethylpiperidide in THF at −78 °C followed by addition to a solution of phenyl phenylthiosulfonate (2.5 equiv at 25 °C) in HMPA gave thioketal ketone **17** in 85% isolated yield. Reduction of **17** with either lithium aluminum hydride or sodium borohydride gave the hydroxy thioketal **18a** in quantitative yield. Conversion of **18a** to acetate **18b** and hydrolysis of the thioketal group with mercuric chloride in aqueous acetonitrile gave keto acetate **14d**; however, silica gel chromatography of **14d** resulted in epimerization. Attempted reduction of a mixture of the epimers with calcium in ammonia (as described by Marshall) or zinc in acetic acid gave a complex mixture of products. Treatment with chromous chloride in refluxing aqueous acetone did produce a small amount of transposed ketone **4** along with a substantial amount of polymer (see Experimental Section).

We felt that a departure from the literature transposition sequence, by way of keto mesylate **8c**, was required. This modification had been considered by Marshall, but attempted preparation of a thioketal mesylate resulted in quantitative elimination–rearrangement to a vinyl sulfide as shown. With the thiophenol derived thioketal alcohol **18a**, however, we were delighted to discover that thioketal mesylate **18c** could be



obtained in quantitative isolated yield. Thioketal hydrolysis proceeded in good yield to give **14c**. Attempted reductive cleavage of the keto mesylate with zinc and acetic acid was ineffective; however, with calcium in ammonia, **4** could be isolated in moderate yield. With chromous chloride in aqueous acetone at 25 °C, transposed ketone **4** was obtained in essentially quantitative yield (58% from **3**).

We also have converted hydroxy thioketal **18a** to **4** in somewhat higher yield using alternate methodology. Hydrolysis of **18a** to give ketol **14b** occurred in high yield without tautomerization to an isomeric ketol! The anticipated instability of **14b** (vide supra, **14a** → **15**) was clearly demonstrated during attempted thick-layer chromatography of **14b** on silica gel, from which rearranged, internal hemiketal **15** was isolated in 85% overall yield from **18a**. However, crude ketol **14b** could be converted to transposed ketone **4**, via keto mesylate **14c**, in 66% isolated yield from **3**.

That the methodology outlined here for the transposition **3** → **4** is useful in even more complex systems was convincingly demonstrated by our recent total synthesis of *dl*-lycoramine **1**.[28] In this case, the carbonyl transposition was performed in 64% overall yield.

Experimental Section

General. All reactions were run under a positive pressure of dry nitrogen. Infrared spectra were recorded on a Perkin-Elmer Model 137B infrared spectrometer. ^{1}H NMR spectra were obtained on either a Varian A-60A or a Varian EM-390 NMR spectrometer (tetramethylsilane internal standard; deuteriochloroform solvent). ^{1}H NMR decoupling experiments were obtained with the Varian EM-390 NMR spectrometer. Low-resolution chemical ionization and electron impact mass spectra were obtained with a Finnigan 3300 gas chromatograph–mass spectrometer. Microanalyses were carried out by Spang Microanalytical Laboratory, Ann Arbor, Mich. Melting points were obtained on a Thomas-Hoover apparatus, in open capillary tubes, and are uncorrected. Preparative thick layer (1.25 mm) plates were made of E. Merck AG Darmstadt silica gel PF-254 or GF-254. A mixture of 15% methanol in methylene chloride was used for extractions from silica gel unless otherwise indicated. The resulting organic solution was usually washed with 50% brine and water and dried over anhydrous magnesium sulfate and the solvent was evaporated to obtain the organic product.

2-(2-Methylphenoxy)-3-methyl-2-cyclohexen-1-one (2). To a suspension of potassium hydride (0.91 g, 0.022 mol) in THF (14 mL) was added a solution of *o*-cresol (21.0 g, 0.195 mol) in THF (14 mL). When gas evolution had subsided, a solution of 2,3-epoxy-3-methylcyclohexanone (20.0 g, 0.195 mol)[29] in THF (14 mL), followed by hexamethylphosphoramide (26 mL), was added, after which the mixture was heated to reflux for 11 h. After cooling, water (100 mL) was added and the mixture was extracted with ether (2 × 200 mL); the organic layer was washed with 1 N sodium hydroxide (2 × 75 mL) and water (3 × 75 mL) and then dried over anhydrous magnesium sulfate. Evaporation of solvent, distillation (bp 130–132 °C at 0.2 mm), and crystallization from ether–petroleum ether gave **2** (27.1 g, 79%, mp 65.5–66.5 °C): IR ($CHCl_3$) 5.95 μm; ^{1}H NMR δ 1.88 (s, 3 H), 1.73–2.74 (m, 6 H), 2.36 (s, 3 H), 6.35–7.28 (m, 4 H).

4-Oxo-6,9β-dimethyl-1,2,3,4,4aβ,9b-hexahydrodibenzofuran (3) was prepared from **2** by the photochemical procedure found in ref 1; crystallization from ether–petroleum ether gave **3** (84%, mp 93.5–94.0 °C): IR ($CHCl_3$) 5.80 μm; ^{1}H NMR δ 1.45 (s, 3 H), 1.50–2.15 (m, 4 H), 2.28 (s, 3 H), 2.28–2.66 (m, 2 H), 4.42 (s, 1 H), 6.77–7.07 (m, 3 H).

Preparation of 3,3-Bis(phenylsulfenyl)-4-oxo-6,9bβ-dimethyl-1,2,3,4,4aβ,9b-hexahydrodibenzofuran (17). To a solution of tetramethylpiperidine (0.465 mL, 2.75 mmol) and THF (5 mL) at 0 °C was added 2.4 M *n*-butyllithium (1.10 mL, 2.64 mmol) in 1 min. After stirring for 20 min, the solution was cooled to −78 °C and a solution of ketone **3** (540 mg, 2.49 mmol) in THF (5 mL) was added over 3 min. The resulting solution was stirred for 30 min and then was added to a vigorously stirred solution of phenylbenzene thiosulfonate[32] (1.56 g, 6.25 mmol) and hexamethylphosphoramide (5 mL), which was cooled by a 25 °C water bath. After 2 h, 50% saturated ammonium chloride (20 mL) was added to the resulting white suspension. Extraction with ether (3 × 50 mL) was followed by washes with 1 N hydrochloric acid (3 × 25 mL), 1 N sodium hydroxide (3 × 25 mL), and water (2 × 25 mL). Drying over anhydrous magnesium sulfate and evaporation of solvent afforded an oily yellow solid which was crystallized from cold ether to give **17** (624 mg, 58%, mp 134.5–136 °C). The resulting mother liquor was chromatographed (thick layer, silica gel 60 GF-254, benzene as elution solvent) to give more **17** (291 mg, 27%, mp 132–135 °C, R_f 0.3, 85% total): IR ($CHCl_3$) 5.80, 6.25 μm; ^{1}H NMR δ 1.40 (s, = H), 1.80–2.32 (m, 4 H), 2.28 (s, 3 H), 5.06 (s, 1 H), 6.68–7.10 (m, 3 H), 7.13–7.79 (m, 10 H).

Anal. Calcd for $C_{26}H_{24}O_2S_2$: C, 72.21; H, 5.59; O, 7.40; S, 14.80. Found: C, 72.25; H, 5.65.

Preparation of 3,3-Bis(phenylsulfenyl)-4β-hydroxy-6,9bβ-dimethyl-1,2,3,4,4aβ,9b-hexahydrodibenzofuran (18a). To a solution of thioketal ketone **17** (915 mg, 2.11 mmol) and ether (40 mL) was added lithium aluminum hydride (500 mg, 13 mmol) in several portions over 5 min. After 1 h, the resulting suspension was cooled to 0 °C and 1 N hydrochloric acid was added until gas evolution ceased. The mixture was extracted with ether (75 mL) and the organic layer was washed with 1 N hydrochloric acid (3 × 30 mL), 1 N sodium hydroxide (3 × 30 mL), and water (2 × 30 mL) and dried over anhydrous magnesium sulfate. Evaporation of solvent gave **18a** (glass, 920 mg, 100%): IR ($CHCl_3$) 2.70, 6.25 μm; ^{1}H NMR δ 1.09–2.41 (m, 4 H), 1.18 (s, 3 H), 2.31 (s, 3 H), 3.25 (db, 1 H, J_{ab} = 6.0 Hz), 3.99 (db of db, 1 H, J_{ba} = 6.0 Hz, J_{bc} = 4.0 Hz), 4.51 (db, 1 H, J_{cb} = 4.0 Hz), 6.82–7.09 (m, 3 H), 7.12–7.75 (m, 10 H) (deuterium exchange experiment: addition

of deuterium oxide results in disappearance of doublet at δ 3.25 (H_a) and collapse of doublet of doublets at δ 3.99 (H_b) to a doublet (J = 4.0 Hz)).

Preparation of 3,3-Bis(phenylsulfenyl)-4β-acetoxy-6,9bβ-dimethyl-1,2,3,4,4aβ-9b-hexahydrodibenzofuran (18b). To a solution of thioketal alcohol **18a** (100 mg, 0.23 mmol) and pyridine (4.5 mL) was added acetic anhydride (0.62 mL, 6.57 mmol). After 48 h, ether (100 mL) was added and the resulting solution was washed with 1 N sodium carbonate (2 × 25 mL), 1 N hydrochloric acid (2 × 25 mL), and water (2 × 25 mL) and dried over anhydrous magnesium sulfate. Evaporation of solvent and thick-layer chromatography (silica gel 60 PF-254, methylene chloride as elution solvent) gave **18b** (104 mg, 95%, R_f 0.8): IR ($CHCl_3$) 5.74, 6.25 μm; ^1H NMR δ 1.19–2.25 (m, 4 H), 1.25 (s, 3 H), 1.84 (s, 3 H), 2.25 (s, = H), 4.66 (db, 1 H, J = 4.0 Hz), 5.49 (db, 1 H, J = 4.0 Hz), 6.63–7.10 (m, 3 H), 7.10–7.94 (m, 10 H).

Preparation of 3-Oxo-4β-acetoxy-6,9bβ-dimethyl-1,2,3,4,4aβ,9b-hexahydrodibenzofuran (14d). To a suspension of **18b** (55 mg, 0.115 mmol), acetonitrile (1.9 mL), and water (0.49 mL) was added mercuric oxide red (280 mg, 1.29 mmol) followed by mercuric chloride (122 mg, 0.45 mmol). The resulting suspension was heated to 55 °C for 6 h. After cooling, the suspension was filtered through glass wool with the aid of methylene chloride (10 mL). The filtrate was diluted with methylene chloride (50 mL) and then was washed with 50% saturated ammonium acetate (3 × 30 mL) and water (2 × 20 mL) and dried over anhydrous magnesium sulfate. Evaporation of solvent gave crude **14d**, but thick layer chromatography (silica gel 60 PF-254 with $CaSO_4$, methylene chloride as elution solvent) effected epimerization to give a mixture of mainly **14d** and the epimer (24 mg, 76%, R_f 0.4): IR ($CHCl_3$) 5.70, 5.78, 6.25 μm; ^1H NMR δ 1.16–2.58 (m, 4 H), 1.58 (s, 3 H), 2.20 (s, 3 H), 2.28 (s, 3 H), 4.49 (db, 0.29 H, J = 8.0 Hz), 4.75 (db, 0.71 H, J = 3.0 Hz), 5.46 (db, 0.29 H, J = 8.0 Hz), 5.68 (db, 0.71 H, J = 3.0 Hz), 6.92 (m, 3 H). Crystallization from ether–petroleum ether gave **14d** (mp 154–155.5 °C); chemical ionization mass spectrum m/e 275.

Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.06; H, 6.61; O, 23.33. Found: C, 70.13; H, 6.66.

Reductive Cleavage of 14d with Chromous Chloride. To a mixture of acetoxy ketone **14d** and the epimer (13 mg, 0.047 mmol) in acetone (3 mL) was added a solution of chromous chloride (3 mL, 2.55 mmol).[31] The resulting solution was heated to reflux for 1.5 h. After cooling, methylene chloride (50 mL) and brine (10 mL) were added. The organic layer was washed with 1 N sodium carbonate (2 × 10 mL) and water (2 × 10 mL) and dried over anhydrous magnesium sulfate. Evaporation of solvent afforded a mixture (11 mg) of **4** (22%) and **14d** (78%) and no epimer of **14d**. Further treatment of this crude product with chromous chloride led to excessive polymerization.

Preparation of 3,3-Bis(phenylsulfenyl)-4β-mesyloxy-6,9bβ-dimethyl-1,2,3,4,4aβ,9b-hexahydrodibenzofuran (18c). To a solution of thioketal alcohol **18a** (150 mg, 0.345 mmol) in pyridine (1.4 mL) at 0 °C was added mesyl chloride (53 μL, 0.680 mmol). After 10 min, the reaction was allowed to warm to 25 °C and stirring was continued for another 20 min. Ether (70 mL) was added and the resulting solution was washed with 1 N hydrochloric acid (2 × 15 mL), 1 N sodium bicarbonate (2 × 15 mL), and water (2 × 15 mL) and dried over anhydrous magnesium sulfate. Evaporation of solvent at 25–35 °C gave **18c** (quantitative yield) of sufficient purity for further operations: IR ($CHCl_3$) 6.25, 7.40, 8.52 μm; ^1H NMR δ 1.05–2.10 (m, 4 H), 1.14 (s, 3 H), 2.28 (s, 3 H), 3.21 (s, 3 H), 4.65 (db, 1 H, J = 4.0 Hz), 5.21 (db, 1 H, J = 4.0 Hz), 6.75–7.13 (m, 3 H), 7.13–7.80 (m, 10 H).

Preparation of 3-Oxo-4β-mesyloxy-6,9bβ-dimethyl-1,2,3,4,4aβ,9b-hexahydrodibenzofuran (14c). To a suspension of **18c** (182 mg, 0.345 mmol), acetonitrile (6 mL), and water (1.5 mL) was added mercuric oxide red (280 mg, 1.29 mmol) followed by mercuric chloride (360 mg, 1.33 mmol). The resulting mixture was heated to 50 °C for 6 h. After cooling, the suspension was filtered through glass wool with the aid of methylene chloride (20 mL). Methylene chloride (50 mL) was added to the filtrate, which was then washed with 50% saturated ammonium acetate (5 × 30 mL) and water (2 × 20 mL) and dried over anhydrous magnesium sulfate. Evaporation of solvent gave crude **14c**, but thick layer chromatography (silica gel 60 GF-254, methylene chloride as elution solvent) effected epimerization to give a mixture of mainly **14c** and the epimer (70 mg, 73%, R_f 0.4): IR (neat) 5.74, 6.25, 7.37, 8.55 μm; ^1H NMR δ 1.20–2.55 (m, 4 H), 1.38 (s, 0.75 H), 1.60 (s, 2.25 H), 2.18 (s, 2.25 H), 2.21 (s, 0.75 H), 3.24 (s, 0.75 H), 3.40 (s, 2.25 H), 4.52 (db, 0.25 H, J = 8.0 Hz), 4.86 (db, 0.75 H, J = 3.0 Hz), 5.20 (db, 0.25 H, J = 8.0 Hz), 5.49 (db, 0.75 H, J = 3.0 Hz), 6.75–7.20 (m, 3 H).

Reductive Cleavage of 14c with Calcium–Ammonia. To a solution of refluxing liquid ammonia (5 mL) was added a small piece of calcium (just enough to impart a blue color), followed by another addition of calcium (30 mg, 7.5 mmol).[7] After 2 min, a solution of mesyloxy ketone **14c** and the epimer (40 mg, 0.129 mmol) in toluene (0.5 mL) was added and stirred for 10 min. To the resulting solution was added bromobenzene (1 mL, 9.4 mmol, stirred for 2 min) and water (10 mL) after which the mixture was allowed to warm up to 25 °C. Ether (50 mL) was added and the resulting solution was washed with 1 N hydrochloric acid (10 mL) and water (2 × 10 mL) and dried over anhydrous magnesium sulfate. Evaporation of solvent gave a mixture (35 mg) of **4** (44%) and polymeric material (56%) by ^1H NMR analysis.

Preparation of 3-Oxo-6,9bβ-dimethyl-1,2,3,4,4aβ,9b-hexahydrodibenzofuran (4). To a solution of mesyloxy ketone **14c** and the epimer (35 mg, 0.125 mmol) in acetone (2.5 mL) was added a solution of chromous chloride (3 mL, 2.55 mmol).[31] After 4 h, methylene chloride (50 mL) and brine (10 mL) were added and the separated organic layer was washed with water (2 × 10 mL) and dried over anhydrous magnesium sulfate. Evaporation of solvent and Kugelrohr distillation gave **4** (25 mg, 93%).

Preparation of 3-Oxo-4β-hydroxy-6,9b-dimethyl-1,2,3,4a,9b-hexahydrodibenzofuran (14b). To a suspension of thioketal alcohol **18a** (250 mg, 0.575 mmol) in acetonitrile (8.5 mL) and water (2.2 mL) was added mercuric oxide red (430 mg, 1.985 mmol) followed by mercuric chloride (530 mg, 1.952 mmol). The resulting mixture was heated to 55 °C for 6 h. After cooling, the suspension was filtered through glass wool with the aid of ether (70 mL) and the filtrate was washed with 50% saturated ammonium acetate (6 × 25 mL) and water (2 × 20 mL) and dried over anhydrous magnesium sulfate. Evaporation of solvent afforded crude **14b** (250 mg, quantitative yield) which was used for further operations without purification: IR (neat) 2.90, 5.80, 6.25 μm; ^1H NMR δ 1.00–1.50 (m, 2 H), 1.55 (s, 3 H), 1.80–2.35 (m, 2 H), 2.19 (s, 3 H), 3.65 (br s, 1 H, replaceable on addition of deuterium oxide), 4.56 (db, 1 H, J = 3.0 Hz), 4.81 (db, 1 H, J = 3.0 Hz), 6.78–7.13 (m, 3 H).

Rearrangement of Ketol 14b to 4-Methyl-4-(2-hydroxy-3-methylphenyl)-1,2-cyclohexanedione Hemiketal (15). A sample of ketol **14b** (250 mg, ca. 0.575 mmol) underwent rearrangement on attempted chromatography (silica gel 60 PF-254 with $CaSO_4$, methylene chloride as elution solvent) to give **15** (114 mg, 85% overall from **18a**).

Preparation of 3-Oxo-4β-mesyloxy-6,9bβ-dimethyl-1,2,3,4,4aβ,9b-hexahydrodibenzofuran (14c). To a solution of crude ketol **14b** (250 mg, ca. 0.575 mmol) in pyridine (3.5 mL) at 0 °C was added mesyl chloride (0.10 mL, 1.283 mmol) dropwise. After 10 min, the mixture was allowed to warm to 25 °C and stirred for another 20 min. Ether (70 mL) was added and the resulting solution was washed with 1 N hydrochloric acid (2 × 20 mL), 1 N sodium bicarbonate (2 × 15 mL), and water (2 × 15 mL) and dried over anhydrous magnesium sulfate. Evaporation of solvent afforded **14c** (230 mg, quantitative yield) which was used for further operations without purification.

Preparation of Ketone 4 (via Ketol 14b). To a solution of crude mesyloxy ketone **14c** (230 mg, ca. 0.575 mmol) in acetone (17 mL) was added a solution of chromous chloride (24 mL, 20.4 mmol).[31] After 3 h, brine (10 mL) was added and the resulting solution was extracted with ether (60 mL). The organic layer was washed with 1 N sodium hydroxide (15 mL) and water (2 × 10 mL) and dried over anhydrous magnesium sulfate. Evaporation of solvent and distillation gave **4** (95 mg, 77% overall from **18a**: bp 75–80 °C (0.05 mm); mp 52–55 °C): IR ($CHCl_3$) 5.83, 6.25 μm; ^1H NMR δ 1.35–2.42 (m, 4 H), 1.50 (s, 3 H), 2.20 (s, 3 H), 2.67 (db of db, 1 H, J_{ab} = 16.0 Hz, J_{ax} = 3.0 Hz), 2.94 (db of db, 1 H, J_{ba} = 16.0 Hz, J_{bx} = 3.0 Hz), 4.74 (db of db, 1 H, J_{xa} = 3.0 Hz, J_{xb} = 3.0 Hz), 6.75–7.12 (m, 3 H) [decoupling experiment–irradiation of the center of two sets of doublet of doublets at δ 2.67 (H_a) and δ 2.94 (H_b) results in collapse of doublet of doublets at δ 4.74 (H_x) to a singlet and irradiation of doublet of doublets at δ 4.74 (H_x) results in collapse of the two sets of doublets at δ 2.67 (H_a) and δ 2.94 (H_b) to two sets of doublets (J = 16.0 Hz for both)]; electron impact mass spectrum m/e 216.

Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46; O, 14.79. Found: C, 77.73; H, 7.30.

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Registry No.—**2**, 68758-17-8; **3**, 68758-18-9; **3a**, 66613-56-7; **3a** enol Me_4Si ether, 68758-19-0; **4**, 68758-20-3; **5a**, 68758-21-4; **5b**, 68758-22-5; **5b** double bond isomer, 68758-23-6; **5c**, 68758-24-7; **5d**, 68758-25-8; **5e**, 68758-26-9; **5f**, 68758-27-0; **6** isomer A, 68758-28-1; **6** isomer B, 68758-29-2; **7** isomer A, 68758-30-5; **7** isomer B, 68758-31-6; **8a**, 68758-32-7; **8b**, 68758-33-8; **8d**, 68758-34-9; **8e**, 68758-35-0; **8f**,

68758-36-1; **9a,** 68758-37-2; **9b,** 68758-38-3; **9c,** 68758-39-4; **9d,** 68758-40-7; **13,** 68758-41-8; **14a,** 68758-42-9; **14b,** 68758-43-0; **14c,** 68758-44-1; **14d,** 68758-45-2; **15,** 68758-46-3; **16b,** 68758-47-4; **17,** 68758-48-5; **18a,** 68758-49-6; **18b,** 68758-50-9; **18c,** 68758-51-0; *o*-cresol, 95-48-7; 2,3-epoxy-3-methylcyclohexanone, 21889-89-4; phenylbenzene thiosulfonate, 1212-08-4; benzenethiol, 108-98-5; pyrrolidine, 123-75-1; piperidine, 110-89-4; trimethylchlorosilane, 75-77-4; *tert*-butyldimethylsilyl chloride, 18162-48-6; phenylselenyl chloride, 5707-04-0.

Supplementary Material Available: Preparation and reactions of **5–9, 14,** and **16** (14 pages). Ordering information is given on any current masthead page.

References and Notes

(1) A. G. Schultz, R. D. Lucci, W. Y. Fu, M. H. Berger, J. Erhardt, and W. K. Hagmann, *J. Am. Chem. Soc.*, **100,** 2150 (1978): A. G. Schultz, W. Y. Fu, R. D. Lucci, B. G. Kurr, K. M. Lo, and M. Boxer, *ibid.*, **100,** 2140 (1978); A. G. Schultz and I-C. Chiu, *Chem. Commun.*, 29 (1978); A. G. Schultz and W. K. Hagmann, *ibid.*, 726 (1976); A. G. Schultz, J. Erhardt, and W. K. Hagmann, *J. Org. Chem.*, **42,** 3458 (1977); A. G. Schultz, *ibid.*, **40,** 3466 (1975); A. G. Schultz and R. D. Lucci, *ibid.*, **40,** 1371 (1975); A. G. Schultz, *ibid.*, **39,** 3185 (1974)

(2) A. G. Schultz and R. D. Lucci, *Chem. Commun.*, 925 (1976).

(3) A. G. Schultz and W. Y. Fu, *J. Org. Chem.*, **41,** 1483 (1976).

(4) H. C. Brown and R. L. Sharp, *J. Am. Chem. Soc.*, **90,** 2915 (1968).

(5) Stotter and Edwards report a ketone carbonyl transposition in three model systems, which is performed by (1) oxygen alkylation of a kinetically generated lithium enolate with chloromethyl methyl ether in HMPA solution, (2) hydroboration–oxidation of the resulting enol ether to give an α-methoxy methoxy ketone, and (3) reductive cleavage with lithium in ammonia; see C. L. Edwards, Ph.D. Dissertation, The University of Texas at Austin, 1974; *Diss. Abstr.*, **35,** 5327-B (1975). Because alkylation of the kinetic lithium enolate of **3** with chloromethyl methyl ether gave a 70:30 mixture of oxygen–carbon alkylation, this methodology was not pursued.

(6) R. S. Rosenfeld and T. F. Gallagher, *J. Am. Chem. Soc.*, **77,** 4367 (1955).

(7) J. H. Chapman, J. Elks, G. H. Phillipps, and L. J. Wyman, *J. Chem. Soc.*, 4344 (1956).

(8) H. O. House and R. G. Carlson, *J. Org. Chem.*, **29,** 74 (1964); H. O. House and E. F. Kinloch, *ibid.*, **39,** 1173 (1974).

(9) D. J. Pasto and Sr. R. Snyder, O. S. F., *J. Org. Chem.*, **31,** 2777 (1966).

(10) I. J. Borowitz and G. J. Williams, *J. Org. Chem.*, **32,** 4157 (1967).

(11) The conversion of enamines to amines by hydroboration and protonolysis of the intermediate β-amino alkylborane in refluxing methanol has been reported; for example, see J. Gore and J.-J. Barieux, *Tetrahedron Lett.*, 2849 (1970); and J.-J. Barieux and J. Gore, *Tetrahedron*, **28,** 1537 (1973).

(12) E. J. Corey and J. W. Suggs, *Tetrahedron Lett.*, 2647 (1975).

(13) S. L. Huang, K. Omura, and D. Swern, *J. Org. Chem.*, **41,** 3329 (1976).

(14) J. Gore, J. P. Drouet, and J.-J. Barieux, *Tetrahedron Lett.*, 9 (1969).

(15) D. J. Cram, M. R. V. Sahyun, and G. R. Knox, *J. Am. Chem. Soc.*, **84,** 1734 (1962).

(16) A. C. Cope and N. A. LeBel, *J. Am. Chem. Soc.*, **82,** 4656 (1960).

(17) J. Klein, R. Levene, and E. Dunkelblum, *Tetrahedron Lett.*, 2845 (1972). Cyclic enol trimethylsilyl ethers have been converted to olefins by hydroboration followed by treatment of the intermediate organoborane with an acid catalyst; see G. L. Larson, E. Hernandez, C. Alonso, and I. Nieves, *Tetrahedron Lett.*, 4005 (1975).

(18) The dimethyl-*tert*-butylsilyloxy group is $\sim 10^4$ times more stable to solvolysis in protic media than trimethylsilyloxy: see L. H. Sommer, "Stereochemistry, Mechanism and Silicon", McGraw-Hill, New York, 1965, pp 132 and 138.

(19) E. J. Corey and A. Venkateswarlu, *J. Am. Chem. Soc.*, **94,** 6190 (1972).

(20) B. M. Trost, K. Hiroi, and S. Kurozumi, *J. Am. Chem. Soc.*, **97,** 438 (1975).

(21) B. M. Trost, T. N. Salzamann, and K. Hiroi, *J. Am. Chem. Soc.*, **98,** 4887 (1976).

(22) H. O. House, L. J. Czuba, M. Gall, and H. D. Olmstead, *J. Org. Chem.*, **34,** 2324 (1969).

(23) H. J. Shine, M. Rahman, H. Seeger, and G. S. Wu, *J. Org. Chem.*, **32,** 1901 (1967).

(24) R. A. Olofson and C. M. Dougherty, *J. Am. Chem. Soc.*, **95,** 582 (1973).

(25) K. B. Sharpless, R. F. Lauer, and A. Y. Teranishi, *J. Am. Chem. Soc.*, **95,** 6137 (1973).

(26) In an apparently analogous reaction, Reich and co-workers report that treatment of 1-phenyl-2-phenylseleno-1-propanone with PhSeLi at −78 °C results in formation of diphenyl diselenide and 1-phenyl-1-propanone: H. J. Reich, J. M. Renga, and I. L. Reich, *J. Am. Chem. Soc.*, **97,** 5434 (1975).

(27) J. A. Marshall and H. Roebke, *J. Org. Chem.*, **34,** 4188 (1969).

(28) A. G. Schultz, Y. K. Yee, and M. H. Berger, *J. Am. Chem. Soc.*, **99,** 8065 (1977).

(29) Prepared from 3-methyl-2-cyclohexen-1-one by the procedure of E. I. Wasson and H. O. House, *Org. Synth.*, **37,** 58 (1957).

(30) R. Ratcliffe and R. Rodehorst, *J. Org. Chem.*, **35,** 4000 (1970).

(31) G. Rosenkranz, O. Mancera, J. Gatica, and C. Djerassi, *J. Am. Chem. Soc.*, **72,** 4077 (1950).

(32) D. Barnard, *J. Chem. Soc.*, 4673 (1957).

Modified Extended Selectivity Treatment for Biphenyl, Naphthalene, and Benzothiophene

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Electrophilic substitution at position 4 in biphenyl, 1 and 2 in naphthalene, and 2 and 3 in benzothiophene is correlated by an equation, $\log f = \rho\{\sigma_1^+ + (\sigma_2^+ - \sigma_1^+)\} + E_R$, which, because of variations in the magnitudes of $\sigma_2^+ - \sigma_1^+$ and E_R, is best applied as two linear equations, $\log f = \rho\sigma_1^+$, for $0 > \rho \geq -4.5$, and $\log f = \rho\sigma_2^+ + E_R$, for $-4.5 > \rho$. The parameters σ_1^+, σ_2^+, and E_R are discussed in terms of dual activation mechanisms for the bicyclic systems, and reactivity in position 1 in naphthalene is explained without invoking steric interaction with the peri hydrogen.

The extended selectivity treatment (EST) of Stock and Brown[1] produces linear plots passing through the origin (hence defining a unique σ^+ constant) for monosubstituted benzenes,[1] furan,[2] thiophene,[3,4] and fluorene,[5] but nonlinear plots have been obtained for 4-biphenyl (I),[5] 1- and 2-naphthalene (II and III),[1,6] and 2- and 3-benzothiophene (IV and V).[6] Attempts to explain the curvature in terms of polarizability or steric effects (for I) or variable mesomeric contributions (for II–V) have not been successful,[6] and the four-parameter Yukawa–Tsuno equation[7] has been found not to improve the correlation, except for III.[6]

Two *linear* equations, eq 1 and 2, give good correlations of the reactivity of I–III in electrophilic substitution, each over a limited range of ρ values:

$$\log f = \rho\sigma_1^+ \quad (1)$$

i.e., the normal EST equation, for $0 > \rho \geq -4.5$, over which range a single σ_1^+ value suffices for II and III, and

$$\log f = \rho\sigma_2^+ + E_R \quad (2)$$

where E_R is constant, for $-4.5 \geq \rho \geq -12.1$. The parameters σ_1^+, σ_2^+, and E_R, evaluated by least squares, are listed in

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