was added slowly with stirring to a solution of **3** (101 mg, 0.20 mmol) and hexamethyldisilazane (100 μL, 0.47 mmol) in dry pentane (3.0 mL) at −20 °C. The reaction mixture was stirred at −20 °C for 20 min and then at 24 °C for 6 h. The solid was removed by centrifugation, and the solvent was removed under vacuum. The 6-silyl enol ether **12** as a colorless oil was the exclusive product, accompanied by 10% of starting ketone **3**.

(3′*S*,1*R*,2*S*,3*R*)-2-(3′-((*tert*-Butyldimethylsilyl)oxy)-3′-cyclohexylprop-1′-ynyl)-3-((*tert*-butyldimethylsilyl)oxy)-7-((trimethylsilyl)oxy)bicyclo[4.2.0]oct-6-ene (12): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.48 (m, 1 H, H-4′), 1.98 (m, 1 H, H-1), 2.0 (m, 1 H, H-2), 2.21 (dd, 1 H, *J* = 2.0, 12.5 Hz, H-8β), 2.66 (ddd, 1 H, *J* = 3.2, 3.2, 12.5 Hz, H-8α), 3.54 (br dd, 1 H, *J* = 9.0, 9.0 Hz, H-3), 4.08 (dd, 1 H, *J* = 1.3, 5.9 Hz, H-3′); GC/MS *m/z* 576 (M^+).

(±)-7-((Trimethylsilyl)oxy)bicyclo[4.2.0]oct-6-ene (16) as a colorless oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.07 (s, 6 H, $SiMe_2$), 0.20 (s, 3 H, SiMe), 1.93 (m, 1 H, H-1), 2.10 (br dd, 1 H, *J* = 1.9, 12.3 Hz, H-8β), 2.62 (ddd, 1 H, *J* = 3.7, 3.7, 12.3 Hz, H-8α); GC/MS *m/z* 196 (M^+).

(3′*S*,1*S*,2*S*,3*R*,6*S*)-2-(3′-((*tert*-Butyldimethylsilyl)oxy)-3′-cyclohexylprop-1′-ynyl)-3-((*tert*-butyldimethylsilyl)-oxy)-6-methyl-8-*exo*-methylbicyclo[4.2.0]octan-7-one (22). A 1.0 M solution of LiHMDS (0.87 mL) in THF was cooled to −78 °C, and a solution of **7** (300 mg, 0.58 mmol) in THF (10 mL) was added dropwise. The reaction mixture was stirred at −78 °C for 30 min, and then methyl iodide (1.0 mL, 16 mmol) in HMPA (0.5 mL) was added in one portion. The reaction conditions and workup were the same as described for the synthesis of compound **7**, and the residue was chromatographed on silica gel, eluting with 2% ethyl acetate in hexane, to give **22** as a colorless gum (235 mg, 76%): $[\alpha]_D$ = −19.78° (*c* 0.425, $CHCl_3$), IR (neat) 1780 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ [0.06 (s, 3 H), 0.08 (s, 6 H), 0.11 (s, 3 H)] (4 SiMe), 0.88, 0.91 (2 s, 18 H, tBu), 1.11 (d, *J* = 7.1 Hz, 3 H, C8-Me), 1.24 (s, 3 H, C6-Me), 1.74 (br d, *J* = 9 Hz, 1 H, H-1), 2.84 (br s, 1 H, H-2), 4.13 (m, 1 H, H-3), 3.96 (dq, *J* = 9.0, 7.1 Hz, 1 H, H-8), 4.06 (dd, *J* = 6.2, 1.9 Hz, 1 H, H-3′); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −4.46, −5.03 (s), −5.03 (s), −5.03 (s, 2 $SiMe_2$), 12.54 (q, 8-Me), 17.94 (s), 18.33 (s), 25.72 (q), 25.86 (q), (2 *t*-Bu), 20.80 (q, 6-Me), 22.32 (t, C-5), 23.80 (t, C-4), 26.03 (t), 26.03 (t, C-6′, C-8′), 26.59 (t, C-7′) 28.62 (t), 28.76 (t, C-5′, C-9′), 31.83 (d, C-2), 43.40 (d, C-1), 45.15 (d, C-4′), 55.26 (d, C-8), 56.52 (s, C-6), 67.79 (d, C-3′), 69.80 (d, C-3), 82.83 (s, C-2′), 86.04 (s, C-1′), 214.65 (s, C-7); MS *m/z* 532 (M^+); HRMS *m/z* 532.378 493 ($C_{31}H_{56}O_3Si_2$ requires 532.376 803). Anal. Calcd for $C_{31}H_{56}O_3Si_2$: C, 69.86; H, 10.59. Found: C, 69.67; H, 10.42.

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Acknowledgment. We wish to acknowledge the help of Syntex Analytical Services and Dr. Kelvin Chan for analytical and GC/Mass spectral data.

Supplementary Material Available: ^{13}C and/or ^{1}H NMR spectra for compounds **9**, **10**, **12**, (**12** + **13**), **16**, (**16** + **17**), and **18** (20 pages). Ordering information is given on any current masthead page.

1,3-Benzodithiolium Cation Mediated Cyclization Reactions

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General protocols for the construction of various ring systems employing cation olefin cyclizations initiated by the readily accessible 1,3-benzodithiolium ion are described. Several substituted tetralones and tetralins can be rapidly assembled by this methodology as can a variety of substituted bicyclo[3.2.1]octane and tricyclic ring systems. The products of these transformations are amenable to interconversion into a range of functionalized species.

Introduction

The readily available 1,3-benzodithiole heterocycle (**1**)[1] exhibits a number of interesting properties which, if properly harnessed, offer considerable appeal in terms of application to rapid and versatile carbon–carbon bond formation. Of particular note is the relative ease with which both the corresponding carbanionic **2** and carbocationic **3** forms can be expressed. The former is generated by simple deprotonation at the C_2 position with a strong base such as *n*-butyllithium. This species can be viewed as a convenient acyl anion equivalent and has been shown to react accordingly.[2] The alternative 1,3-benzodithiolium carbocation (**3**) exhibits considerable stability and can be produced, among other ways, by a hydride exchange with triphenylmethyl fluoroborate.[1,3] Several studies attesting to the useful electrophilicity of **3** have appeared recently.[4] The unique stability of carbocation **3** has been attributed to the presence of a cyclic 10π electron array that renders the system aromatic in character. Indeed, ^{13}C NMR studies on **3** and related sulfur stabilized carbocations have been cited in support of this contention.[5] Experimental evidence places the stability of the 1,3-benzodithiolium ion **3** somewhere between that of the tropylium and trityl carbocations.[1,3]

The notion of combining this dichotomy of reactivity into a sequence in which the nucleophilic and electrophilic

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(2) (a) Ncube, S.; Pelter, A.; Smith, K. *Tetrahedron Lett.* **1979**, 1893, 1895. (b) Ncube, S.; Pelter, A.; Smith, K.; Blatcher, P.; Warren, S. *Ibid.* **1978**, 2345. (c) Brown, C. A.; Miller, R. D.; Lindsay, C. M.; Smith, K. *Ibid.* **1984**, *25*, 991.

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(4) (a) Nakayama, J. *Synthesis* **1975**, 170. (b) Nakayama, J.; Fujiwara, K.; Hoshino, M. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 3567. (c) Degani, I.; Fochi, R. *Synthesis* **1976**, 759. (d) Degani, I.; Fochi, R. *Ibid.* **1977**, 263. (e) Degani, I.; Fochi, R. *J. Chem. Soc., Perkin Trans. 1* **1978**, 1133. (f) Degani, I.; Fochi, R.; Regondi, V. *Tetrahedron Lett.* **1981**, *22*, 1821. (g) Ncube, S.; Pelter, A.; Smith, K. *Ibid.* **1977**, 255. (h) Pelter, A.; Rupani, P.; Stewart, P. *J. Chem. Soc., Chem. Commun.* **1981**, 164.

(5) (a) Sakamoto, K.; Nakamura, N.; Oki, M.; Nakayama, J. *Chem. Lett.* **1977**, 1133. (b) Hirai, K. *Tetrahedron* **1971**, *27*, 4003. (c) Olah, G. A.; Grant, J. L. *J. Org. Chem.* **1977**, *42*, 2237.

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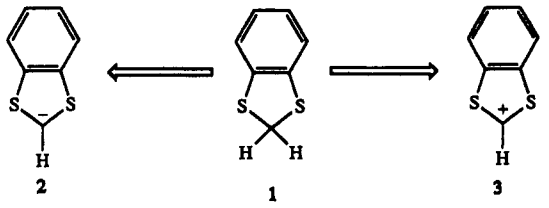
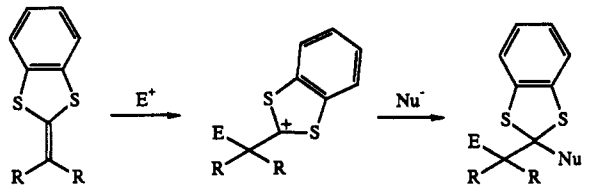


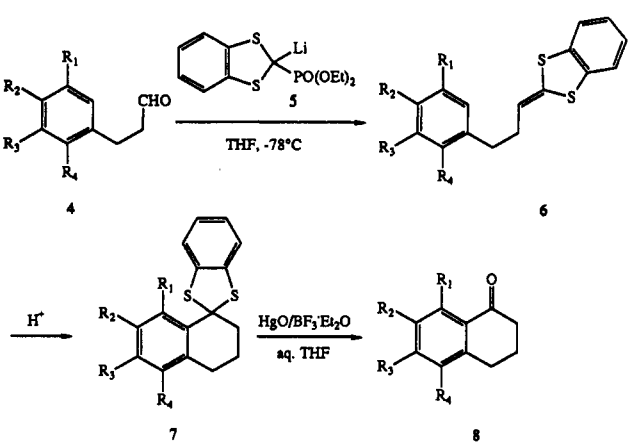
characteristics of this substrate were exploited in successive steps for carbon bond formation was intriguing, and the results of our studies on certain aspects of this concept are presented in the following account. From the outset, it was envisioned that a mild and convenient access to carbocations similar to **3** could be realized through the intermediacy of an appropriate ketene dithioacetal derivative.[6a] The process could be triggered with an electrophilic species (i.e. proton), which would result in the formation of a substituted benzodithiolium ion, which would subsequently be trapped by a suitable carbon nucleophile. The following studies were initiated to examine in detail the general viability of employing of this set of manipulations in the construction of synthetically significant ring systems.



Preparation of Substituted Tetralones and Tetralins. A useful first generation testing ground for this concept would be the cyclization of a tethered ketene dithioacetal onto an aromatic nucleus (Scheme I). The resultant product would possess a protected ketone that could be removed hydrolytically to reveal a tetralone product. Alternatively, the benzodithiole moiety could be conveniently cleaved reductively to provide the corresponding tetralin. Over the years, an impressive list of methods for effecting the cyclization of carbonyl-derived functionality onto an aromatic ring has appeared.[6] In many instances, however, relatively harsh conditions have been necessary to bring about the desired bond formation. The methodology described herein provides an alternative cyclization protocol that is experimentally convenient and sufficiently mild that most functionality will survive intact.

The requisite 3-aryl-1-propanals (**4**) were easily prepared by employing a standard two-carbon homologation sequence. The commercially available benzaldehydes were treated, in succession, with lithiotriethylphosphonoacetate, lithium aluminum hydride, and, finally, pyridinium dichromate to provide the corresponding known aldehyde building blocks. Exposure of these propanals to the readily available 1,3-benzodithiole carbanion source, 2-lithio-2-(diethoxyphosphinyl)-1,3-benzodithiole (**5**)[7] yielded the key cyclization precursors, ketene dithioacetals **6**. The yields for these transformations were exceptionally high, and the

Scheme I



reaction mixtures were free of virtually any side products. Typically, these somewhat labile ketene dithioacetals were used immediately upon isolation.

In light of our expectation that 1,3-benzodithiolium ion mediated cyclization could proceed under mild conditions, we were gratified to learn that only a few crystals of *p*-toluenesulfonic acid at 0 °C were required to trigger ring formation in most of the ketene dithioacetals examined to date. Typically, most reactions were complete at this temperature in a few hours. Filtration of the precipitated product and recrystallization provided pure adducts **7a–f**. The results of this study are compiled in Table I.[8] Examination of the data in this table reveals a number of interesting features of this cyclization protocol. Not surprisingly, the facility of the process was somewhat dependent on the level of activation in the aromatic ring. For example, the reaction in entry 1, wherein no electron-donating substituents are present on the benzene ring, required larger quantities of acid catalyst and warming to 50 °C for a short time to effect efficient bond formation. No product was observed in the absence of heat in this case. The same was true for entry 6, where cyclization was obliged to occur at a position meta to the methoxy substituent. An intriguing trend in substitution patterns could also be discerned which suggested that steric hindrance strongly influences the course of these reactions. This phenomenon was evidenced by the production of the less hindered regioisomeric product in every case where an option was available (entries 2, 4, 5). A more dramatic illustration of this steric inhibition of cyclization was the complete absence of product formation even under the most forcing conditions in the reaction of **6g** (entry 7). This useful site selectivity was exploited to synthetic advantage in another context that will be described in detail below.

While the cyclization step in this process generally proceeded without incident to deliver the desired products, efforts to hydrolyze the respective benzodithiole ketals to expose the corresponding tetralones initially proved to be somewhat problematic. Indeed, after examination of most of the known repertoire of dithioketal cleavage reactions, only treatment with red mercury(II) oxide–boron trifluoride etherate in aqueous THF was routinely successful in the cases studied[9] (Table I). In contrast, the reductive removal of the 1,3-benzodithiole moiety with Raney nickel (W-2) to provide the corresponding tetrahydronaphthalenes **9** was a high-yielding process which was

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(7) (a) Akiba, K.; Ishikawa, K.; Inamoto, N. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 2674. (b) Nakayama, J. *Synthesis* **1975**, 38.

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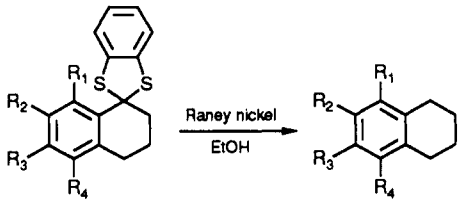
Table I. Preparation and Cyclization of Ketene Benzodithioacetals (Scheme I)

entry	4	yield, % 6	7	8
1	a: R_1, R_2, R_3, R_4 = H	99	70[a]	62
2	b: R_1, R_4 = H; R_2, R_3 = OMe	93	76[b]	60
3	c: R_1, R_2 = H; R_3, R_4 = OMe	99	56	55
4	d: R_1, R_4 = H; R_2, R_3 = $-OCH_2O-$	95	75[b]	55
5	e: R_1, R_2, R_4 = H; R_3 = OMe	99	77[b]	62
6	f: R_1, R_3, R_4 = H; R_2 = OMe	90	74[a]	56
7	g: R_2, R_3 = H; R_1, R_4 = OMe	98	–[c]	–

[a] Approximately twice the normal quantity of *p*-TsOH and warming to 40–50 °C was required for efficient cyclization to occur. [b] None of the other possible regioisomer was observed. [c] No cyclization took place under any conditions examined.

Table II. Desulfurization of Benzodithioles 7b–e

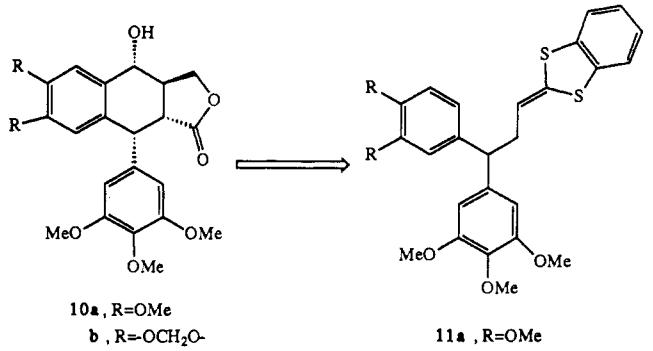


7 9

entry	benzodithiole 7	tetralin 9 yield, %
1	b	69
2	c	75
3	d	91
4	e	95

virtually trouble free in all instances (see Table II).

Synthetic Applications of 1,3-Benzodithiolium Ion Mediated Cyclizations. The reluctance of the 1,3-benzodithiolium ion to undergo cyclization at aryl ring positions that are sterically encumbered suggested that this protocol would be particularly well-suited for assembly of the carbon skeleton of certain lignan natural products. Typical examples of this class of compounds that would appear to lend themselves to this strategy include sikkimotoxin (**10a**) and podophyllotoxin (**10b**).[10] Based on previous results in related systems, our approach into these interesting compounds was predicated on the *selective* cyclization of the benzodithiolium ion from **11a** onto the



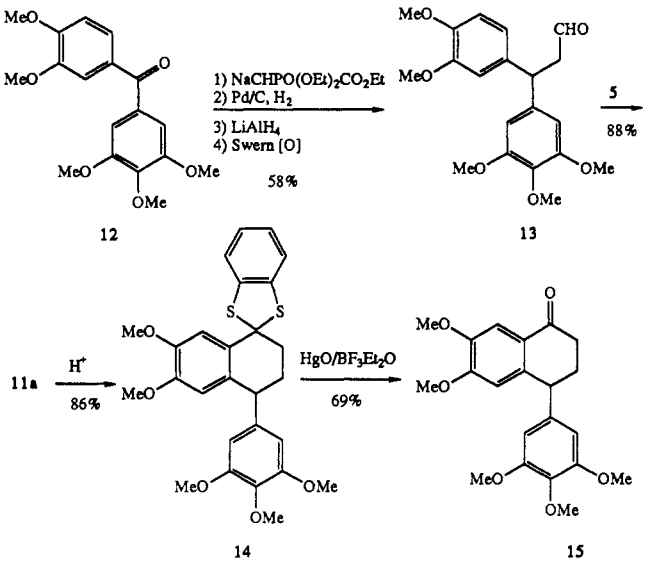
10a, R=OMe
b, R=-OCH2O-

11a, R=OMe

dimethoxy substituted aryl ring in preference to the trimethoxy system even though reaction with the latter would be expected to be favored on electronic grounds. We were confident that the desired selectivity would prevail in this case by virtue of the obligatory bond formation at an ortho ring position if the trimethoxy-substituted benzene were to intercept the dithiolium carbocation.

The requisite substrate for testing this hypothesis was readily available in six steps from veratrole (Scheme II). Stannic chloride mediated Friedel–Crafts coupling pro-

Scheme II



vided the known benzophenone **12** in 84% yield.[11] Routine conversion to the aldehyde **13** followed in good overall yield and the labile ketene dithioacetal **11a** was accessed in typically high yield by standard one-carbon homologation with reagent **5** as in previous cases. Exposure of **11a** to the standard cyclization conditions (trace of *p*-TsOH, 0 °C, several hours) provided the expected benzodithiole **14** as a single product in 86% yield. No trace of the alternative cyclization product could be detected. This result clearly demonstrates the greater dependence on steric access over electronic factors for the success of the 1,3-benzodithiolium ion mediated aryl cyclizations. Routine hydrolysis of intermediate **14** under standard conditions led to the tetralone **15** in 69% yield. Unfortunately, efforts to extend this approach to the total synthesis of sikkimotoxin or other related lignans were thwarted by difficulties associated with the convenient elaboration of the elements of the *trans*-butyrolactone unit onto the tetralone framework.

Initiation of polyolefin cyclizations is another attractive potential application for 1,3-benzodithiolium ion participation.[12] To explore this possibility, a rapid synthesis of the tricyclic ketone **20** was performed.[13] Allylic alcohol **16** was obtained in 92% yield by addition of isopropenylmagnesium bromide to 3-(*p*-methoxyphenyl)-1-

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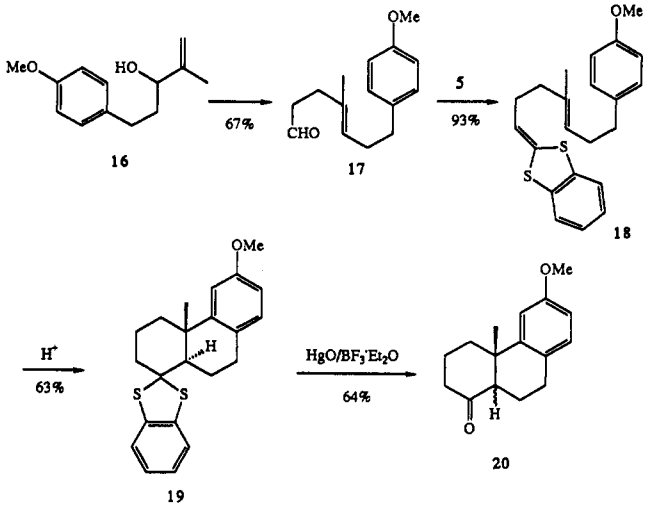
(11) Schreier, E. *Helv. Chem. Acta* **1963**, *46*, 75.

(12) For some related cyclizations, see: (a) Amupitan, J.; Sutherland, J. K. *J. Chem. Soc., Chem. Commun.* **1980**, 398. (b) Trost, B. M.; Murayama, E. *Tetrahedron Lett.* **1982**, *23*, 1047. (c) Berrier, C.; Jacquesy, J. C.; Gesson, J. P.; Renoux, A. *Tetrahedron* **1984**, *40*, 1983. (d) Snider, B. B.; Mohan, R.; Kates, S. A. *J. Org. Chem.* **1985**, *50*, 3659. (e) Janssen, C. G. M.; Godefroi, E. F. *Ibid.* **1984**, *49*, 3600.

(13) Amupitan, V.; Santos, A.; Sutherland, J. K. *J. Chem. Soc., Chem. Commun.* **1980**, 399.

Scheme III

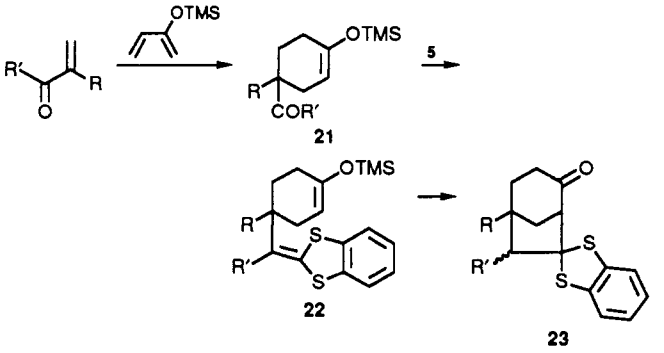


propanal. Subsequent ortho ester Claisen rearrangement, ester reduction, and Swern oxidation provided the requisite γ,δ-unsaturated aldehyde **17** exhibiting an *E* double bond in 67% overall yield for the three steps (Scheme III). Installation of the ketene dithioacetal employing the usual conditions gave compound **18** in 93% yield. Acid-catalyzed cyclization of **18** required somewhat longer exposure to *p*-TsOH at 0 °C (50 h); however, the reaction proceeded with typical efficiency to give the requisite benzodithiole **19** as a single isomer in 63% yield. It is presumed, based on the well-established stereochemical course of olefin cyclizations via *E* double bonds that the relative stereochemistry at the AB ring fusion is trans.[14] Hydrolysis of **19** gave tricyclic ketone **20** in 64% yield as an inseparable 66:34 mixture of isomeric ring fusions.[13]

Construction of Bicyclo[3.2.1]octane Ring Systems. We envisioned that the 1,3-benzodithiolium ion mediated olefin cyclization in tandem with a Diels–Alder reaction would represent a potentially efficient strategy into the bicyclo[3.2.1]octane ring system[15–17] (Table III). Thermally induced [4 + 2] cycloaddition of 2-[(trimethylsilyl)oxy]butadiene[18] with an appropriate α,β-unsaturated carbonyl partner provided the cyclization precursor. Condensation with **5** and exposure of the resultant ketene dithioacetal to trifluoroacetic acid (1 equiv, 0 °C) gave the bicyclic products **23**.

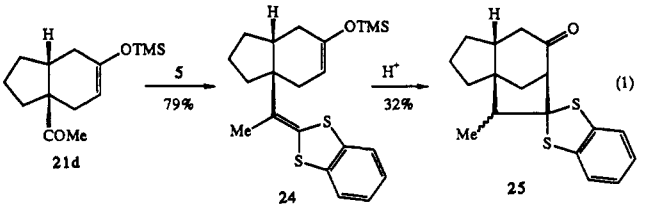
This particular reaction sequence can also be extended to more elaborate systems as depicted in eq 1. The tricycle **25** produced in this sequence was selected as a target because of the close resemblance to the basic carbon skeleton of the sesquiterpene, khusimone.[19] The uncharacteristically depressed yield in the cyclization step in this instance is due, in large measure, to conformational restrictions stemming from the cis-fused hydrindan system in **24** which compels the cyclization to proceed through a boat cyclohexene. Models suggest the development of some strain during the bond formation.

Table III. Preparation of Bicyclo[3.2.1]octane Systems via Benzodithiolium Ion Cyclization



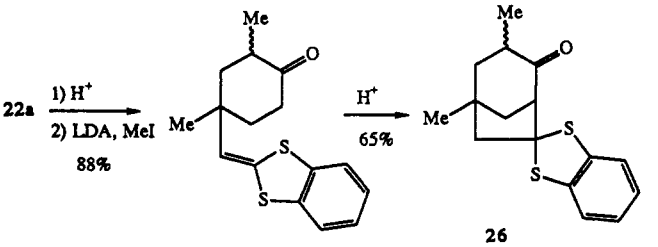
entry	yield,[a] % 21	22	23
a: R = Me; R′ = H	54	90	83
b: R = H; R′ = Me	57	88	77[b]
c: R, R′ = H	68	91	71

[a] Yield of purified product. [b] Stereochemistry of methyl substituent is undefined.



It is interesting to note at this juncture that the cyclization to bicycles **23a–c** could be achieved under identical conditions with equal efficiency starting from the corresponding ketones. This observation suggests that the actual nucleophile that intercepts the benzodithiolium ion in this process may be the enol form of the ketone rather than the trimethylsilyl enol ether.

To further study the characteristics of this ring-forming operation, the ketone derived from silyl enol ether **22a** was monomethylated (LDA, THF, −78 °C, MeI) and subjected to the standard cyclization conditions. The resultant product, **26**, was formed exclusively. None of the alternative regioisomer, where bonding occurred at the more substituted carbon center, could be detected. The pattern of sensitivity to the steric environment at the bond-forming center has continued to emerge as a central feature of these



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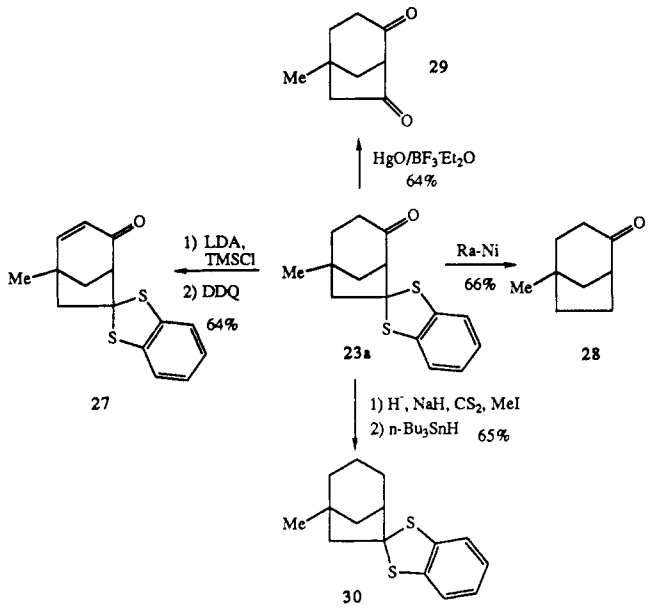
Scheme IV



reactions and should prove to be a useful tool to exploit in more complex applications.

The bicyclic benzodithioles that result from this variant of ketene dithioacetal cyclization protocol exhibit two functionally differentiated ketones and as such are versatile intermediates for subsequent manipulation. Scheme IV displays some of the transformations that can be easily performed on these adducts. Of particular note, the benzodithiole can be easily removed reductively or can undergo hydrolysis to provide a range of bicyclo[3.2.1]-octane species (**27–30**).

Conclusion

Ring-forming reactions mediated by the 1,3-benzodithiolium carbocation can be utilized to construct a wide range of cyclic systems under experimentally convenient and exceptionally mild conditions. The resultant benzodithiole products are versatile precursors for a number of useful functional group interconversions.

Experimental Section

All melting points are uncorrected. ^1H and ^{13}C NMR were determined at 300 and 75 MHz, respectively. Solvents and reagents were dried and purified prior to use: tetrahydrofuran, diethyl ether (distilled from sodium/benzophenone ketyl); methylene chloride; acetonitrile (distilled from CaH_2). All reactions were run in flame-dried flasks under an atmosphere of nitrogen except in those cases where water was present. Analytical thin-layer chromatography was performed utilizing E. Merck hard-surfaced layer glass plates of 0.25 mm thickness with a 254 mm fluorescent indicator. Column chromatography was carried out on SiO_2 (silica gel, Merck, 230–400 mesh).

1-[4,4-(1,2-Benzenediyldithio)but-3-enyl]-4-dimethoxybenzene (6b). To a cold (−78 °C) solution of 2-(diethoxyphosphinyl)-1,3-benzodithiole[7] (0.3 g, 1.03 mmol) in dry THF (25 mL) was added *n*-butyllithium (0.69 mL, 1.03 mmol in hexanes). The resultant pale yellow solution was stirred for 15 min at this temperature, at which time 3-(3,4-dimethoxyphenyl)-1-propanal (0.20 g, 1.03 mmol) was added. This mixture was allowed to warm to room temperature, and the reaction was quenched with water. The THF was evaporated in vacuo, and the residue was extracted from water with methylene chloride (3 × 50 mL). These extracts were combined, washed with saturated aqueous sodium chloride solution (2 × 20 mL), and dried ($MgSO_4$). The solvent was removed in vacuo, and the resultant yellow residue was isolated via flash column chromatography (10% THF/hexane) to give 0.316 g (93%) of a viscous yellow oil: IR (CCl_4) ν 3060, 3000, 2955, 2930, 2832, 1504, 1495, 1257, 1028 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.10–2.50 (m, 2 H), 2.50–2.80 (m, 2 H), 3.83 (s, 3 H), 3.86 (s, 3 H), 5.44 (t, J = 7.03 Hz, 1 H), 6.51–6.92 (m, 3 H), 7.00–7.21 (m, 4 H); MS m/e 330 (6.5), 302 (10), 287 (13), 179 (100), 151 (43), 91 (77).

[4,4-(1,2-Benzenediyldithio)but-3-enyl]benzene (6a). Prepared in the same manner as **6b** and isolated by flash column chromatography (5% ether/hexane) (R_f = 0.18) to give a viscous oil (0.27 g, 99%): IR (CCl_4) ν 3065, 3030, 2925, 2860, 1495, 1448, 1120 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.21–2.62 (m, 4 H), 5.46 (t, J = 6.64 Hz, 1 H), 6.92–7.39 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 34.00, 34.28, 113.86, 115.19, 117.32, 120.98, 125.43, 125.62, 125.88, 128.92, 129.48; MS m/e (%) 270 (12), 179 (100), 91 (23), 77 (11); HRMS calcd for $C_{16}H_{14}S_2$ 270.0539, found 270.0521.

1-[4,4-(1,2-Benzenediyldithio)but-3-enyl]-2,3-dimethoxybenzene (6c). Isolated via flash column chromatography (10% THF/hexane) to give a viscous yellow oil (0.31 g, 95%): IR (CCl_4) ν 3065, 3000, 2960, 2935, 2838, 1473, 1448, 1260, 1220, 1083, 1006 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.10–2.50 (m, 2 H), 2.51–2.92 (m, 2 H), 3.84 (s, 6 H), 5.49 (t, J = 7.14 Hz, 1 H), 6.63–7.20 (m, 7 H); MS m/e 330 (4.8), 302 (10), 299 (15), 179 (100), 105 (40), 91 (77).

3-[4,4-(1,2-Benzenediyldithio)but-3-enyl]-3,4-(methylenedioxy)benzene (6d). Isolated via flash column chromatography (15% THF/hexane) to give a viscous yellow oil (0.16 g, 95%): IR (CCl_4) ν 3060, 3015, 2924, 2875, 2770, 1485, 1441, 1240, 1118, 1041, 937 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.10–2.50 (m, 2 H), 2.52–2.83 (m, 2 H), 5.43 (t, J = 7.03 Hz, 1 H), 5.90 (s, 2 H), 6.54–6.81 (m, 3 H), 6.90–7.22 (m, 4 H); MS m/e 314 (6), 286 (5), 179 (100), 135 (40), 105 (43), 91 (70).

1-[4,4-(1,2-Benzenediyldithio)but-3-enyl]-3-methoxybenzene (6e). Isolated via flash column chromatography (10% THF/hexane) to give a viscous yellow oil (0.25 g 99%): IR (CCl_4) ν 3070, 3000, 2940, 2849, 2838, 1485, 1446, 1258, 1150, 1117, 1065, 1043 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.21–2.52 (m, 2 H), 2.60–2.90 (m, 2 H), 3.79 (s, 3 H), 5.46 (t, J = 7.03 Hz, 1 H), 6.60–7.30 (m, 8 H); MS m/e 300 (5.8), 272 (5), 179 (100), 105 (43), 91 (77).

1-[4,4-(1,2-Benzenediyldithio)but-3-enyl]-4-methoxybenzene (6f). The compound was isolated by flash column chromatography (10% ether/hexane) (R_f = 0.14) to give 0.28 g (90%) of a yellow viscous oil: IR (CCl_4) ν 3068, 3008, 2960, 2935, 2839, 1507, 1447, 1242, 1174, 1120 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.33–2.38 (m, 2 H), 2.69–2.74 (m, 2 H), 3.82 (s, 3 H), 5.48 (t, J = 7.15 Hz, 1 H), 6.86–7.21 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 34.00, 34.33, 55.37, 113.96, 115.09, 121.66, 125.41, 125.66, 125.92, 129.45, 129.51; MS m/e (%) 300 (9), 272 (15), 257 (18), 179 (100), 121 (51), 105 (23), 77 (36); HRMS calcd for $C_{17}H_{16}OS_2$ 300.0645, found 300.0632.

1-[4,4-(1,2-Benzenediyldithio)but-3-enyl]-2,5-dimethoxybenzene (6g). Prepared in the same manner as **6b** and isolated by flash column chromatography (10% ether/hexane) (R_f = 0.13) to give a viscous oil (0.35 g, 98%): IR (CCl_4) ν 3063, 3000, 2940, 2909, 2827, 1491, 1445, 1217, 1119, 1047 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.11–2.52 (m, 2 H), 2.52–2.88 (m, 2 H), 3.73 (s, 6 H), 5.47 (t, J = 7.03 Hz, 1 H), 6.78–7.19 (m, 7 H); ^{13}C NMR ($CDCl_3$) δ 34.27, 34.49, 55.96, 56.02, 111.43, 111.92, 115.04, 120.40, 121.31, 121.66, 125.47, 125.72, 130.85, 134.05, 136.07; MS m/e (%) 330 (7), 179 (100), 105 (12), 91 (11), 77 (16); HRMS calcd for $C_{18}H_{18}O_2S_2$ 330.0758, found 330.0762.

1,1-(1,2-Benzenediyldithio)-1,2,3,4-tetrahydronaphthalene (7a). Several crystals (approximately 20–30 mg) of *p*-toluenesulfonic acid were added at room temperature to a solution of [4,4-(1,2-benzenediyldithio)but-3-enyl]benzene (0.27 g, 1.0 mmol) in acetonitrile (10 mL). The solution was warmed at 50–60 °C for 30 min, cooled to room temperature, and then placed in a refrigerator (5 °C) for 14 h, at which time the reaction was shown to be complete by TLC examination. There was no solid cyclized crystalline product obtained. The acetonitrile was removed under reduced pressure, and the residue was dissolved in diethyl ether (50 mL). The ether extract was washed with saturated aqueous sodium bicarbonate solution (1 × 30 mL), water (2 × 30 mL), and saturated aqueous sodium chloride solution (1 × 30 mL). The organic phase was dried (Na_2SO_4), and the solvent was removed under reduced pressure to leave a viscous oil, which was purified by flash column chromatography (15% ether/hexane) (R_f = 0.15) to give 0.19 g (70%) of the cyclized product: IR (CCl_4) ν 2925, 1604, 1592, 1470 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.02–2.10 (m, 2 H), 2.66–2.70 (m, 2 H), 2.88 (t, J = 6.36 Hz, 2 H), 7.08–7.25 (m, 7 H),

8.46–8.49 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ 20.49, 29.72, 40.02, 71.34, 122.24, 125.91, 126.02, 128.44, 129.38, 130.44, 137.85, 138.25; MS *m/e* (%) 270 (100), 243 (15), 242 (71), 237 (20), 182 (20), 167 (63), 129 (30), 128 (34); HRMS calcd for $C_{16}H_{14}S_2$ 270.0536, found 270.0531.

1,1-(1,2-Benzenediyldithio)-6,7-dimethoxy-1,2,3,4-tetrahydronaphthalene (7b). Method A. Several crystals (approximately 10 mg) of *p*-toluenesulfonic acid monohydrate were added at room temperature to a stirred solution of 1-[4,4-(1,2-benzenediyldithio)but-3-enyl]-3,4-dimethoxybenzene (0.33 g, 1.0 mmol) in acetonitrile (10 mL). This solution was stirred at room temperature until the reaction was shown to be complete by TLC examination, typically 6–12 h. At this time, crystals were already observed, and the reaction mixture was placed in a refrigerator (5 °C) for 5 h to maximize crystallization. The crystals were collected in two crops to give a total isolated yield of 0.25 g (76%) of clean colorless cyclized product.

Method B. When the reaction was shown to be complete by TLC examination, but crystallization did not occur spontaneously, the solution was diluted with a 1:1 diethyl ether/benzene mixture and extracted with saturated aqueous sodium bicarbonate solution (2 × 50 mL), once with water (50 mL), and once with saturated aqueous sodium chloride solution (50 mL). The organic layer was dried ($MgSO_4$), and the solvent was removed in vacuo to leave a solid mass, which was recrystallized from methanol, yielding 76% of colorless needles: mp 138.5–139.5 °C; IR (CCl_4) ν 2942, 2847, 1612, 1510, 1462, 1439, 1250, 1225, 1199, 1117, 1070, 1022, 945 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.81–2.10 (m, 2 H), 2.45–2.91 (m, 4 H), 3.85 (s, 6 H), 6.50 (s, 1 H), 6.90–7.20 (m, 4 H), 7.91 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 20.77, 29.44, 42.35, 56.22, 71.91, 112.04, 113.77, 122.27, 125.83, 127.04, 131.20, 138.22, 147.58, 149.92; MS *m/e* 330 (100), 302 (62), 297 (46), 287 (33), 266 (24), 221 (14), 190 (20), 189 (45), 115 (17), 77 (13); UV (THF) λ_{max} 294 (log ε = 3.82), 241 (log ε 4.6), λ_{max} (log ε = 4.4). Anal. Calcd for $C_{18}H_{18}O_2S_2$: C, 65.42; H, 5.49; S, 19.40. Found: C, 65.45; H, 5.47; S, 19.50.

1,1-(1,2-Benzenediyldithio)-5,6-dimethoxy-1,2,3,4-tetrahydronaphthalene (7c). Method A provided colorless needles (0.17 g, 56%): mp 129.5–130.5 °C; IR (CCl_4) ν 3060, 2941, 2846, 2840, 1484, 1441, 1280, 1250, 1228, 1112, 1085, 1014, 956 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.70–2.11 (m, 2 H), 2.45–2.63 (m, 2 H), 2.79 (t, *J* = 6.15 Hz, 2 H), 3.78 (s, 3 H), 3.82 (s, 3 H), 7.48 (dd, *J* = 14.7, *J* = 8.9 Hz, 2 H), 6.93–7.22 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 20.02, 23.58, 41.69, 55.85, 59.81, 71.25, 110.60, 122.04, 125.68, 126.03, 128.46, 132.79, 137.90, 146.05, 152.03; MS *m/e* 330 (100), 302 (10), (4), 297 (56), 287 (51), 266 (26), 221 (12), 190 (20), 189 (36), 115 (16), 77 (13); UV (THF) λ_{max} 302 (log ε = 3.4), 241 (log ε = 4.6), 222 (log ε = 4.5). Anal. Calcd for $C_{18}H_{18}O_2S_2$: C, 65.42; H, 5.49; S, 19.40. Found: C, 65.50; H, 5.53; S, 19.42.

1,1-(1,2-Benzenediyldithio)-6,7-(methylenedioxy)-1,2,3,4-tetrahydronaphthalene (7d). Method A provided colorless crystals (0.12 g, 75%): mp 132.7–133.5 °C; IR (CCl_4) ν 3064, 2943, 2890, 2844, 1504, 1480, 1443, 1235, 1117, 1041, 961, 951 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.73–2.10 (m, 2 H), 2.45–2.81 (m, 4 H), 5.88 (s, 2 H), 6.46 (s, 1 H), 6.91–7.20 (m, 4 H), 7.85 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 20.77, 30.05, 42.36, 71.91, 101.21, 108.32, 109.96, 122.19, 125.83, 128.60, 132.24, 138.05, 145.94, 148.19; MS *m/e* 314 (100), 286 (98), 281 (34), 174 (21), 173 (45), 115 (45), 77 (12); UV (THF) λ_{max} 298 (log ε = 3.9), 240 (log ε = 4.4). Anal. Calcd for $C_{17}H_{14}O_2S_2$: C, 64.94; H, 4.49; S, 20.39. Found: C, 65.03; H, 4.40; S, 20.29.

1,1-(1,2-Benzenediyldithio)-6-methoxy-1,2,3,4-tetrahydronaphthalene (7e). Method A provided colorless crystals (0.19 g, 77%): mp 127.5–128.5 °C; IR (CCl_4) ν 3070, 3010, 2943, 2870, 2842, 1610, 1495, 1443, 1280, 1252, 1239, 1111, 1041, 1003, 972, 946 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.75–2.10 (m, 2 H), 2.42–2.91 (m, 4 H), 3.75 (s, 3 H), 6.41–6.81 (m, 2 H), 6.83–7.21 (m, 4 H), 8.34 (d, *J* = 8.79 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 20.77, 30.22, 42.53, 55.44, 71.39, 112.91, 113.69, 122.19, 125.83, 127.82, 131.89, 138.31, 139.70, 159.80; MS *m/e* 300 (100), 272 (74), 267 (66), 160 (17), 159 (39), 115 (37), 77 (11); UV (THF) λ_{max} 302 (log ε = 3.4), 289 (log ε = 3.6), 240 (log ε = 4.6). Anal. Calcd for $C_{17}H_{16}OS_2$: C, 67.96; H, 5.37; S, 21.34. Found: C, 67.87; H, 5.35; S, 21.33.

1,1-(1,2-Benzenediyldithio)-7-methoxy-1,2,3,4-tetrahydronaphthalene (7f). The crystalline product was collected in two crops to give a total isolated yield of 0.222 g (74%) of clean colorless cyclized product: mp 95–97 °C; IR (CCl_4) ν 2920, 2840, 1600, 1490, 1308, 1263, 1252, 1231 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.01–2.04 (m, 2 H), 2.63–2.67 (m, 2 H), 2.78–2.82 (m, 2 H), 3.82 (s, 3 H), 6.82–7.21 (m, 6 H), 7.99 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 20.55, 28.91, 41.94, 55.49, 71.75, 114.17, 116.86, 122.26, 125.91, 130.37, 130.89, 135.93, 137.84, 157.44; MS *m/e* (%) 300 (100), 272 (64), 257 (35), 176 (38), 159 (58), 158 (31), 120 (30), 115 (43); HRMS calcd for $C_{17}H_{16}OS_2$ 300.0642, found 300.0639.

6,7-Dimethoxy-1-tetralone (8b). To a vigorously stirred suspension of red mercury(II) oxide (0.26 g, 1.21 mmol) and freshly distilled boron trifluoride etherate (1.7 g, 1.21 mmol) in aqueous THF (10 mL) (0.5 g of water/1 g of substrate) was added tetrahydronaphthalene **7b** (0.20 g, 0.60 mmol) dissolved in a minimal amount of THF (1 mL). The resultant mixture was allowed to stir for 7 h, at which time it was diluted with diethyl ether (30 mL), and the solids were removed by filtration. The solids were washed with diethyl ether (2 × 50 mL) and filtered again. The filtrate was washed twice with saturated aqueous sodium bicarbonate solution (30 mL) and once with saturated aqueous sodium chloride solution (30 mL) and then dried ($MgSO_4$). The solvent was evaporated in vacuo to leave a white solid, which was further purified by flash column chromatography (20% THF/hexane), yielding 0.072 g (60%) of the tetralone: mp 93.5–95.5 °C (lit.[20] mp 96 °C).

α-Tetralone (8a). Prepared in the same manner as **8b** and purified by flash column chromatography (15% ether/hexane) (R_f = 0.17) to give an oil (57 mg, 56%): Identical with the authentic compound sold by Aldrich Chemical Co., Milwaukee, WI.

5,6-Dimethoxy-1-tetralone (8c). Purified via flash column chromatography (20% THF/hexane) to provide a white solid (50 mg, 55%): mp 101–102 °C (lit.[21a] mp 104–105 °C).

6,7-(Methylenedioxy)-1-tetralone (8d). Purified via flash column chromatography (25% THF/hexane) to provide a white solid (42 mg, 55%): mp 73.5–75.0 °C (lit.[21b] mp 71–72 °C).

6-Methoxy-1-tetralone (8e). Purified via flash column chromatography with 20% THF/hexane to provide a white solid (0.065 g, 62%): mp 76–78 °C (lit.[22] mp 77–78.5 °C).

7-Methoxy-1-tetralone (8f). Obtained as a white solid 0.065 g (62%) of the tetralone: mp 61–63 °C; identical with the authentic compound sold by Aldrich, Milwaukee, WI.

6,7-Dimethoxytetralin (9b). To a stirred solution of 1,1-(1,2-benzenediyldithio)-6,7-dimethoxy-1,2,3,4-tetrahydronaphthalene (0.10 g, 0.30 mmol) in 95% ethanol (20 mL) was added 1–2 g of activated (W-2) Raney nickel. This mixture was refluxed for 2 h, at which time it was cooled to room temperature, and the ethanol was filtered through Celite to separate the unsettled nickel. The remaining nickel was washed twice with 10 mL of ethanol. The filter cake was then washed with 5 mL more of ethanol, and the solvent was evaporated in vacuo to leave 0.04 g (69%) of the colorless solid tetralin: mp 52.0–54.5 °C (lit.[20] mp 55–57 °C); IR (CCl_4) ν 2940, 2865, 2845, 1510, 1253, 1217, 1115, 1010 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.61–1.93 (m, 4 H), 2.50–2.83 (m, 4 H), 3.83 (s, 6 H), 6.56 (s, 2 H).

5,6-Dimethoxytetralin (9c).[23a] Obtained as a colorless oil (0.048 g, 75%): IR (CCl_4) ν 2940, 2870, 2845, 1490, 1280, 1225, 1093, 1078, 1050, 1004 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.53–1.91 (m, 4 H), 2.50–2.90 (m, 4 H), 3.79 (s, 3 H), 3.82 (s, 3 H), 6.74 (AB q, *J* = 1.98, *J'* = 8.42 Hz, 2 H).

6,7-(Methylenedioxy)tetralin (9d). Obtained as a colorless solid (0.033 g, 91%): mp 38–42 °C; IR (CCl_4) ν 2930, 2890, 2865, 1479, 1232, 1165, 1041 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.53–1.91 (m, 4 H), 2.42–2.82 (m, 4 H), 5.85 (s, 2 H), 6.52 (s, 2 H).

6-Methoxytetralin (9e). Obtained as a colorless oil (0.054 g, 95%): IR (CCl_4) ν 2938, 2864, 2844, 1610, 1499, 1251, 1228, 1151, 1040 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.52–1.91 (m, 4 H), 2.51–2.92 (m, 4 H), 3.75 (s, 3 H), 6.54–7.03 (m, 3 H).

3,3',4,4',5'-Pentamethoxybenzophenone (12). To an ice-cold solution of veratrole (27.6 g, 100 mmol) in 1,2-dichloroethane (200 mL) was added anhydrous stannic chloride (24 mL), followed by

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(23) Sprenger, W. K.; Cannon, J. G.; Koelling, H. F. *J. Org. Chem.* **1966**, *31*, 2402.

dropwise addition of 3,4,5-trimethoxybenzoyl chloride (46 g, 100 mmol) in 1,2-dichloroethane (90 mL). The mixture was stirred at room temperature for 6 h, at which time it was treated with 18% aqueous hydrochloric acid solution (50 mL) and steam distilled. The residue from steam distillation was extracted with benzene. The extract was washed with 5% aqueous sodium hydroxide solution, water, saturated aqueous sodium chloride solution and dried (Na_2SO_4). The solvent was evaporated under reduced pressure to give a solid, which after recrystallization from acetone/methanol gave 56 g (84%) yield of the known benzophenone: mp 122–123 °C (lit.[24] mp 122–123 °C).

2-(3,3′,4,4′,5′-Pentamethoxybenzhydryl)ethanal (13). To a suspension of sodium hydride (3.6 g, 150 mmol) (50% dispersion in oil, prewashed with pentane) in toluene (60 mL) at 0–10 °C was added dropwise triethyl phosphonoacetate (16.8 g, 75 mmol) in toluene (40 mL) over a period of 45 min. After evolution of hydrogen gas has ceased, a solution of the benzophenone **12** (16.6 g, 50 mmol) in toluene (100 mL) was added over a period of 30 min. The resulting solution was stirred and heated to reflux for 5 h, at which time the reaction was shown to be complete by TLC examination. The reaction mixture was cooled to room temperature and poured into 100 mL of saturated aqueous ammonium chloride solution. The organic layer was separated, and the aqueous layer was extracted with toluene (2 × 50 mL). The combined organic layers were washed with water and saturated aqueous sodium chloride solution and dried (Na_2SO_4). The solvent was removed under reduced pressure to give a solid, which was recrystallized from diethyl ether to give 17.09 g (85%) of a white solid: mp 112–114 °C, as a mixture of double bond isomers in a ratio of 69:31, as determined by ^1H NMR; IR (CCl_4) ν 2938, 2835, 1710, 1580, 1512, 1462, 1415, 1322, 1268, 1160 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.10–1.18 (m, 3 H), 3.77–3.96 (m, 15 H), 4.04–4.11 (m, 2 H), 6.24–7.46 (m, 6 H); ^{13}C NMR ($CDCl_3$) δ 14.15, 14.21, 55.88, 56.02, 56.23, 60.06, 60.12, 60.97, 61.02, 106.14, 106.85, 110.47, 110.76, 111.02, 112.97, 115.76, 116.56, 122.25, 122.62, 131.18, 133.28, 134.59, 136.79, 152.84, 153.01, 166.38, 166.42; MS *m/e* (%) 332 (16), 165 (12), 74 (17), 59 (30), 57 (36), 56 (11), 45 (36), 43 (23), 41 (21), 31 (100); HRMS calcd for $C_{22}H_{26}O_7$ 402.1678, found 402.1683.

To a solution of the α,β-unsaturated ester (8.04 g, 20 mmol) in a minimum amount of absolute ethanol (60 mL) was added a catalytic amount of 10% palladium on carbon (20–50 mg), and the suspension was placed under an atmosphere of hydrogen at room temperature. The mixture was stirred for a few hours, at which time the reaction was shown to be complete by TLC examination. The reaction mixture was allowed to stand, and the catalyst was removed by filtration. The catalyst was washed three times with 10-mL portions of ethanol, and the combined organic layers were then evaporated under reduced pressure to give a solid, which was recrystallized from diethyl ether to give 7.51 g (93%) of a white solid: mp 81 °C; IR (CCl_4) ν 1735, 1636, 1205, 1157 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.09 (t, J = 7.12 Hz, 3 H), 2.96 (d, J = 8.04 Hz, 2 H), 3.73–3.82 (m, 15 H), 4.00 (q, J = 7.12 Hz, 2 H), 4.40 (t, J = 7.91 Hz, 1 H), 6.42 (s, 2 H), 6.73–6.76 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 14.18, 41.35, 46.94, 55.89, 56.12, 60.50, 60.79, 104.86, 105.09, 111.30, 111.38, 119.44, 135.96, 139.51, 147.38, 148.97, 153.23, 171.86; MS *m/e* (%) 404 (23), 330 (5), 318 (19), 317 (100), 314 (7), 165 (6), 163 (5), 144 (5), 87 (8); HRMS calcd for $C_{22}H_{28}O_7$ 404.1835, found 404.1841.

To a suspension of lithium aluminum hydride (0.95 g, 25 mmol) in diethyl ether (25 mL) at 0 °C was added dropwise a solution of the saturated ester (7.51 g, 18.6 mmol) in diethyl ether (20 mL) over a period of 15 min. The reaction was stirred at 0 °C for 20 min, at which time the reaction was shown to be complete by TLC examination. To the reaction mixture at 0 °C was slowly added 0.95 mL water, 0.95 mL of 15% sodium hydroxide, and 2.85 mL of water, and the resultant suspension was stirred vigorously for 15 min to give a gummy white residue. The mixture was filtered, and the residue was washed three times with 10-mL portions of ether. The combined ether solution was evaporated under reduced pressure to give a viscous oil, which was purified by flash column chromatography (60% ether/hexane) (R_f = 0.19) to give 6.2 g (92%) of the desired alcohol: IR (CCl_4) ν 3630, 2940, 2818, 1578, 1510, 1461, 1415, 1234, 1130 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.98 (br s, 1 H), 2.25 (m, 2 H), 3.59 (t, J = 6.39 Hz, 2 H), 3.79–3.84 (m, 15 H), 4.00 (t, J = 7.92 Hz, 1 H), 6.45 (s, 2 H), 6.76–6.81 (m, 3 H); ^{13}C NMR ($CDCl_3$) δ 38.67, 47.22, 55.97, 56.19, 60.90, 61.05, 104.94, 111.36, 111.50, 119.64, 120.97, 137.01, 140.65, 147.67, 149.02, 153.24; MS *m/e* (%) 362 (26), 318 (24), 317 (100), 287 (8), 57 (9), 55 (67); HRMS calcd for $C_{20}H_{26}O_6$ 362.1729, found 362.1736.

To a solution of oxalyl chloride (1.39 g, 11 mmol) in methylene chloride (22 mL) at −60 °C was added dropwise dimethyl sulfoxide (1.88 g, 24 mmol) in methylene chloride (4.5 mL). The mixture was allowed to stir at −60 °C for 15 min, a solution of the alcohol (3.32 g, 10 mmol) in methylene chloride (2.5 mL) was then added, and the mixture was stirred at −60 °C for 15 min. Triethylamine (5.06 g, 50 mmol) was then added at −60 °C, and the cooling bath was removed. The mixture was then allowed to warm to room temperature. To this reaction mixture was added 30 mL of water, and the mixture was stirred vigorously for 30 min. The organic layer was separated, and the aqueous layer was extracted with methylene chloride (3 × 20 mL). The combined organic extracts were washed with saturated aqueous sodium chloride solution and dried (Na_2SO_4). The solvent was then evaporated under reduced pressure to give a solid, which was recrystallized (diethyl ether) to give 2.88 g (80%) of the desired aldehyde as a white solid (mp 103–104 °C): IR (CCl_4) ν 2720, 1732, 1510, 1261, 1238, 1029 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.10 (m, 2 H), 3.80–3.84 (m, 15 H), 4.50 (t, J = 7.77 Hz, 1 H), 6.42 (s, 2 H), 6.73–6.79 (m, 3 H), 9.72 (t, J = 1.83 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 44.84, 49.89, 55.97, 56.01, 56.23, 60.89, 104.94, 105.10, 111.40, 119.50, 135.62, 139.28, 148.01, 149.18, 153.41, 166.73, 201.98; MS *m/e* (%) 360 (32), 317 (100), 181 (29), 149 (31), 105 (32), 71 (31), 69 (66), 57 (33), 51 (23); HRMS calcd for $C_{20}H_{24}O_6$ 360.1572, found 360.1567.

3-(3,3′,4,4′,5′-Pentamethoxybenzhydryl)-2-ethylidene-1,3-benzodithiole (11a). To a cold (−78 °C) solution of 2-(diethoxyphosphinyl)-1,3-benzodithiole (**5**) (2.9 g, 10 mmol) in THF (100 mL) was added *n*-butyllithium (4 mL, 10 mmol). This solution was stirred at −78 °C for 15 min, at which time a solution of the ethanal **13** (3.60 g, 10 mmol) in THF (4 mL) was added. This solution was allowed to warm to room temperature, and the THF was evaporated under reduced pressure to give a gummy residue. The residue was suspended in water and extracted with methylene chloride (4 × 30 mL). The extracts were combined, washed with saturated aqueous sodium chloride solution, and dried (Na_2SO_4). The solvents were removed under reduced pressure to give a yellow residue, which was isolated by flash column chromatography (35% ether/hexane) (R_f = 0.17) to give 4.37 g (88%) yield of a viscous oil: IR (CCl_4) ν 3057, 3001, 2955, 2930, 2832, 1505, 1493, 1257, 1025 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.74 (t, J = 7.42 Hz, 2 H), 3.82–3.88 (m, 15 H), 3.94 (t, J = 9.96 Hz, 1 H), 5.37 (t, J = 6.99 Hz, 1 H), 6.46 (s, 2 H), 6.77–7.22 (m, 7 H); ^{13}C NMR ($CDCl_3$) δ 39.01, 50.28, 55.99, 56.05, 56.26, 60.91, 105.91, 111.39, 114.09, 119.83, 121.34, 121.62, 125.50, 125.80, 131.39, 135.82, 136.18, 136.82, 140.06, 147.82, 149.05, 153.29; MS *m/e* (%) 332 (12), 318 (25), 317 (100), 165 (9), 153 (10), 105 (48), 77 (15); HRMS calcd for $C_{27}H_{28}O_5S_2$ 496.1377, found 496.1380.

1,1-(1,2-Benzenediyldithio)-4-(3,4,5-trimethoxyphenyl)-6,7-dimethoxy-1,2,3,4-tetrahydronaphthalene (14). Several crystals (approximately 15 mg) of *p*-toluenesulfonic acid were added at room temperature to a solution of ketene dithioacetal **11a** (0.5 g, 1.01 mmol) in acetonitrile (10 mL). A deep red color was produced immediately. The red solution was placed in a refrigerator (5 °C) for 6–8 h, at which time the reaction was shown to be complete by TLC examination. The cyclized solid crystalline product was collected as two crops to give a total yield of 0.43 g (86%) of colorless product (mp 192–193 °C): IR (CCl_4) ν 2942, 2847, 1612, 1510, 1462, 1439, 1250, 1225, 1199, 1117, 1070, 1022 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.12–2.73 (m, 4 H), 3.72–3.92 (m, 15 H), 4.05 (t, J = 6.28 Hz, 1 H), 6.29 (s, 2 H), 6.35 (s, 1 H), 7.08–7.20 (m, 4 H), 8.01 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 30.07, 39.41, 45.05, 56.02, 56.26, 60.97, 71.91, 105.92, 112.07, 112.14, 122.35, 122.44, 126.01, 126.96, 133.12, 137.74, 141.86, 147.92, 149.38, 153.26; MS *m/e* (%) 496 (69), 494 (18), 356 (36), 355 (82), 324 (22), 181 (21), 161 (61), 153 (18); HRMS calcd for $C_{27}H_{28}O_5S_2$ 496.1377, found 496.1372. Anal. Calcd for $C_{27}H_{28}O_5S_2$: C, 65.32; H, 5.69; S, 12.89. Found: C, 65.00; H, 5.68; S, 12.93.

4-(3,4,5-Trimethoxyphenyl)-6,7-dimethoxy-1-tetralone (15). To a vigorously stirred suspension of red mercury(II) oxide (0.26 g, 1.21 mmol) and boron trifluoride etherate (0.17 g, 1.21 mmol)

(24) Schreier, E. *Helv. Chem. Acta* **1963**, *46*, 75.

in aqueous THF (5 mL) (15% water by volume) was added tetrahydronaphthalene 14 (0.25 g, 0.5 mmol) in a minimum amount of THF (0.25 mL). The solution was heated to reflux for 30 min, at which time the reaction was judged to be complete by TLC examination. The solution was diluted with 2 volumes of ether, and the solids were washed twice with ether and filtered. The filtrate was extracted twice with a saturated aqueous sodium bicarbonate solution, washed with a saturated aqueous sodium chloride solution, and dried (Na_2SO_4). The solvent was evaporated under reduced pressure to give 0.13 g (69%) of an oily residue after flash column chromatography (50% ether/hexane) (R_f = 0.16): IR (CCl_4) ν 1678, 1601, 1507, 1268, 1220, 1033 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.24–2.67 (m, 4 H), 3.79–3.96 (m, 15 H), 4.16–4.21 (m, 1 H), 6.33 (s, 2 H), 6.47 (s, 1 H), 7.60 (s, 1 H); ^{13}C NMR ($CDCl_3$) δ 30.42, 32.45, 36.28, 45.54, 56.12, 56.34, 60.90, 105.83, 106.11, 108.62, 111.26, 126.45, 139.51, 140.82, 149.34, 153.52, 153.88, 196.84; MS *m/e* (%) 372 (100), 314 (14), 205 (41), 135 (7), 83 (11), 81 (10), 71 (15), 69 (23), 57 (41); HRMS calcd for $C_{21}H_{24}O_6$ 372.1577, found 372.1577.

5-(4-Methoxyphenyl)-2-methylpent-1-en-3-ol (16).[25] To a suspension of magnesium metal (0.03 g, 1.25 mmol) in diethyl ether (3 mL) at 0 °C was added dropwise 2-propenyl bromide (0.15 g, 1.25 mmol) over a period of 15 min. The mixture was stirred at 0 °C for an additional 30 min until the solution became cloudy and then 3-(4-methoxyphenyl)-1-propanal (0.13 g, 0.8 mmol) in ether (1 mL) was added. The resultant mixture was stirred at 0 °C for 30 min, at which time the reaction was shown to be complete by TLC examination. The mixture was then poured into saturated aqueous ammonium chloride solution (10 mL). The organic layer was separated, and the aqueous layer was extracted with diethyl ether (2 × 10 mL). The combined organic layers were washed with water and saturated aqueous sodium chloride solution and dried (Na_2SO_4). The solvent was evaporated under reduced pressure to give 0.15 g (92%) yield of a clear oily residue of the allylic alcohol **16**: IR (CCl_4) ν 3635, 3510, 1509, 1260, 1032 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.77 (s, 3 H), 1.83–1.90 (m, 3 H), 2.55–2.70 (m, 2 H), 3.81 (s, 3 H), 4.11 (t, J = 6.38 Hz, 1 H), 4.94 (dd, J = 1.63, 1.77 Hz, 2 H), 6.84–7.17 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 17.72, 31.08, 36.93, 55.36, 75.32, 111.23, 113.97, 129.45, 134.20, 147.63, 157.94.

(*E*)-7-(4-Methoxyphenyl)-4-methylhept-4-en-1-al (17). To a solution of the allylic alcohol **16** (0.147 g, 0.72 mmol) in triethyl orthoformate (0.7 g, 4.32 mmol) was added two drops of propionic acid. The reaction mixture was stirred and heated to reflux for 5–6 h, at which time the reaction was shown to be complete by TLC examination. The excess triethyl orthoformate was removed by distillation, and the residue was purified by flash column chromatography (25% ether/hexane) (R_f = 0.14) to give 0.154 g (78%) of the desired unsaturated ester as its *E* isomer: IR (CCl_4) ν 1733, 1636, 1205, 1158, cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (t, J = 7.14 Hz, 3 H), 1.69 (s, 3 H), 2.27–2.62 (m, 8 H), 3.81 (s, 3 H), 4.14 (q, J = 7.13 Hz, 2 H), 5.23 (t, J = 7.03 Hz, 1 H), 6.82–7.13 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 14.35, 15.96, 30.19, 33.35, 34.77, 35.13, 55.35, 60.30, 113.80, 124.61, 129.43, 134.18, 134.41, 157.90, 173.53; MS *m/e* (%) 276 (4), 231 (3), 155 (3), 122 (15), 121 (100), 91 (4), 78 (5); HRMS calcd for $C_{17}H_{24}O_3$ 276.1725, found 276.1728.

To a solution of the unsaturated ester (0.15 g, 0.54 mmol) in diethyl ether (5 mL) at 0 °C was added lithium aluminum hydride (0.21 g, 0.55 mmol). The reaction mixture was stirred for 20 min, at which time the reaction was shown to be complete by TLC examination. To the reaction mixture was added water (0.02 mL), 15% aqueous sodium hydroxide solution (0.02 mL), and water (0.06 mL), and the mixture was stirred vigorously for 15 min. The mixture was filtered, and the residue was washed with ether (3 × 10 mL). The combined ether solution was then evaporated under reduced pressure to give 0.12 g (94%) of a thick clear viscous oil of the alcohol: IR (CCl_4) ν 3633, 3505, 1510, 1253, 1029, cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.59 (s, 3 H), 1.62–1.68 (m, 2 H), 1.85 (br s, 1 H), 2.08 (t, J = 7.48 Hz, 2 H), 2.27–2.35 (m, 2 H), 2.62 (t, J = 7.73 Hz, 2 H), 3.62 (t, J = 6.52 Hz, 2 H), 3.81 (s, 3 H), 5.24 (t, J = 7.04 Hz, 1 H), 6.84–7.14 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 15.96, 30.19, 30.89, 35.23, 36.03, 55.37, 62.76, 113.83, 124.27, 129.45, 134.53, 135.43, 157.87; MS *m/e* (%) 234 (7), 122 (14), 121 (100), 120 (4), 78 (6), 77 (5); HRMS calcd for $C_{15}H_{22}O_2$ 234.1619, found 234.1625.

To a solution of oxalyl chloride (0.072 g, 0.56 mmol) in methylene chloride (1.2 mL) at −60 °C was added dropwise dimethyl sulfoxide (0.11 g, 1.35 mmol) in methylene chloride (0.25 mL). The mixture was allowed to stir at −60 °C for 15 min and then the *E* alcohol (0.12 g, 0.51 mmol) was added in minimum amount of methylene chloride and stirred at −60 °C for 15 min. Triethylamine (0.29 g, 2.82 mmol) was then added at −60 °C, and the cooling bath was removed. The mixture was then allowed to warm to room temperature, at which time 2 mL of water was added, and the resultant mixture was vigorously stirred for 30 min. The organic layer was separated, and the aqueous layer was extracted with methylene chloride (2 × 10 mL). The combined organic layers were washed with saturated aqueous sodium chloride solution and dried (Na_2SO_4). The solvent was then evaporated under reduced pressure to give an oily residue, which was purified by flash column chromatography (30% ether/hexane) (R_f = 0.19) to give 0.108 g (91%) of the *E* aldehyde **17**: IR (CCl_4) ν 2717, 1729, 1505, 1362, 1241, 1033 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.57 (s, 3 H), 2.28–2.62 (m, 8 H), 3.81 (s, 3 H), 5.22 (t, J = 7.0 Hz, 1 H), 6.83 (d, J = 9 Hz, 2 H), 7.15 (d, J = 9 Hz, 2 H), 9.75 (t, J = 1.73 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 16.10, 30.13, 31.95, 35.07, 42.21, 55.35, 113.86, 124.95, 129.43, 133.80, 134.31, 157.98, 202.47; MS *m/e* (%) 232 (7), 122 (15), 121 (100), 91 (5), 78 (8), 77 (8); HRMS calcd for $C_{15}H_{20}O_2$ 232.1463, found 232.1459.

(*E*)-1-[8,8-(1,2-Benzenediyldithio)-4-methylocta-3,7-dienyl]-4-methoxybenzene (18). This material was prepared in the same manner as previously described and was isolated by flash column chromatography (20% ether/hexane) (R_f = 0.15) to give the desired product **18** (0.065 g, 93%): IR (CCl_4) ν 3058, 3004, 2955, 2839, 1507, 1447, 1246, 1174, 1123 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.60 (s, 3 H), 2.11–2.36 (m, 6 H), 2.63 (t, J = 7.65 Hz, 2 H), 3.82 (s, 3 H), 5.24 (t, J = 7.04 Hz, 1 H), 5.43 (t, J = 6.4 Hz, 1 H), 6.85–7.20 (m, 8 H); ^{13}C NMR ($CDCl_3$) δ 15.95, 30.25, 30.87, 35.22, 38.55, 55.36, 113.82, 115.83, 121.29, 121.64, 124.79, 125.39, 125.64, 129.49, 134.55, 134.76, 157.88; MS *m/e* (%) 368 (6), 179 (24), 153 (47), 122 (9), 121 (100), 91 (5), 77 (9); HRMS calcd for $C_{22}H_{24}OS_2$ 368.1263, found 368.1258.

1,1-(1,2-Benzenediyldithio)-4a-methyl-6-methoxy-1,2,3,4,4a,9,10,10a-octahydrophenanthrene (19). Several crystals (approximately 20–30 mg) of *p*-toluenesulfonic acid were added at room temperature to a solution of ketene dithioacetal **18** (0.065 g, 0.18 mmol) in acetonitrile (3 mL). The reaction mixture was placed in the refrigerator (5 °C) for 40–42 h, at which time the reaction was shown to be complete by TLC examination. The cyclized solid crystalline product was washed with cold acetonitrile and dried to give an isolated yield of 0.041 g (63%) of a colorless cyclized product: mp 178–179 °C; IR (CCl_4) ν 2915, 2833, 1601, 1486, 1309, 1261, 1247, 1228 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.34 (s, 3 H), 1.53–1.72 (m, 3 H), 1.93–2.11 (m, 3 H), 2.35 (d, J = 8 Hz, 1 H), 2.62–3.01 (m, 4 H), 3.81 (s, 3 H), 6.71–7.19 (m, 7 H); ^{13}C NMR ($CDCl_3$) δ 19.62, 22.85, 24.66, 28.95, 37.82, 39.71, 45.08, 49.46, 55.41, 75.34, 110.31, 111.39, 121.97, 122.73, 125.12, 125.36, 127.22, 130.12, 136.83, 138.22, 149.15, 157.97; MS *m/e* (%) 368 (15), 367 (59), 324 (24), 193 (30), 179 (100), 176 (94), 175 (48), 173 (25), 170 (52), 153 (69), 140 (25), 121 (19); HRMS calcd for $C_{22}H_{24}OS_2$ 368.1263, found 368.1270.

4a-Methyl-6-methoxy-3,4,4a,9,10,10a-hexahydro-1(2*H*)-phenanthrone (20).[13] This compound was obtained in the same manner as described previously as a mixture of inseparable isomers in the ratio of 66:34 by NMR (0.17 g, 64%): IR (CCl_4) ν 2945, 1718, 1595, 1493, 1255, 1023 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.06 (s, 3 H), 1.33 (s, 3 H), 1.41–1.61 (m, 6 H), 2.21–3.01 (m, 5 H), 3.84 (s, 3 H), 6.63–7.21 (m, 3 H).

General Procedure for Cycloaddition (Diels–Alder) Reaction for Preparation of 21a–d. To a solution of 5.68 g (40 mmol) of 2-[(trimethylsilyl)oxy]-1,3-butadiene[18] in 40 mL of toluene was added 40 mmol of the appropriate dienophile and a few crystals of *p*-hydroquinone to avoid any radical-induced polymerization, and the reaction mixture was heated to reflux with stirring for 45 h. The flask was cooled to room temperature, and a short-path distillation was carried out to remove toluene to give the cycloadduct as a colorless oil.

1-[(Trimethylsilyl)oxy]-4-formyl-4-methyl-1-cyclohexene (21a). Obtained after distillation as a colorless oil (0.54 g, 54%):

(25) Karasch, M.; Reinmuth, S. *Grignard Reactions of Nonmetallic Substances*; Prentice-Hall: New Jersey, 1954.

bp 103 °C (3 Torr); IR (CCl_4) ν 2900, 2750, 1725, 1665, 1352, 1233, 1187 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.14 (s, 9 H), 1.01 (s, 3 H), 1.31–2.51 (m, 6 H), 4.74 (br t, J = 4.01 Hz, 1 H), 9.41 (s, 1 H).

1-[(Trimethylsilyl)oxy]-4-acetyl-1-cyclohexene (21b).[25] Obtained after distillation as a colorless oil (0.49 g, 57%): bp 115 °C (3 Torr); IR (CCl_4) ν 3029, 1712, 1669, 1358, 1251, 1189 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.17 (s, 9 H), 1.61–2.49 (m, 7 H), 2.07 (s, 3 H), 4.73 (br t, J = 3.98 Hz, 1 H).

1-[(Trimethylsilyl)oxy]-4-formyl-1-cyclohexene (21c). Obtained after distillation as a colorless oil (0.61 g, 68%). The reaction was complete in 24 h: bp 67–70 °C (1.2 Torr); IR (CCl_4) ν 2900, 2751, 1730, 1660, 1351, 1234, 1186 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.21 (s, 9 H), 1.81–2.51 (m, 7 H), 4.92 (m, 1 H), 9.78 (s, 1 H).

2-[(Trimethylsilyl)oxy]-4a-acetyl-2-hydrindene (21d). A mixture of 0.4 g (2.76 mmol) of the diene and 0.22 g (2 mmol) of 1-acetyl-1-cyclopentene were heated in a sealed tube at 250 °C for 46 h. The excess diene was removed to give 0.2 g (40%) yield of a dark colored cycloadduct. No further purification was attempted: IR (CCl_4) ν 2900, 2849, 1715, 1665, 1342, 1259, 1158 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.19 (s, 9 H), 1.61–2.52 (m, 11 H), 2.06 (s, 3 H), 4.72 (br t, J = 4.02 Hz, 1 H).

General Procedure for Preparation of 2-Alkylidene-1,3-benzodithioles (Ketene Dithioacetals, 22a–c, 24). To a cold (−78 °C) solution of 2-(diethoxyphosphinyl)-1,3-benzodithiole (**5**) (0.58 g, 2 mmol) in THF (3 mL) was added n-butyllithium (1.4 mL, 2.05 mmol). This solution was stirred for 15 min at which time 2 mmol of the appropriate carbonyl compound **21a–d** in THF (2 mL) was added. The reaction mixture was stirred at −78 °C for 5–6 h and then allowed to warm to room temperature. The THF was evaporated to give a gummy residue. The gummy residue was diluted with cold water (20 mL) and extracted very quickly with methylene chloride (3 × 20 mL). The extracts were combined, washed once with saturated aqueous sodium chloride solution, and dried (Na_2SO_4). The solvent was then evaporated under reduced pressure to give an oily residue of the 2-alkylidene-1,3-benzodithioles.

1-[(Trimethylsilyl)oxy]-4-methyl-4-(1,3-benzodithiol-2-ylidenemethyl)cyclohexene (22a). Obtained as a viscous light yellow oil (0.77 g, 90%): IR (CCl_4) ν 3000, 2850, 1717*, 1665, 1446, 1350, 1250, 1125 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.15 (s, 9 H), 1.21 (s, 3 H), 1.31–2.49 (m, 6 H), 4.74 (m, 1 H), 5.30 (s, 1 H), 6.81–7.21 (m, 4 H) [* arises from partial hydrolysis of the silyl enol ether during aqueous workup].

1-[(Trimethylsilyl)oxy]-4-[1-(1,3-benzodithiol-2-ylidene)-ethyl]cyclohexene (22b). Obtained as a yellow oil (0.71 g, 88%): IR (CCl_4) ν 3000, 2831, 1715*, 1661, 1442, 1361, 1249, 1170 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.24 (s, 9 H), 1.92 (s, 3 H), 1.61–2.59 (m, 6 H), 4.81 (m, 1 H), 7.00–7.29 (m, 4 H) [* arises from partial hydrolysis of the silyl enol ether during aqueous workup].

1-[(Trimethylsilyl)oxy]-4-(1,3-benzodithiol-2-ylidene-methyl)cyclohexene (22c). Obtained as a pale yellow viscous oil (0.61 g, 91%): IR (CCl_4) ν 3000, 2831, 1720*, 1662, 1443, 1247, 1121 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.28 (s, 9 H), 1.71–2.62 (m, 7 H), 4.81 (m, 1 H), 5.32 (m, 1 H), 7.01–7.29 (m, 4 H) [* arises from partial hydrolysis of the silyl enol ether during aqueous workup].

2-[(Trimethylsilyl)oxy]-4a-[1-(1,3-benzodithiol-2-ylidene)ethyl]hydrindene (24). Obtained as a dark viscous oil (0.33 g, 79%): IR (CCl_4) ν 3000, 2822, 1720*, 1663, 1444, 1248, 1121 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.24 (s, 9 H), 1.81 (s, 3 H), 1.91–2.95 (m, 11 H), 4.81 (m, 1 H), 6.98–7.28 (m, 4 H) [* arises from partial hydrolysis of the silyl enol ether during aqueous workup].

General Procedure for Preparation of Bicyclo[3.2.1]octanes (Cyclization Reactions) (23a–c, 25). To a solution of 1 mmol of the appropriate precursor (the enol ether, or the carbonyl compound) in acetonitrile (4 mL) was added trifluoroacetic acid (0.125 g, 1.1 mmol). The light yellow solution immediately turned dark red. The reaction mixture was placed in a refrigerator (5 °C) for 12–48 h, at which time the reaction was shown to be complete by TLC examination. The acetonitrile was removed under reduced pressure to give a dark viscous oily residue. The residue was dissolved in 20 mL of ethyl acetate, and the solution was then washed with saturated aqueous sodium bicarbonate solution (2 × 20 mL), water, and saturated aqueous sodium chloride solution and dried (Na_2SO_4). The solvent was then evaporated under reduced pressure to give a semisolid residue, which was purified by flash column chromatography and recrystallized from petroleum ether to give white crystalline bicyclo[3.2.1]octanes.

7,7-(1,2-Benzenediyldithio)-5-methylbicyclo[3.2.1]octan-2-one (23a). Purified by flash column chromatography (15% ether/hexane) (R_f = 0.11), recrystallized (petroleum ether) to give a white solid (0.11 g, 83%): mp 136–137 °C; IR (CCl_4) ν 2950, 2872, 1715, 1429, 1340, 1275, 1110 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.21 (s, 3 H), 2.15–2.76 (m, 8 H), 3.21 (d, J = 4.49 Hz, 1 H), 6.95–7.21 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 25.91, 36.12, 38.53, 39.64, 42.85, 66.89, 71.72, 122.02, 122.71, 125.96, 137.94, 208.32; MS m/e (%) 276 (100), 261 (26), 220 (18), 219 (53), 206 (25), 179 (61), 166 (38), 165 (35), 153 (31); HRMS calcd for $C_{15}H_{16}OS_2$ 276.0642, found 276.0642. Anal. Calcd for $C_{15}H_{16}OS_2$: C, 65.20; H, 5.84. Found: C, 65.03; H, 5.86.

7,7-(1,2-Benzenediyldithio)-6-methylbicyclo[3.2.1]octan-2-one (23b). Purified by flash column chromatography (15% ether/hexane) (R_f = 0.12) and recrystallized (petroleum ether) to give a white solid in as a mixture of inseparable isomers (0.09 g, 77%): mp 121–122 °C; IR (CCl_4) ν 2950, 2870, 1715, 1440, 1368, 1119 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.33–1.45 (m, 3 H), 1.67–2.69 (m, 8 H), 3.29 (d, J = 4.06 Hz, 1 H), 3.33 (d, J = 4.17 Hz, 1 H), 6.95–7.21 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 15.29, 20.21, 25.20, 31.12, 34.31, 35.07, 36.00, 36.38, 38.82, 41.91, 43.97, 44.49, 67.69, 68.15, 78.99, 122.13, 122.63, 122.95, 125.96, 126.06, 126.19, 136.39, 136.62, 208.78; MS m/e (%) 276 (100), 218 (73), 217 (96), 205 (65), 192 (79), 180 (80), 179 (99), 178 (97), 165 (97), 153 (99), 77 (99), 32 (92), 28 (97); HRMS calcd for $C_{15}H_{16}OS_2$ 276.0642, found 276.0640. Anal. Calcd for $C_{15}H_{16}OS_2$: C, 65.20; H, 5.84. Found: C, 65.37; H, 5.87.

7,7-(1,2-Benzenediyldithio)bicyclo[3.2.1]octan-2-one (23c). Purified by flash column chromatography (10% ether/hexane) (R_f = 0.12), recrystallized (petroleum ether) to give the product as a white solid (0.07 g, 71%): mp 112–114 °C; IR (CCl_4) ν 2950, 2880, 1716, 1441, 1255 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.79–2.85 (m, 9 H), 3.26 (d, J = 4.45 Hz, 1 H), 7.02–7.21 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 20.33, 33.67, 33.88, 36.53, 41.12, 66.49, 71.67, 122.24, 122.98, 126.18, 208.54; MS m/e (%) 262 (100), 206 (34), 205 (85), 193 (21), 192 (25), 179 (90), 166 (43), 153 (51), 77 (20); HRMS calcd for $C_{14}H_{14}OS_2$ 262.0485, found 262.0481.

5,5-(1,2-Benzenediyldithio)-4-methyl-1,2,3,3a,4,5,6,8aα-octahydro-3aα,6α-methanoazulen-7(8*H*)-one (25). Purified by flash column chromatography (15% ether/hexane) (R_f = 0.12), recrystallized (petroleum ether) to give the product as an inseparable mixture of isomers, as a white solid (0.021 g, 32%): mp 195–196 °C; IR (CCl_4) ν 2948, 2860, 1715, 1443, 1260 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28–2.82 (m, 11 H), 1.45 (d, J = 7 Hz, 1.5 H), 1.47 (d, J = 7 Hz, 1.5 H), 3.34 (m, J = 3.79 Hz, 2 H), 7.01–7.21 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 15.29, 20.19, 25.21, 29.78, 31.12, 32.97, 34.09, 34.32, 35.06, 35.56, 36.00, 36.26, 36.38, 38.82, 41.91, 43.94, 44.46, 67.02, 67.70, 68.14, 122.14, 122.63, 122.96, 123.13, 125.95, 126.07, 126.21, 208.99; MS m/e (%) 316 (11), 276 (46), 220 (11), 219 (21), 193 (17), 181 (14), 180 (39), 179 (100), 166 (19), 153 (49), 140 (13), 91 (19), 77 (25), 69 (22), 55 (22); HRMS calcd for $C_{18}H_{20}OS_2$ 316.0955, found 316.0951.

7,7-(1,2-Benzenediyldithio)-3,5-dimethylbicyclo[3.2.1]octan-2-one (26). To a solution of 1 mmol of silylenol ether **22a** in THF (5 mL) at room temperature was added 5% aqueous trifluoroacetic acid solution (0.1 mL). The resultant mixture was stirred for 5 min, at which time the reaction was shown to be complete by TLC examination. The reaction mixture was diluted with diethyl ether (15 mL), and the ether solution was washed with saturated aqueous sodium bicarbonate solution, water, and saturated aqueous sodium chloride solution (20 mL each) and then dried (Na_2SO_4). The ether was evaporated under reduced pressure to give an oil of the crude cyclohexanone, which was purified by flash column chromatography (10% ether/hexane) (R_f = 0.13) to give a viscous oil (0.27 g, 98%): IR (CCl_4) ν 3050, 2969, 2841, 1718, 1560, 1440, 1367, 1325, 1119 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (s, 3 H), 1.49–2.61 (m, 8 H), 5.63 (s, 1 H), 6.99–7.28 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 16.81, 26.12, 38.70, 42.99, 122.25, 122.94, 125.95, 126.20, 138.18, 208.75; MS m/e (%) 276 (73), 261 (33), 220 (40), 219 (100), 207 (21), 206 (23), 179 (37), 166 (29), 153 (34), 80 (21); HRMS calcd for $C_{15}H_{16}OS_2$ 276.0642, found 276.0636.

To a solution of diisopropylamine (0.11 g, 1.1 mmol) in THF (3 mL) at −5 °C was added n-butyllithium (0.44 mL, 1.1 mmol), and the mixture was stirred for 20 min. The temperature of the

bath was lowered to −78 °C, and a solution of the cyclohexanone (prepared above) (0.27 g, 1 mmol) in THF (1 mL) was added. The resultant solution was stirred at −78 °C for 1 h, at which time iodomethane (0.14 g, 1.1 mmol) was added. The solution was stirred at −78 °C for 1 h and then allowed to warm to room temperature with stirring for an additional 6 h. The reaction mixture was then poured into 10 mL of saturated aqueous ammonium chloride solution. The organic layer was separated, and the aqueous layer was extracted with diethyl ether (3 × 10 mL). The combined organic extracts were washed with saturated aqueous sodium chloride solution and dried (Na_2SO_4). The solvent was then evaporated under reduced pressure, and the residue was purified by flash chromatography (15% ether/hexane) to give a 0.26-g (90%) yield of a pale yellow oil as an inseparable mixture of epimers (R_f = 0.12): IR (CCl_4) ν 3070, 2974, 2885, 1715, 1448, 1375, 1120 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.98 (d, J = 6.45 Hz, 3 H), 1.15 (s, 3 H), 1.21–2.91 (m, 7 H), 5.64 (s, 1 H), 6.97–7.28 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 14.44, 16.39, 19.91, 22.71, 25.74, 26.49, 27.25, 31.58, 37.26, 37.98, 38.36, 38.65, 39.04, 39.19, 41.44, 47.14, 49.82, 53.31, 120.38, 120.77, 120.88, 121.13, 121.45, 121.61, 121.95, 125.35, 125.51, 125.66, 125.74, 125.91, 131.24, 212.08; MS m/e (%) 290 (77), 275 (46), 266 (50), 220 (40), 219 (100), 206 (41), 193 (25), 166 (50), 153 (66), 41 (27); HRMS calcd for $C_{16}H_{18}OS_2$ 290.0793, found 290.0798.

The cyclization was performed in a manner analogous to previously described to give compound **26**, which was purified by flash column chromatography (20% ether/hexane) (R_f = 0.13) and recrystallization (petroleum ether) to give a white crystalline solid as a mixture of inseparable C_3 epimers (0.17 g, 65%): mp 128–129 °C; IR (CCl_4) ν 2960, 2881, 1720, 1445, 1260, cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.09 (d, J = 6.47 Hz, 3 H), 1.19 (s, 3 H), 1.25–2.71 (m, 7 H), 3.26* (d, J = 4.51 Hz, 1 H), 6.95–7.24 (m, 4 H) [* the bridge head proton in both isomers displayed the same chemical shift value]; ^{13}C NMR ($CDCl_3$) δ 14.56, 25.90, 27.91, 31.37, 32.74, 39.86, 40.31, 43.67, 48.31, 48.70, 53.02, 66.44, 66.91, 71.96, 122.01, 122.22, 122.84, 122.89, 125.74, 125.93, 126.06, 126.14, 138.10, 138.14, 210.14; MS m/e (%) 290 (100), 219 (45), 179 (68), 166 (47), 153 (58), 77 (40), 41 (50), 39 (40), 28 (32); HRMS calcd for $C_{16}H_{18}OS_2$ 290.0798, found 290.0790. Anal. Calcd for $C_{16}H_{18}OS_2$: C, 66.16; H, 6.25; S, 22.04. Found: C, 65.95; H, 6.12; S, 22.29.

7,7-(1,2-Benzenediyldithio)-5-methylbicyclo[3.2.1]oct-3-ene (27). To a solution of diisopropylamine (0.10 g, 1 mmol) in THF (3 mL) at −5 °C was added n-butyllithium (0.65 mL, 1 mmol), and the resultant solution was stirred for 20 min. The temperature of the bath was lowered to −78 °C, and a solution of bicyclo[3.2.1]octane **23a** (0.236 g, 0.86 mmol) in THF (2 mL) was added. The solution was stirred at −78 °C for 45 min, at which time chlorotrimethylsilane (0.164 g, 1.5 mmol) was added. The reaction mixture was slowly warmed to room temperature. The mixture was then stirred for an additional 3 h and poured into ice-cold, saturated aqueous ammonium chloride solution. The organic layer was separated, and the aqueous layer was extracted with pentane (3 × 10 mL). The combined organic extracts were then very quickly washed with cold saturated aqueous sodium chloride solution (20 mL) and dried (Na_2SO_4). The pentane was evaporated under reduced pressure to give a 0.284-g (95%) yield of the crude silyl enol ether: IR (CCl_4) ν 3040, 2942, 2851, 1665, 1435, 1347, 1189, 1019 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.21 (s, 9 H), 1.22 (s, 3 H), 1.31–2.82 (m, 7 H), 4.74 (m, 1 H), 6.97–7.21 (m, 4 H).

To a stirred solution of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (0.30 g, 1.3 mmol) in benzene (5 mL) was added dropwise a solution of collidine (0.17 g, 1.4 mmol) in benzene (1 mL), and the resultant mixture was stirred at room temperature for 30 min. At this time a solution of the silyl enol ether (0.088 g, 0.25 mmol) in benzene (2 mL) was added dropwise over 20 min, and the mixture was stirred for an additional 24 h. The resultant black reaction mixture was then partitioned between 10 mL of 1 M aqueous sodium hydroxide solution and 10 mL of diethyl ether. The aqueous layer was extracted with ether (3 × 10 mL). The combined ether extracts were then washed with 5% aqueous sodium hydroxide solution, 10% aqueous hydrochloric acid solution, saturated aqueous sodium bicarbonate solution, water, and saturated aqueous sodium chloride solution (15 mL each). The organic layer was dried (Na_2SO_4), and the solvent was evaporated under reduced pressure to give an oily residue. The residue was purified by flash column chromatography with 15% ether/petroleum ether as eluent to give 0.044 g (64%) of the enone, which was recrystallized (diethyl ether) to give a white solid: mp 128–129 °C; IR (CCl_4) ν 3060, 2951, 2862, 1696, 1443, 1372, 1113 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.20–2.60 (m, 4 H), 1.35 (s, 3 H), 3.43 (d, J = 4.08 Hz, 1 H), 5.88 (d, J = 9.24 Hz, 1 H), 6.98 (d, J = 7.45 Hz, 1 H), 7.03–7.19 (m, 4 H); ^{13}C NMR ($CDCl_3$) δ 28.91, 36.13, 37.53, 44.81, 63.42, 71.72, 122.13, 124.63, 136.84, 138.93, 139.21, 207.43; MS m/e (%) 274 (42), 260 (28), 247 (21), 232 (35), 194 (30), 180 (23), 148 (76), 77 (100), 52 (34); HRMS calcd for $C_{15}H_{14}OS_2$ 274.0475, found 274.0476.

5-Methylbicyclo[3.2.1]octan-2-one (28).[26] To a solution of bicyclobenzodithiole **23a** (82.8 mg, 0.30 mmol) in absolute ethanol (5 mL) was added 2–3 g of activated Raney nickel (W-2). The dark colored mixture was heated to reflux for 6 h, at which time the reaction was shown to be complete by TLC examination. The flask was then cooled, and the contents were filtered through Celite. The remaining nickel was washed with ethanol (2 × 10 mL), and the combined ethanol washings were evaporated under reduced pressure to give the desulfurized compound **28** after flash column chromatography with 10% ether/hexane as eluent (R_f = 0.11) (27 mg, 66%): IR (CCl_4) ν 2939, 2857, 1717, 1128, 1023 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.18 (s, 3 H), 1.28–2.01 (m, 10 H), 2.29 (br, 1 H); ^{13}C NMR ($CDCl_3$) δ 21.83, 28.67, 29.87, 35.24, 36.67, 37.26, 38.54, 39.42, 209.89; HRMS calcd for $C_9H_{14}O$ 138.1047, found 138.1041.

5-Methylbicyclo[3.2.1]octane-2,7-dione (29). To a vigorously stirred suspension of red mercury(II) oxide (0.11 g, 0.5 mmol) and boron trifluoride etherate (0.071 g, 0.5 mmol) in aqueous THF (15% water by volume) (3 mL) was added bicyclo[3.2.1]octane **23a** (69 mg, 0.25 mmol). The reaction mixture was heated to reflux for 1–2 h, during which time the orange-red solution changed to light yellow and then to a greenish color. At this time the reaction was shown to be complete by TLC examination. The flask was then cooled to room temperature, ether (10 mL) was added to the reaction mixture, and the contents of the flask were filtered. The green residue was washed a few times with ether and once again filtered. The combined ether washings were then washed with saturated aqueous sodium bicarbonate solution, water, and saturated aqueous sodium chloride solution (15 mL each). The ether layer was then dried (Na_2SO_4), and the solvent was evaporated under reduced pressure to give an oily residue, which was purified by flash column chromatography (25% ether/hexane) to give 25 mg of compound **29** (64% yield) as a light colored oil: IR (CCl_4) ν 2972, 2937, 2880, 1757, 1722, 1174 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.19 (s, 3 H), 1.70–2.58 (m, 8 H), 3.29 (d, J = 5.16 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 22.92, 29.74, 36.90, 37.87, 42.96, 50.62, 63.55, 206.61, 210.75; MS m/e (%) 152 (33), 95 (11), 87 (12), 82 (23), 71 (40), 67 (54), 57 (40), 55 (90), 43 (100); HRMS calcd for $C_9H_{12}O_2$ 152.0837, found 152.0844.

7,7-(1,2-Benzenediyldithio)-5-methylbicyclo[3.2.1]octane (30). To a solution of bicyclo[3.2.1]octane **23a** (0.28 g, 1 mmol) in diethyl ether (5 mL) at 0 °C was added lithium aluminum hydride (0.04 g, 1.05 mmol). The reaction mixture was stirred for 30 min, at which time the reaction was shown to be complete by TLC examination. To the reaction mixture at 0 °C was added 0.04 mL water, 0.04 mL of 15% aqueous sodium hydroxide solution, and 0.12 mL of water, and the resultant mixture was stirred vigorously for 30 min to give a gummy white residue. The ether was filtered off, and the residue was washed with ether (3 × 10 mL). The combined ether washings were evaporated under reduced pressure to give 0.26 g (94%) yield of a viscous oil, after flash column chromatography (25% ether/hexane): IR (CCl_4) ν 3515, 2940, 2862, 1461, 1444, 1118, 1065 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.09 (s, 3 H), 1.27–2.37 (m, 8 H), 2.78 (m, 1 H), 3.20 (d, J = 10.5 Hz, 1 H), 6.99–7.21 (m, 4 H); MS m/e (%) 278 (75), 263 (24), 219 (42), 179 (45), 166 (52), 153 (100), 137 (25), 95 (31), 93 (23), 79 (21), 77 (38), 72 (45), 71 (50), 69 (37); HRMS calcd for $C_{15}H_{18}OS_2$ 278.0798, found 278.0797.

To a suspension of sodium hydride (50% dispersion in oil, prewashed with pentane) (0.29 g, 0.6 mmol) in THF (3 mL) at room temperature was added 0.1033 g (0.36 mmol) of the alcohol (0.103 g, 0.36 mmol) in THF (2 mL). After the evolution of hydrogen ceased (15 min), the reaction mixture was treated with

(26) Belikova, N. A.; Bobyleva, A. A.; Dzhigirkhanova, A. V.; Pehk, T.; Lippmaa, F.; Plate, A. F. *Zh. Org. Khim.* **1977**, *13*, 1898.

carbon disulfide (1 mL), and the mixture was refluxed for 30 min and then was treated with 1 mL of iodomethane. The entire mixture was refluxed for 6 h, at which time the reaction was judged to be complete by TLC examination. The reaction mixture was then cooled to room temperature and diluted with saturated aqueous ammonium chloride solution (10 mL), and the organic layer was extracted with diethyl ether (3 × 10 mL). The combined organic layers were washed with saturated aqueous sodium chloride solution (15 mL) and dried (Na_2SO_4). The ether was removed under reduced pressure to give a 0.11-g (83%) yield of the xanthate after flash column chromatography (5% ether/hexane) (R_f = 0.18): IR (CCl_4) ν 2965, 2880, 1445, 1215, 1065 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.13 (s, 3 H), 1.21–2.51 (m, 8 H), 2.60 (s, 3 H), 3.19 (d, J = 8.72 Hz, 1 H), 5.67 (m, 1 H), 6.97–7.21 (m, 4 H); MS m/e (%) 290 (13), 261 (56), 205 (26), 167 (34), 153 (21), 95 (100), 77 (25); HRMS calcd for $C_{16}H_{20}OS_4$ 368.0397, found 368.0399.

To a solution of the xanthate (0.085 g, 0.23 mmol) in toluene (3 mL) at room temperature was added tri-*n*-butyltin hydride (0.876 g, 0.3 mmol). The mixture was refluxed for 24 h, at which time the reaction was shown to be almost complete by TLC examination. The toluene was removed under reduced pressure to give 0.034 g (56%) of the deoxygenated product **30** after flash column chromatography (hexane): IR (CCl_4) ν 2950, 2925, 2863, 1458, 1442 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.07 (s, 3 H), 1.21–2.51 (m, 10 H), 2.31 (d, J = 4.21 Hz, 1 H), 6.99–7.20 (m, 4 H); MS m/e (%) 262 (73), 247 (44), 219 (40), 193 (34), 179 (28), 166 (67), 153 (100), 121 (40), 91 (26), 79 (25), 77 (49); HRMS calcd for $C_{15}H_{18}S_2$ 262.0849, found 262.0854.

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Supplementary Material Available: ^1H and ^{13}C NMR spectra for **7a,f**, **13**, **15**, **17**, **19**, and **25** (14 pages). Ordering information is given on any current masthead page.

Total Syntheses of (+)-Thyrsiferol, (+)-Thyrsiferyl 23-Acetate, and (+)-Venustatriol

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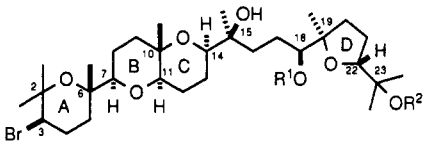
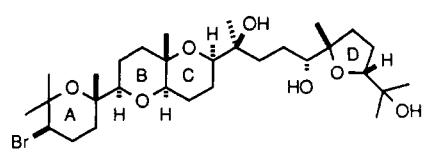
The first total syntheses of (+)-thyrsiferol (**1**), (+)-thyrsiferyl 23-acetate (**3**), and (+)-venustatriol (**5**) have been accomplished in a stereoselective manner. An effective synthetic scheme to construct the BC ring system, which adopts a chair/twist-boat conformation, was first developed by means of a model study. This method involves stereoselective formation of the strained C ring by intramolecular attack of the C_7-hydroxyl group at the C_3-position of the 2,3-epoxy alcohol, employing titanium tetraisopropoxide as an acidic activator. Based on the information accumulated in the model study and retrosynthetic considerations, the total syntheses of **1**, **3**, and **5** were performed in the sequence of (1) construction of the BC ring system equipped with a C_1–C_6 carbon unit, (2) elongation of the C_{17}–C_{24} carbon chain, (3) formation of a D ring through the stereoselective epoxidation of the 4-en-1-ol system and successive cyclization, and (4) construction of the A ring by bromonium ion induced cyclization of the 4-en-1-ol system.

Introduction

Thyrsiferol (**1**) and its 18-acetate (**2**), squalene-derived metabolites from *Laurencia thyrsiferia*, were isolated as a new type of triterpene–polyether by Munro's group in 1978.[1] Their relative stereochemistries were determined by X-ray diffraction. In 1985, Kurosawa and his coworkers isolated related polyethers such as thyrsiferyl 23-acetate (**3**),[2] 18,23-diacetate (**4**), $\Delta^{15,16}$- and $\Delta^{15,28}$-anhydrothyrsiferyl diacetates, and magireols from *Laurencia obtusa*, and found that these bromine-containing polyethers show strong citotoxicity against P388 murine leukemia in vitro.[3] Particularly, **3** exhibited ED_{50} values of 0.3 ng/mL in a P388 in vitro assay. Venustatriol (**5**), a diastereomeric isomer of **1**, was found as a metabolite of a congenial *Laurencia venusta* by Higa's group in 1986.[4] This tetracyclic polyether **5** exhibits significant antiviral activity against the vesicular stomatitis virus (VSV) and herpes simplex virus type 1 (HSV-1). X-ray structural analysis of **5** disclosed the absolute configuration depicted in formula **5**. These results permit the correct assignments of the absolute configurations of thyrsiferol (**1**) and its congeners.



1 $R^1 = R^2 = H$ (thyrsiferol)
2 R^1 = Ac, R^2 = H
3 R^1 = H, R^2 = Ac
4 R^1 = Ac, R^2 = Ac



5 (venustatriol)

All members of this family are characterized by a (bromotetrahydropyranyl)-2,7-dioxabicyclo[4.4.0]decane

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