A Total Synthesis of the Methyl Ester of the 9,11-Dithia Analogue of 13,14-Dehydro-PGH_2

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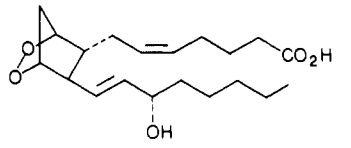
A total synthesis of the disulfide analogue **2** of 13,14-dehydro-PGH_2 methyl ester is described. A key intermediate is the mesylate of the 3-phenyl-2,4-dithia[3.2.1]bicyclooctane derivative **37b**, which undergoes alkynylation via an episulfonium intermediate to form the desired product **41** as well as the isomers **39** and **40** resulting from alternative openings of the episulfonium intermediate. The use of the 2-anisyl substituent on the model compound **19** leads exclusively to **21**, the product corresponding to **39**. Functional group manipulation and deprotection steps on **41** lead to the parent dithiol, which cyclizes spontaneously to the target compound **2**. This facile intramolecular disulfide formation is ascribed to steric hindrance by the two side chains, which interfere with polymerization.

The prostaglandin endoperoxide **1** is a pivotal intermediate in the biosynthesis of prostaglandins, prostacyclin, and thromboxanes.[1] While this cyclooxygenase-derived product of arachidonic acid possesses interesting biological properties,[2] its short half-life of only 5 min in aqueous buffer has presented a problem in studying its biological action, as well as the enzymology involved in the processing of these compounds.[1,3] Thus, while the chemical synthesis of PGH_2 has been reported,[4a,b] a considerable amount of effort has recently been focused on the synthesis of stable analogues of the bicyclic system present in these substances.[4c] A bicycloheptene analogue was shown to cause platelet aggregation and to inhibit the enzyme that catalyzes the isomerization of PGH_2 to PGE_2.[5] The 9,11-azo analogue, obtained by both partial and total synthesis, was likewise shown to cause aggregation of platelets.[5,6]

Our decision to synthesize a 9,11-disulfide analogue of PGH_2 was influenced by the precedence of substantial literature on obtaining active analogues of biological molecules by substitution of oxygen by sulfur and vice versa. Examples of active thia compounds in the steroid field,[7] the equivalence of biotin and oxybiotin in biotin-utilizing reactions,[8] similar biological properties of 7-thiaprostaglandin $F_{1\alpha}$ and 7-oxaprostaglandin $F_{1\alpha}$,[9] and the comparable potency of 6,9-thiaprostacyclin[10] to natural prostacyclin in inhibiting platelet aggregation have been documented in the literature. A particularly attractive feature was the possibility that the disulfide system would possess sufficient stability to find its way to bind to endoperoxide receptors or to enzymes that utilize the endoperoxide for further processing into the prostaglandins. When bound at the appropriate sites, an adventitiously present thiol functionality might then by sulfide exchange open the dithiolane ring and cause covalent attachment of the analogue to the enzyme or receptor, causing irreversible inhibition or antagonism. Since it is known that one of the major metabolic pathways for the inactivation of natural prostaglandins is due to 15-hydroxyprostaglandin dehydrogenase,[11] we focused our attention on the synthesis of the 13,14-dehydro-9,11-disulfide analogue **2**. As a rule, 13,14-dehydroprostaglandins are not substrates for this enzyme.[11b]



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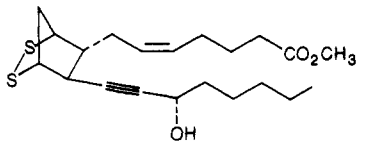

2

During the course of our research, two partial syntheses of the disulfide analogue of PGH_2 methyl ester have been reported.[12,13] The compound was found to be a strong mimic of thromboxane A_2 in contracting rabbit aorta strips and in causing rapid, irreversible aggregation of platelets. The synthetic route reported in this paper represents a total synthesis of **2** and permits structural modifications to produce prostaglandin analogues not available from the syntheses reported earlier.

Strategy and Retrosynthetic Studies. Since cyclic disulfides are prone to polymerization due to torsional strain resulting from the distortion of the dihedral angle

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(2) (a) Hamberg, M.; Samuelsson, B. *Proc. Natl. Acad. Sci. U.S.A.* **1973**, *70*, 899. (b) Hamberg, M.; Svensson, J.; Wakabayashi, T.; Samuelsson, B. *Proc. Natl. Acad. Sci. U.S.A.* **1974**, *71*, 345. (c) Hamberg, M.; Samuelsson, B. *Proc. Natl. Acad. Sci. U.S.A.* **1974**, *71*, 3400.
(3) (a) Dewitt, D. L.; Smith, W. L. *J. Biol. Chem.* **1983**, *258*, 3285. (b) Haurand, M.; Ullrich, V. *J. Biol. Chem.* **1985**, *260*, 15059.
(4) (a) Johnson, R. A.; Nidy, E. G.; Baczynskj, L.; Gorman, G. G. *J. Am. Chem. Soc.* **1977**, *99*, 7738. (b) Porter, N. A.; Byers, J. D.; Mebane, R. C.; Gilmire, D. W.; Nixon, J. R. *J. Org. Chem.* **1978**, *43*, 2088. (c) Nicolaou, K. C.; Gasic, G. P.; Barnette, W. E. *Angew. Chem., Int. Ed. Engl.* **1978**, *17*, 293.
(5) (a) Corey, E. J.; Shibasaki, M.; Nicolaou, K. C.; Malmsten, C. L.; Samuelsson, B. *Tetrahedron Lett.* **1976**, 737. (b) Corey, E. J.; Nicolaou, K. C.; Machida, Y.; Malmsten, C. L.; Samuelsson, B. *Proc. Natl. Acad. Sci. U.S.A.* **1975**, *72*, 3355.
(6) Corey, E. J.; Narasaka, K.; Shibasaki, M. *J. Am. Chem. Soc.* **1976**, *98*, 6417.
(7) (a) Wolff, M. E.; Zanati, G. *J. Med. Chem.* **1969**, *12*, 629; (b) **1971**, *14*, 958; (c) **1972**, *15*, 368.
(8) White, A.; Handler, P.; Smith, E. L. *Principles of Biochemistry*, 4th ed.; McGraw-Hill: New York, 1970; p 1034.
(9) Fried, J.; Mehra, M. M.; Kao, W. L. *J. Am. Chem. Soc.* **1971**, *93*, 5594.
(10) Nicolaou, K. C.; Barnette, W. E.; Gasic, G. P.; Magolda, R. L. *J. Am. Chem. Soc.* **1977**, *99*, 7736.
(11) (a) Braithwaite, S. S.; Jarabak, J. *J. Biol. Chem.* **1975**, *250*, 2315. (b) Fried, J.; Lee, M.; Gaede, B.; Sih, J. C.; Yoshikawa, Y.; McCracken, J. A. In *Advances in Prostaglandin and Thromboxane Research*; Samuelsson, B., Paoletti, R., Eds.; Raven: New York, 1976; Vol. 1, p 183.
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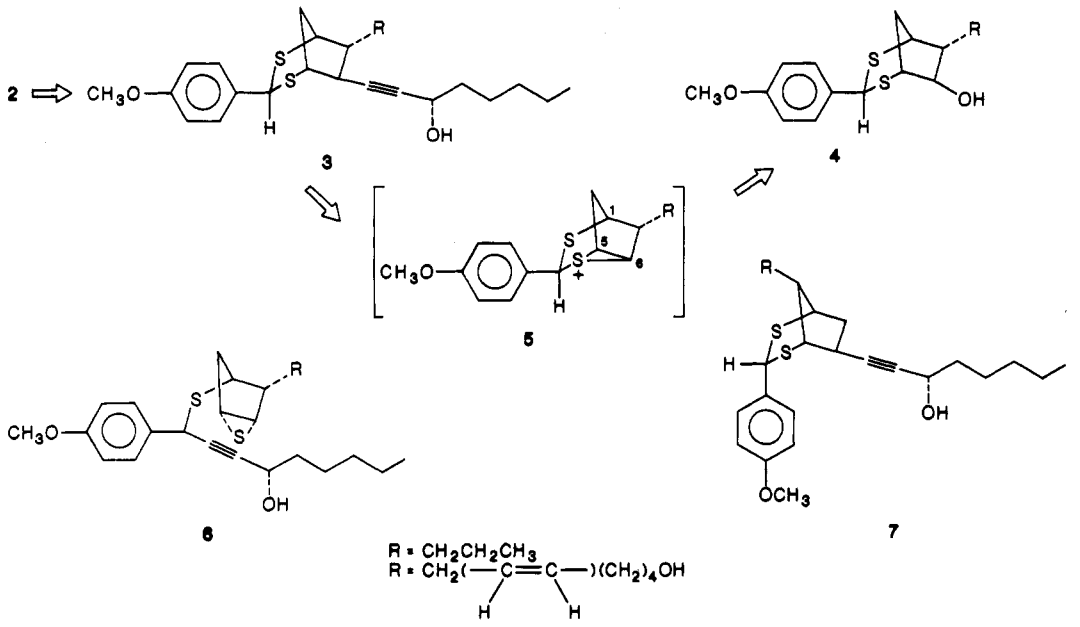
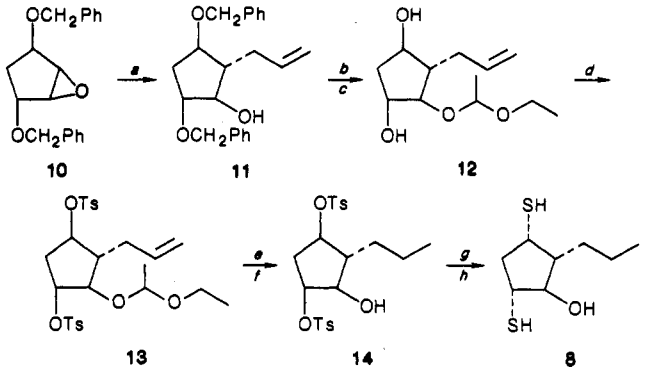
Scheme I



of the disulfide bond from the favored 90°,[14] we elected to leave the construction of this crucial bond until the last stages of the synthesis. An additional factor was the observation that branching near the disulfide bond in cyclic systems imparted greater stability to the ring system.[15] Consequently, a multistep synthetic sequence (Scheme I) was envisioned in which the thiol functionality was to be introduced in a suitably protected form at an early stage. The elegant approach developed by Kishi and co-workers for the construction of the epidithiodiketopiperazine ring systems of gliotoxin and sporidesmins A and B appeared particularly attractive,[16] since it provided a very stable *p*-methoxybenzylidene protecting group for a dithiol system which could be liberated with concomitant oxidation to the disulfide upon treatment of the thioacetal with peracid, followed by exposure to acid. Our synthetic analysis thus called for the *p*-methoxybenzylidene derivative **3** as a precursor to **2** (Scheme I).

The other critical reaction in this synthetic scheme was a stereospecific alkynylation reaction for the introduction of a suitably functionalized eight-carbon chain at the C-6 position of a bicyclic thioacetal system **4**. It was hoped that conversion of the hydroxyl functionality to a leaving group followed by a nucleophilic displacement reaction would be facilitated by the intermediacy of an episulfonium ion **5** to give **3**, with retention of configuration. If **5** is indeed an intermediate in this reaction, then two additional possibilities must be considered. Thus, attack could occur at C-5 rather than C-6, with formation of **7**. Additionally, the episulfonium ion could rearrange to the benzylic cation, which upon alkynylation would give **6**, with the driving force for such a rearrangement being the resonance stabilization afforded by the electron-donating aromatic system. Since no firm prediction could be made about the course of the reaction, we first investigated the chemistry of a simpler model system possessing a propyl side chain to establish the conditions and course of the alkynylation reaction before proceeding to the synthesis of the target molecule **2**.

Scheme II



[a] Allyllithium, ether, −78 °C, then warm to −30 °C for quench. [b] α-Chlorodiethyl ether, *N,N*-diethylaniline, methylene chloride, 22 °C. [c] Sodium in ethanol/ether/ammonia, −78 °C. [d] *p*-Toluenesulfonyl chloride, pyridine, 0 °C. [e] *p*-Toluenesulfonic acid, methanol, 22 °C. [f] H_2, 5% palladium on carbon, 1:3 ethyl acetate/ethanol. [g] Potassium thioacetate, dimethylformamide, 84 °C. [h] 4.6% methanolic HCl, 55 °C.

Chemistry of the Propyl Hydroxy Dithioacetal System. The synthesis of the dithiol precursor **8** to the hydroxy *p*-methoxybenzylidene thioacetal **9** began with the all-cis dibenzyl ether epoxide[9] **10** and followed the sequence of steps outlined in Scheme II. Opening of the epoxide was effected with allyllithium at −78 °C to afford the alcohol **11** in 99% yield. Protection of the secondary alcohol as the ethoxyethyl ether, followed by reductive cleavage of the benzyl groups with sodium in ethanol/ether/ammonia, provided the cis diol **12** in excellent yield. The choice of the ethoxyethyl ether was dictated by the observation that acetyl and benzoyl groups migrated to adjacent hydroxyl groups during debenzylation.

Tosylation of **12** was quantitatively achieved to afford **13**, which upon acid hydrolysis followed by hydrogenation (H_2, 5% Pd/C) provided the ditosylate alcohol **14**.

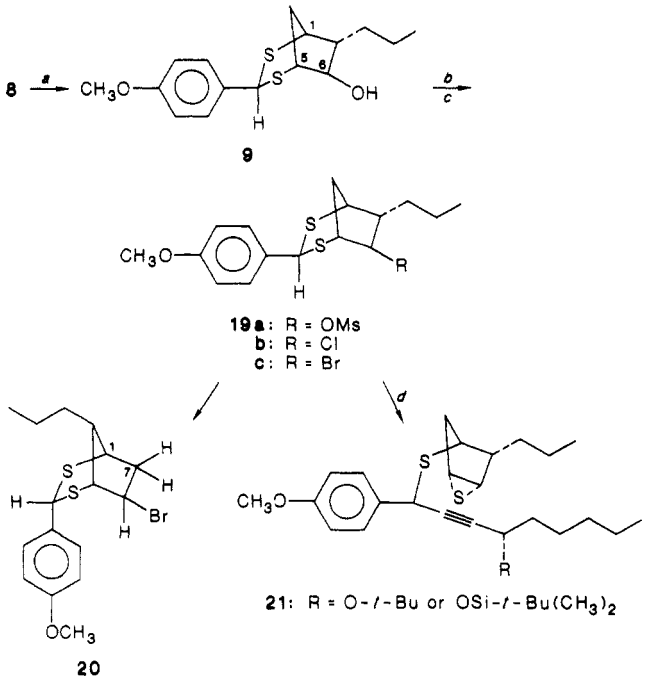
One might have thought that preservation of the allyl side chain would have provided a better system. Such an attempt was abandoned when it was discovered that re-

(14) (a) Barltrop, J.; Hayes, P. A.; Calvin, M. *J. Am. Chem. Soc.* **1954**, *76*, 4348. (b) Field, L.; Barbee, R. B. *J. Org. Chem.* **1969**, *34*, 36. (c) Foss, O. In *Organic Sulfur Compounds*; Kharasch, N., Ed.; Pergamon: London, 1961; Vol. 1, p 75. (d) Calvin, M.; Barltrop, J. A. *J. Am. Chem. Soc.* **1952**, *74*, 6153.

(15) Isenberg, N.; Herbrandson, H. F. *Tetrahedron* **1965**, *21*, 1067.

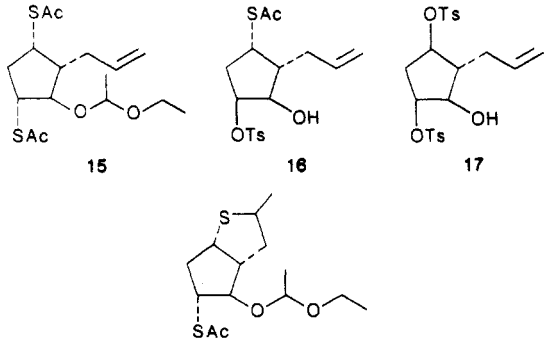
(16) (a) Fukuyama, T.; Kishi, Y. *J. Am. Chem. Soc.* **1976**, *98*, 6773. (b) Kishi, Y.; Nakatsuka, S.; Fukuyama, T.; Havel, M. *J. Am. Chem. Soc.* **1973**, *95*, 6493. (c) Nakatsuka, S.; Fukuyama, T.; Kishi, Y. *Tetrahedron Lett.* **1974**, 1549.

Scheme III



[a] p-Anisaldehyde, BF_3·OEt_2, chloroform, 22 °C. [b] (To give **19a**) methanesulfonyl chloride, triethylamine, dichloromethane, 0 °C. [c] (To give **19c**) lithium bromide dimethoxyethane on **19a**. [d] Alanate of (*S*)-3-hydroxy-1-octyne derivatives, ethyl chloride, 0 °C.

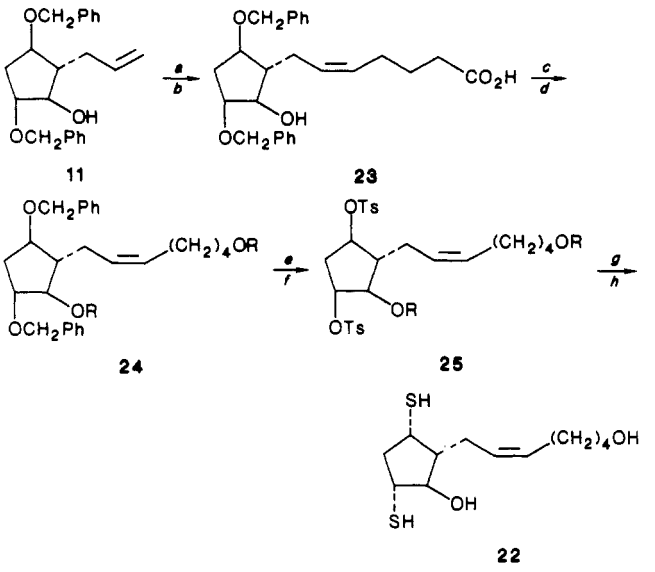
action of the ditosylate **13** with potassium thioacetate in DMF not only led to the desired dithioacetate **15** but also produced the monothioacetate **16**, the ditosylate alcohol **17**, and the tetrahydrothiophene derivative **18**. Fortunately, this cyclization side reaction turned out to be inconsequential in the synthesis of the disulfide **2**.



Nucleophilic displacement of the tosylate groups in **14** with potassium thioacetate at 84 °C led to the dithioacetate, which upon hydrolysis with methanolic HCl at 55 °C afforded the dithiol **8**. The dithiol proved to be extremely unstable and polymerized readily upon contact with air; hence, no purification was attempted.

Treatment of crude **8** with p-anisaldehyde and BF_3·OEt_2 furnished the model bicyclic thioacetal **9**, whose p-methoxybenzylidene group was assigned the thermodynamically stable exo or equatorial orientation. The ^1H NMR spectrum of **9** displayed striking similarities of proton–proton coupling to norbornane systems,[17] clearly indicating the trans relationship of the propyl and hydroxyl substituents, as well as their endo and exo orientations, respectively.

Scheme IV



[a] O_3, 1:1 methylene chloride/methanol, −78 °C, then dimethyl sulfide. [b] Dimsyl anion, (4-carboxybutyl)triphenylphosphonium bromide, 22 °C. [c] Lithium aluminum hydride, ether, 22 °C. [d] Chloromethyl methyl ether, diethylaniline, methylene chloride. [e] Sodium/liquid ammonia, ether, ethanol. [f] Tosyl chloride, pyridine, 0 °C. [g] Potassium thioacetate, dimethylformamide, 63 °C. [h] 4.8% methanolic HCl, 53 °C.

Analogous to norbornanes, the H-6 endo proton α to the hydroxyl group appeared at δ 4.47 (d, J = 5 Hz), coupled only to the H-7 exo proton.

Reaction of **9** with methanesulfonyl chloride and triethylamine afforded the mesylate **19a** instead of the expected chloride **19b** (Scheme III). However, the intermediacy of the episulfonium ion became evident when **19a** was reacted with lithium bromide in DME to furnish the bromide **19c** with retention of configuration. Upon standing, **19c** rearranged to the isomeric **20**, displaying the expected coupling pattern of H-6 endo (dd, $J_{6\text{-endo},7\text{-exo}}$ = 3 Hz, $J_{6\text{-endo},7\text{-endo}}$ = 8 Hz), H-7 endo (dd, J_{gem} = 15 Hz), and H-7 exo (ddd, $J_{7\text{-exo},1}$ = 8 Hz).

A variety of conditions was tried in order to achieve alkynylation at the C-6 position. A modification of the procedure[18] of Negishi and Baba using lithium tetraoctynylalanates proved successful. However, inspection of the ^1H NMR and mass spectra of the alkynylated product strongly suggested that alkynylation had proceeded with attack at the benzylic carbon to afford the episulfide **21**. While the benzylic proton absorption of **9** and its derivatives appeared at δ 5.30, the benzylic proton signal of **21** was shifted upfield to δ 4.60. The characteristic splitting patterns of the H-1 and H-5 bridgehead protons were also absent.

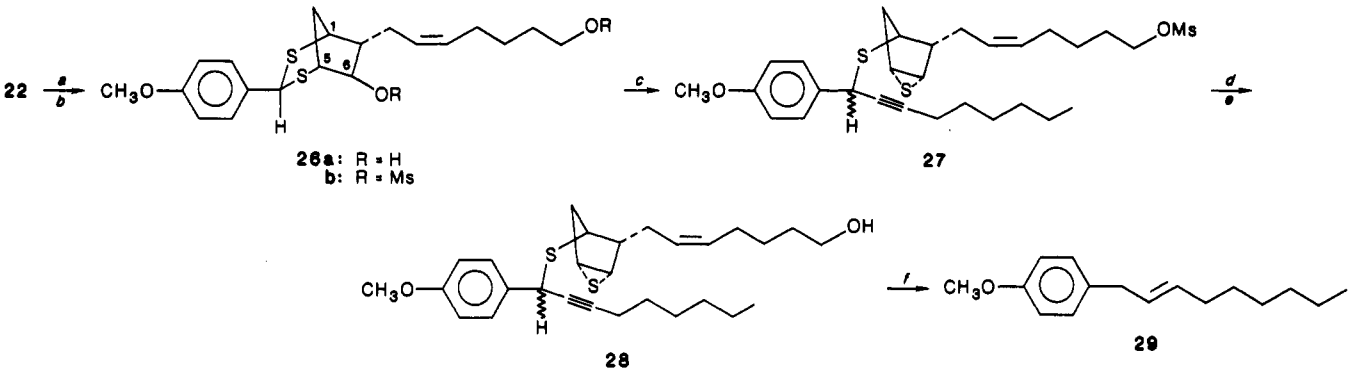
Considering the possibility that perhaps the use of the model system had led us astray, we decided to shift our attention to the dithioacetal system possessing the complete upper side chain, and we used a degradation approach to unambiguously establish the course of the alkynylation reaction. The synthesis of the dithiol precursor **22** is outlined in the sequence of steps in Scheme IV. Ozonolysis of the olefinic dibenzyl ether **11**, followed by reductive workup,[19] afforded the crude aldehyde, which was treated without purification with the ylid derived from (4-carboxybutyl)triphenylphosphonium bromide to yield

(17) Jackman, L. M.; Sternhill, S. *Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry*, 2nd ed.; Pergamon: London, 1969; p 289.

(18) Negishi, E.; Baba, S. *J. Am. Chem. Soc.* **1975**, *97*, 7385.

(19) Pappas, J. J.; Keaveney, W. P.; Gaucher, E.; Berger, M. *Tetrahedron Lett.* **1966**, 4273.

Scheme V



[a] *p*-Anisaldehyde, chloroform, BF_3·OEt_2, 22 °C. [b] Methanesulfonyl chloride, triethylamine, dichloromethane, 0 °C. [c] Alanate of 1-octyne, ethylene chloride, 0 °C. [d] Tetra-*n*-butylammonium formate, dimethylformamide, 60 °C. [e] Sodium bicarbonate, methanol, 22 °C. [f] Sodium, liquid ammonia.

the acid **23** in 75% yield. Reduction with lithium aluminum hydride furnished the diol in 92% yield, whose hydroxyl groups were then protected as the methoxymethyl ethers to give **24**. Reductive cleavage of the benzyl groups was achieved with sodium in ethanol/THF/ammonia to afford the diol in quantitative yield, which was then tosylated to give **25** in 91% isolated yield. Treatment of **25** with potassium thioacetate in degassed DMF produced the dithioacetate, which, upon hydrolysis in 4.8% methanolic HCl solution, afforded the dithiol diol **22**. A trace of EDTA was used in the reaction to inhibit dithiol oxidation.

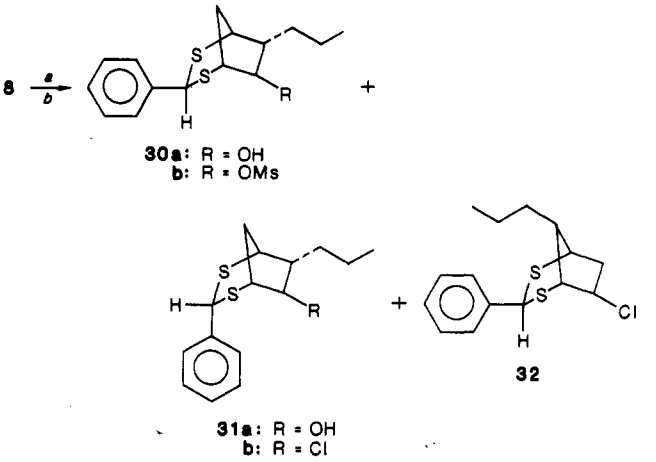
The air-sensitive dithiol diol **22** was used without purification in the BF_3·OEt_2-catalyzed thioacetalization reaction with *p*-anisaldehyde to afford the expected single epimer **26a** as an oil in 55% overall yield from the ditosylate **25** (Scheme V).

The observed lack of reactivity of primary mesylates toward alane-derived acetylenic nucleophiles[18] prompted conversion of the diol to the dimesylate **26b**, which proceeded in quantitative yield. Treatment with the lithium alanate of 1-octyne[20] resulted in the selective displacement of the secondary mesylate group, generating an alkynylated product **27** whose ^{1}H NMR characteristics closely resembled those of the product **21** in the propyl system. Conversion of the primary mesylate functionality into a hydroxyl group[21] was achieved in two steps by displacement with formate, followed by hydrolysis, to afford **28** in 37% yield from the diol **26a**.

Reduction with sodium in liquid ammonia failed to give *p*-methylanisole, ruling out any dithioacetalic product arising from attack at the C-5 or C-6 position. Instead, the olefin **29** was obtained in 75% yield and its structure proved by independent synthesis, providing firm chemical evidence of the site of attachment of the alkynyl side chain at the benzylic position.

Since the direction of attack was being dictated by the intermediacy of a strongly resonance-stabilized benzylic carbonium ion, irrespective of the nature of the upper side chain, we decided to return to the propyl model and modulate this resonance stabilization by using alternate benzylidene protecting groups. Perhaps attack would then occur at the desired C-6 position. The choice of the unsubstituted benzylidene protecting group seemed appropriate, since a phenyl substituent was not expected to stabilize a benzylic cation to the extent observed in the *p*-anisyl case; hence, rearrangement of an episulfonium ion to the benzylic cation would be less likely. Since it was anticipated that the benzylidene protecting group might present problems in the application of the Kishi method of disulfide formation, an alternate strategy of acetal cleavage and disulfide formation would have to be devised.

Interestingly, and in contrast to the previously described cases using the *p*-anisyl protecting group, two alcohols, **30a** and **31a**, epimeric at the benzylic position, were obtained in the BF_3·OEt_2-catalyzed reaction of the propyl dithiol **8** with benzaldehyde. Structure **30a** (obtained in 22% yield from ditosylate, **14**) was assigned to the exo isomer on the basis of the close similarity of its ^{1}H NMR spectrum to that of the *p*-anisyl analogue **9**. This isomer was very susceptible to oxidation to the *S*-4-sulfoxide, so the precaution of degassing solvents during its isolation was necessary. The endo isomer **31a**, in which the phenyl group is axial, was obtained in 16% yield and also displayed the coupling characteristics of norbornane systems in its ^{1}H NMR spectrum. A third product (22% yield) was deduced to be **32** on the basis of its mass spectrum and distinctive proton–proton coupling pattern.



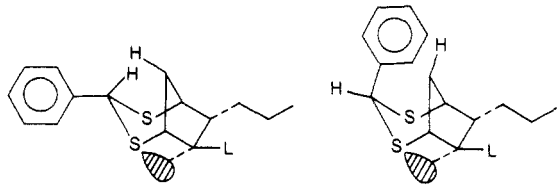
[a] Benzaldehyde, BF·OEt_2, chloroform, 23 °C. [b] Methanesulfonyl chloride, triethylamine, dichloromethane, 0 °C.

Analogous to the *p*-anisyl case, mesylation of the exo isomer **30a** gave rise to the mesylate **30b**. Under the same conditions, the endo isomer **31a** afforded the chloride **31b** exclusively, and longer reaction times led to partial rearrangement to **32**. The difference in behavior of these two isomeric alcohols in the mesylation reaction could be rationalized from inspection of molecular models for the

(20) While reaction of the dimesylate with the alanate derived from (*S*)-3-[(*tert*-butylsilyl)oxy]-1-octyne also furnished an alkynylated product in good yield, reductive cleavage with sodium in ammonia failed to give well-characterized products, presumably due to the presence of the propargylic alcohol functionality.

(21) Corey, E. J.; Terashima, S. *Tetrahedron Lett.* **1972**, 111.

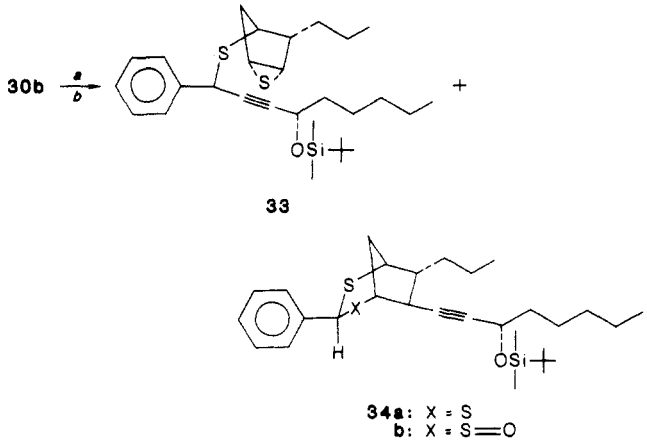
transition state requirements for formation of the episulfonium ion intermediate. Anchimeric assistance of sulfur is possible only when the bicyclic system adopts a conformation in which the six-membered ring is boatlike, permitting one of the sulfur lone pairs to lend assistance to the group L to leave. Participation of sulfur would therefore be expected to be quite facile for the endo isomer (hydrogen–hydrogen flagpole interaction), as opposed to the more destabilizing phenyl–hydrogen interaction in the exo case. The formation of the rearranged chloride **32** in



endo exo

the thioacetalization step could then be explained by the attack of residual HCl from the previous hydrolysis reaction on the endo alcohol **31a**.

We then investigated the behavior of **30b** and **31b** toward acetylenic nucleophiles. Reaction of the exo mesylate **30b** with an alanate derived from [3-(silyloxy)octynyl]-lithium and aluminum chloride gave rise to an inseparable mixture of products **33** and **34a**. Stirring with silica gel in oxygenated ethyl acetate effected selective oxidation of **34a** to its sulfoxide **34b**, thereby facilitating separation by preparative thin-layer chromatography of the episulfide **33** (58% from **24a**) as the predominant product and **34b** in 12–20% yield. The assignment of the sulfoxide structure as **34b** was based on the perturbing effect of the sulfoxide oxygen on the chemical shifts of the benzylic and H-5 protons, as well as the similarity of its ^{1}H NMR spectrum to that of the sulfoxide of **30a**.



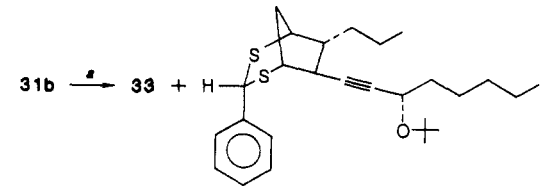
33

34a: X = S
b: X = S=O

[a] Alanate of (*S*)-3-[(*tert*-butyldimethylsilyl)oxy]-1-octyne, ethylene chloride, 0 °C. [b] Silica gel, oxygenated ethyl acetate, 23 °C.

Treatment of the endo chloride **31b** with the alanate did not result in any alkynylation. However, reaction with the alkynyl alane derived from dimethylaluminum chloride and the lithium acetylide of *tert*-butoxyoctyne[22] furnished **33** and the desired product **35** in 5% and 16% yields, respectively.

The chemistry of the *p*-nitrobenzylidene thioacetal system was also investigated, since the electron-withdrawing nature of the nitro group was expected to strongly destabilize a benzylic cation in the alkynylation reaction.



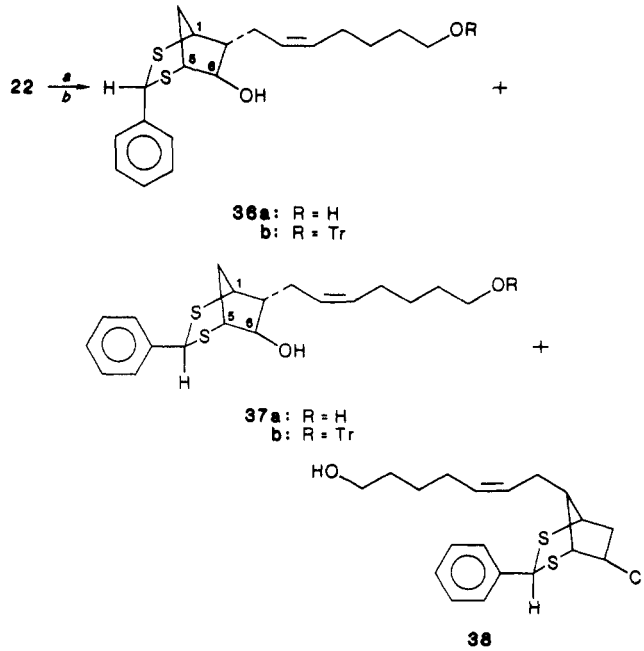
35

[a] (*S*)-(3-*tert*-Butoxy-1-octynyl)dimethylalane, toluene, 0 °C.

Furthermore, selective reduction of the nitro group would afford an aminobenzylidene dithioacetal, which could be utilized in the Kishi reaction. Just as in the benzylidene case, the exo and endo epimeric alcohols were obtained, which displayed the same pattern of reactivity in the mesylation reaction. However, when their chloride and mesylate derivatives were subjected to various alkynylating conditions, rapid abstraction of the benzylic proton occurred, and the deeply red-colored anion decomposed during the course of the reaction.

Once it was established that the benzylidene protecting group in the thioacetal model system was effective in directing partial attack to the C-6 position, attention was focused on the chemistry of the dithioacetal possessing the complete seven-carbon side chain.

Synthesis of 9,11-Dithia-13,14-dehydro-PGH$_2$ Methyl Ester. Treatment of the dithiol **22** with benzaldehyde in the presence of BF_3·OEt_2 produced an inseparable mixture of epimeric alcohol (**36a** and **37a**) in 30–37% yield from the ditosylate **25** and the rearranged chloride **38** in 5–10% yield. The ^{1}H NMR spectrum of the epimeric alcohol mixture indicated that the exo alcohol **37a** was the major product, a result analogous to that found in the model system.



36a: R = H
b: R = Tr

37a: R = H
b: R = Tr

38

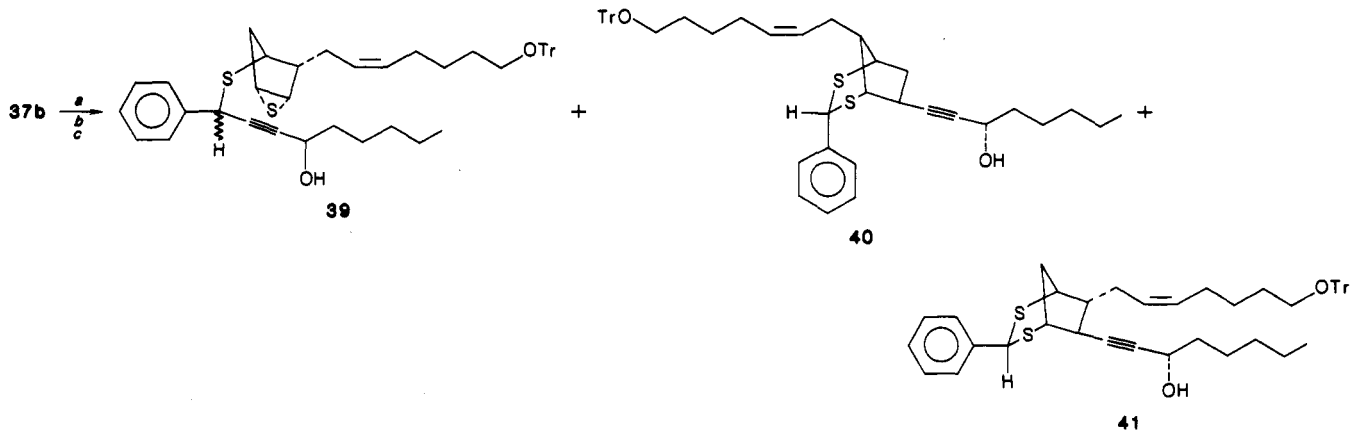
[a] Benzaldehyde, BF_3·OEt_2, chloroform, 23 °C. [b] Triphenylmethyl chloride, pyridine, 23 °C.

Selective tritylation of the primary hydroxyl groups of **36a** and **37a** proceeded uneventfully to afford the monotritylated derivatives **36b** and **37b** in 80–87% yield, which were now amenable to separation by preparative thin-layer chromatography.

It was of interest to ascertain whether the predominantly formed exo **37a** could be epimerized to the endo **36a**. According to the procedure of Eliel et al.[23] for converting

(22) Fried, J.; Sih, J. C.; Lin, C. H.; Dalven, P. *J. Am. Chem. Soc.* **1972**, *94*, 4343.

Scheme VI



[a] Methanesulfonyl chloride, triethylamine, dichloromethane, 0 °C. [b] (*S*)-3-[(*tert*-Butyldimethylsilyl)oxy]-1-octynyldimethylalanine, toluene, 0 °C. [c] Tetra-*n*-butylammonium fluoride, tetrahydrofuran, 0 °C.

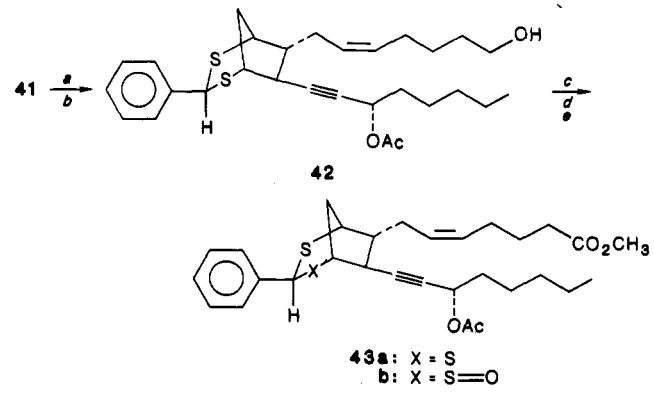
an equatorially 2-substituted anomeric dithiane to its axial epimer, **37a** was treated with *n*-butyllithium at −30 °C and then rapidly quenched with 0.1 N HCl to give **36b** in greater than 90% purity. The reverse isomerization was achieved when the acetate of **36b** was treated with 10% anisole in trifluoroacetic acid, followed by acetylation, to afford the acetate of **37b** in 50% yield. This demonstrated that the equatorial exo isomer is indeed the more stable compound.

As expected, treatment of endo **36b** with methanesulfonyl chloride and triethylamine provided the chloride in quantitative yield. However, we were disappointed to find that this compound was quite unreactive with various acetylenic nucleophiles, and longer reaction times only led to the formation of the rearranged chloride **38**.

The mesylate of exo **37b** (Scheme VI) reacted with (*S*)-dimethyl[3-(silyloxy)-1-octynyl]alane in toluene to give a mixture of products, which upon desilylation with tetra-*n*-butylammonium fluoride afforded the episulfide **39** (13% from **37b**), rearranged alcohol **40** (36%), and the desired compound **41** (37%).

From the foregoing, it was abundantly clear that the reactions of the bicyclic system with nucleophilic reagents could take a variety of courses. The two variables exerting a decisive influence on the reaction were the nature and stereochemistry of the aromatic group on the thioacetalic carbon and the nature of the nucleophile. While the results of the mesylation and reaction with bromine could be explained by the transition state conformations discussed earlier, more complex circumstances attended the alkynylation reaction. Here, assistance to bond-breaking by the Lewis acid character of the alane reagents blurred the difference in reactivity between the endo- and exo-substituted thioacetals. Thus, it appeared that the Lewis acid assisted breaking of a benzylic carbon sulfur bond or the bond between C-6 and the leaving group could lead to substitution at the benzylic center, at C-6, or by rearrangement at the C-5 position. However, the ratio of products could be influenced in favor of substitution at the C-6 position by varying the aromatic substituent at the thioacetalic center. Although substitution at the C-6 position was always exo, it did not provide compelling evidence of anchimeric assistance by sulfur, since endo attack was not favored per se and in addition was impeded by the eclipsing interaction with the propyl or seven-carbon side chain.

Scheme VII



[a] Acetic anhydride, pyridine, 23 °C. [b] 90% acetic acid in water, 23 °C. [c] Oxalyl chloride, dimethyl sulfoxide, dichloromethane, −70 °C, then triethylamine. [d] Pyridinium dichromate, dimethylformamide, 23 °C. [e] Diazomethane in 2:1 ether/methanol.

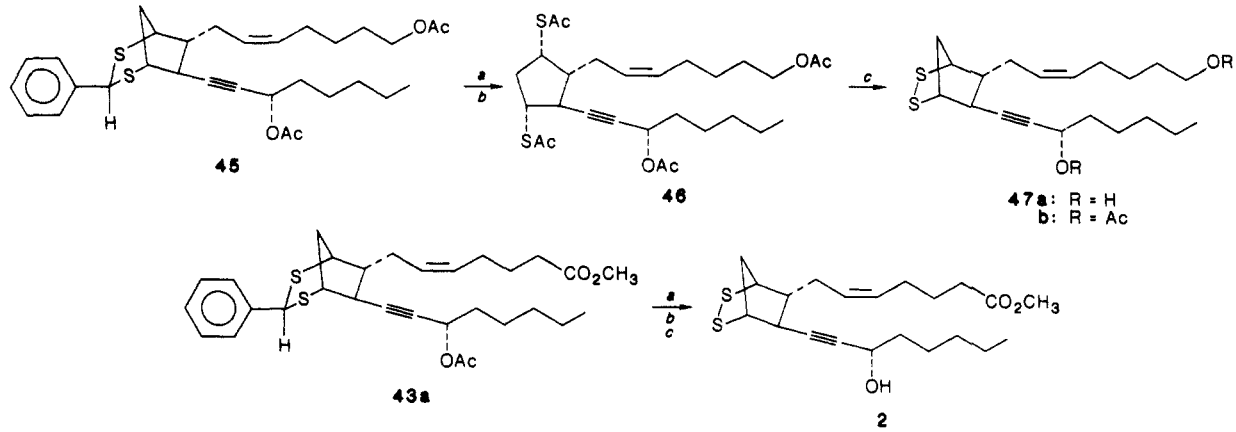
Conversion of the secondary hydroxyl group of **41** (Scheme VII) to its acetate, followed by detritylation with 90% acetic acid in water, provided the alcohol **42**. Selective oxidation of the terminal hydroxyl group with pyridinium dichromate[24] in DMF was slow, and prolonged reaction times led to decomposition. However, oxidation of the alcohol to the aldehyde by using the Swern method,[25] followed by pyridinium dichromate, afforded the acid, which was isolated as the methyl ester **43a** in 36% yield, along with 10% of its sulfoxide **43b**.

There remained the task of removing the benzylidene protecting group and the oxidation of the dithiol to the disulfide. From the work of Kishi and co-workers,[16] it was known that the presence of an electron-donating aromatic system at the thioacetalic center was essential for the acid-catalyzed decomposition of dithioacetal monosulfoxides to cyclic disulfides via a postulated resonance-stabilized carbonium ion. Hence, it seemed doubtful that a sulfoxide of our unsubstituted benzylidene thioacetal (e.g., **43b**) would undergo such an acid-catalyzed transformation. It appeared likely, however, that cyclic disulfide formation might be facilitated by weakening one of the carbon–sulfur bonds by attaching an electron-withdrawing substituent at the sulfoxide oxygen.[26] Model studies with the dithiane oxide **44** showed that while this compound was inert to

(23) (a) Eliel, E. L.; Hartman, A. A.; Abatjoglou, A. J. *J. Am. Chem. Soc.* **1974**, *96*, 1807. (b) Abatjoglou, A. J.; Eliel, E. L.; Kuyper, L. F. *J. Am. Chem. Soc.* **1977**, *99*, 8262.

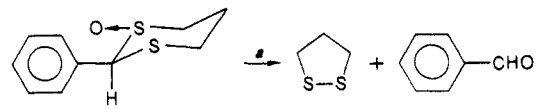
(24) Corey, E. J.; Schmidt, G. *Tetrahedron Lett.* **1979**, 399.
(25) Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651.
(26) For proposed mechanism of reaction, see: Zwanenberg, B.; Kielbasinski, P. *Tetrahedron* **1979**, *35*, 169.

Scheme VIII



[a] 1,3-Propanedithiol, BF_3·OEt_2, chloroform, 23 °C. [b] Acetic anhydride, pyridine, 23 °C. [c] Potassium carbonate, methanol, 23 °C.

various acids, treatment with trifluoroacetic anhydride or methanesulfonic anhydride at low temperature effected an extremely rapid cleavage to dithiolane and benzaldehyde.



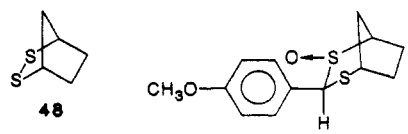
44

[a] Trifluoroacetic anhydride, chloroform, −50 °C.

However, under the same conditions, deoxygenation of the bicyclic thioacetal sulfoxide **43b** to **43a** took place. This unexpected result could only be explained if a redox reaction was invoked, in which the activated sulfoxide was being reduced by a divalent sulfur moiety.[27]

The failure of the above approach led us to explore a trans-acetalization reaction with 1,3-propanedithiol to generate the dithiol analogue of 13,14-dehydro-PGF_2, which could then be oxidized under the reported conditions to **2**. Reaction with excess 1,3-propanedithiol in the presence of BF_3·OEt_2 of the model diacetate **45** (Scheme VIII), followed by acetylation, provided the tetraacetate **46**. To our pleasant surprise, hydrolysis of the acetyl groups with potassium carbonate in methanol provided the dithiol diol, which spontaneously cyclized under the conditions of the workup to afford the disulfide diol **47a**. The diacetate derivative **47b** showed the diagnostic proton–proton coupling pattern of norbornane systems and displayed excellent agreement of the molecular ion peak in its high-resolution mass spectrum with its calculated molecular weight. Encouraged by the success in obtaining the model disulfide **47b**, the same conditions were applied to the methyl ester acetate **43a** to yield the target **2** in 20% overall yield, thus completing the synthesis.

The extremely facile formation of the disulfide **2** deserves some comment. In laying the groundwork for the above synthesis, model experiments were performed with the objective of preparing the bicyclic dithianorbornane nucleus **48** by reaction of the *p*-anisyl sulfoxide **49** with BF_3·OEt_2. These attempts led only to polymeric products.



48 49

In contrast, the monocyclic *p*-anisyl analogue of **44** cleanly yielded dithiolane under these conditions. The presence of the two bulky side chains in the prostaglandin case favors intramolecular rather than intermolecular disulfide formation in spite of the strain introduced in forming the bicylic system.

Experimental Section

Instrumentation and Materials. Infrared spectra were recorded on a Perkin-Elmer Model 283 spectrophotometer. Samples were run in solution cells at a concentration of ca. 1 mg/mL. Proton magnetic resonance (^{1}H NMR) spectra were obtained on solutions in deuteriochloroform containing chloroform (δ 7.26) as internal standard. Chemical shifts are reported in δ; coupling constants (J) are reported in hertz; and the abbreviations s, d, t, q, p, and m signify singlet, doublet, triplet, quartet, pentet, and multiplet, respectively. ^{1}H NMR spectra were recorded on a Bruker HX-270 (270 MHz) instrument or the University of Chicago DS 1000 (500 MHz) spectrometers operating in the pulsed Fourier transform mode. Free induction decay data were accumulated and processed with the Nicolet 1080 (at 270 MHz) or 1180 (at 500 MHz) Data Acquisition System. Low-resolution mass spectra were determined by using a Finnigan 1015 quadrupole mass spectrometer equipped with VPC, gas, and solid-phase inlets; the data were recorded and processed by a Systems Industries Computer Interface System/150 and plotted as bar graphs. High-resolution mass spectra were determined by using an AE1 Model MS-9 instrument or a Kratos MS-50 instrument interfaced with an Incos data system. Thin-layer chromatography was carried out by using 20 cm × 20 cm × 0.25 mm Merck silica gel analytical plates containing a fluorescent indicator. The eluting and extracting solvents were distilled and degassed with argon for 30 min. Melting points are uncorrected. Microanalyses were performed by Baron Consulting Co., Orange, CN.

(1*RS*,2*RS*,3*RS*,5*SR*)-3,5-Bis(phenylmethoxy)-2-(2-propenyl)-1-cyclopentanol (11). To 200 mL of dry ether cooled in dry ice was added 84 mL (1.07 M, 90 mmol) of an allyllithium solution. A solution of 8.85 g (29.9 mmol) of the epoxide **10** in 1100 mL of dry ether was then added over 35 min. The solution was magnetically stirred for 1.5 h at −78 °C and then warmed gradually over 2 h to −30 °C. The reaction was then quenched with 300 mL of saturated aqueous $(NH_4)_2SO_4$. The layers were separated, and the organic phase was washed with 200 mL of water, dried over Na_2SO_4, and concentrated to give 11.94 g of a crude oil. Successive recrystallizations gave 8.71 g (86.2%) of **11** as white needles, mp 34.5–36 °C. The remaining impure oil (ca 2 g) was chromatographed over 53 g of silica gel eluting with 10% and 14% ethyl acetate in hexane. The eluents were combined to give an additional 1.25 g (12.4%) of the alcohol **11** as a clear oil. The total yield of pure alcohol **11** was 98.6%. ^{1}H NMR: δ 7.23–7.4 (m, 10 H, aromatic), 5.76–5.93 (m, 1 H, C*H*=CH_2), 4.98–5.09 (m, 2 H, CH=CH_2), 4.48 and 4.56 (AB, J = 6, 2 H, benzylic), 4.34 and 4.72 (AB, J = 12, 2 H, benzylic), 3.80 (q, J = 6, 1 H, H-5α), 3.68 (br s, 1 H, H-1α), 3.55 (m, 1 H, H-3α), 3.38

(27) Tanikaga, R.; Nakayama, K.; Tanaka, K.; Koji, A. *Chem. Lett.* **1977**, 395.

(br s, 1 H, OH), 2.10–2.29 (m, 4 H, H-2β, H-4α, and CH_2CH=CH$_2$), 1.95 (dt, J_{gem} = 14, $J_{3\alpha,4\beta} = J_{4\beta,5\alpha}$ = 6, 1 H, H-4β). IR: 3600 (s), 995 (m), 905 (s), 735 (s), 690 (s). Mass spectrum: m/z 338 (M^+, 1%), 247 (M – $C_6H_5CH_2$, 31%), 91 (C_7H_7, 100%).

Anal. Calcd for $C_{22}H_{26}O_3$: C, 78.07; H, 7.74. Found: C, 78.33; H, 7.94.

(1*RS*,2*SR*,3*RS*,4*SR*)-3-(2-Propenyl)-1,2,4-cyclopentanetriol 2-*O*-Ethoxyethyl Ether (12). A solution of 8.22 g (24.3 mmol) of the alcohol **11** in 200 mL of CH_2Cl_2 was treated under N_2 with 6.4 mL (40.1 mmol) of *N,N*-diethylaniline and 3.9 mL (34.1 mmol) of α-chlorodiethyl ether for 22 h at 22 °C, at which point the reaction was complete as indicated by thin-layer chromatography (alcohol, R_f 0.14; ether, R_f 0.33; 3:7 ethyl acetate/hexane). The dark green solution was treated with 50 mL of saturated $NaHCO_3$, the layers were separated, and the aqueous phase was extracted with three 25-mL portions of CH_2Cl_2. The combined organic phases were dried over Na_2SO_4 and concentrated to give a green oil weighing 17 g. A solution of the oil in 600 mL of 1:1 ether/hexane containing 5 drops of pyridine was filtered through 25 g of silica gel. The trace of pyridine was essential to prevent partial hydrolysis of the acetal. The eluent was concentrated to give a yellow oil (16.6 g), which was taken up in 200 mL of hexane and washed quickly with three 50-mL portions of 10% HCl followed immediately by two 50-mL portions of saturated $NaHCO_3$. Two drops of pyridine were then added to the hexane solution, which was dried over Na_2SO_4 and concentrated to give the ethoxyethyl ether (mixture of diastereomers) as a yellow oil weighing 10.17 g (quantitative). An analytical sample was obtained by TLC (3:7 ether/hexane plus a trace of pyridine). ^{1}H NMR: δ 7.22–7.38 (m, 1 OH, aromatic), 5.73–5.94 (m, 1 H, CH=CH$_2$), 4.9–5.1 (m, 2 H, CH=CH_2), 4.77 (q, J = 5, 1 H, acetal), 4.4–4.68 (m, 4 H, benzylic), 3.79 (q, J = 5, 1 H, H-1α), 3.44–3.73 (m, 4 H, H-3α, H-5α, and CH_3CH_2O), 2–2.5 (m, 5 H, H-2β, H-4, and CH_2CH=CH$_2$), 1.33 (m, 3 H, CHCH_3), 1.16 (m, 3 H, CH_3CH_2O). IR: 995 (m), 910 (s), 735 (s), 700 (s). Mass spectrum: m/z 337 (M – $CH_3CH_2OCH(CH_3)$, 3%), 91 (C_7H_7, 100%), 73 ($CH_3CH_2OCH(CH_3)$, 38%), 45 (CH_3CH_2O, 36%).

Anal. Calcd for $C_{26}H_{34}O_4$: C, 76.06; H, 8.35. Found: C, 75.80; H, 8.59.

A solution of 3.91 g (9.52 mmol) of the above ethoxyethyl ether of **11** in 100 mL of dry ether and 3.5 mL (60 mmol) of absolute ethanol was cooled in a dry ice/acetone bath, and ca. 600 mL of NH_3 (dried over Na) was distilled into the solution. Na (1.39 g, 60 mmol) was added to the reaction mixture, and after 15 min, the solution turned completely blue. The solution was magnetically stirred for an additional 1 h at –78 °C and then quenched with 25 g of NH_4Cl. After evaporation of the NH_3, the residue was taken up in 600 mL of ether and 200 mL of water and the layers were separated. The aqueous phase was saturated with NaCl and extracted with three 200-mL portions of ether. The combined ether phases were dried over Na_2SO_4 and concentrated to give 2.32 g (quantitative) of the oily diol **12**. The diol was pure by ^{1}H NMR and hence was generally used in the following tosylation reaction without purification. An analytical sample was prepared by distillation, bp 105 °C (1 torr). Thin-layer chromatography separated the diastereomers, R_f 0.28 and 0.34 with ethyl acetate. ^{1}H NMR **12**: δ 5.78–6.0 (m, 1 H, CH=CH$_2$), 5.06–5.24 (m, 2 H, CH=CH_2), 4.67 and 4.81 (2 q, J = 5, each 0.5 H, acetal), 4.16 (m, 1 H, H-2α), 3.5–3.89 (m, 4 H, H-1α, H-4α, and CH_3CH_2), 2.7 (br s, 2 H, OH), 1.92–2.47 (m, 5 H, H-3β, H-5, and CH_2CH=CH$_2$), 1.4 (m, 3 H, CHCH_3), 1.23 (m, 3 H, CH_2CH_3). IR: 3400 (s). Mass spectrum: m/z 73 ($CH_3CH_2OCH(CH_3)$, 100%), 45 (CH_3CH_2O, 75%).

Anal. Calcd for $C_{12}H_{22}O_4$: C, 62.58; H, 9.63. Found: C, 62.32; H, 9.57.

(1*RS*,2*RS*,3*RS*,5*SR*)-3,5-Bis[(*p*-toluenesulfonyl)oxy]-2-(2-propenyl)-1-cyclopentyl Ethoxyethyl Ether (13). A solution of 2.19 g (9.52 mmol) of the crude oily diol **12** in 100 mL of dry pyridine was cooled under N_2 in an ice/water bath, and 9 g (47 mmol) of *p*-toluenesulfonyl chloride was added. The solution was stored at 0 °C for 5 days and poured into 500 mL of ice/water. The mixture was extracted with ether, and the ether extracts were washed with 10% HCl, saturated $NaHCO_3$, and brine, dried over Na_2SO_4, and concentrated to give the ditosylate **13** as a pink solid weighing 5.34 g (quantitative). Since the ditosylate was pure by ^{1}H NMR, it was used in subsequent reactions without further purification. An analytical sample was prepared by recrystallization from a mixture of CH_2Cl_2, ether, and hexane (1:15:15), mp 79–81 °C. ^{1}H NMR: δ 7.72–7.84 (m, 4 H, aromatic), 7.34 (d, J = 8, 4 H, aromatic), 5.47–5.63 (m, 1 H, CH=CH$_2$), 4.43–4.51 and 4.67–5.0 (m, 5 H, H-3α, H-5α, CH=CH_2, and acetal), 3.4–3.73 (m, 3 H, H-1α and CH_2CH_3), 2.47 (s, 7 H, H-4α and CH_3), 2.02–2.17 (m, 4 H, H-2β, H-4β, and CH_2CH=CH$_2$), 1.22–1.33 (m, 3 H, CHCH_3), 1.1–1.2 (m, 3 H, CH_2CH_3). IR: 1350 (s), 1185 (s), 1170 (s), 820 (s), 810 (s). Mass spectrum: m/z 383 (M – $CH_3C_6H_4SO_2$, 24%), 155 ($CH_3C_6H_4SO_2$, 25%), 91 (C_7H_7, 48%), 73 ($CH_3CH_2OCH(CH_3)$, 100%), 45 (42%), 44 (54%), 43 (65%).

Anal. Calcd for $C_{26}H_{34}O_8S_2$: C, 57.97; H, 6.36; S, 11.90. Found: C, 57.70; H, 6.15; S, 11.97.

(1*RS*,2*RS*,3*RS*,5*SR*)-2-Propyl-3,5-bis[(*p*-toluenesulfonyl)oxy]-1-cyclopentanol (14). A solution of 5.13 g (9.53 mmol) of the ethoxyethyl ether **13** in 150 mL of methanol was treated with 250 mg (ca. 0.01 N) of *p*-toluenesulfonic acid for 4 h at 22 °C, whereupon TLC showed the reaction to be complete. The solution was taken up in ether, washed with one-fourth-saturated $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated to give the unsaturated alcohol as a yellow oil (4.66 g, quantitative). It was used in subsequent reactions without further purification. For analysis it was crystallized from ether/hexane, mp 74.5–76 °C. ^{1}H NMR: δ 7.38 and 7.81 (AA'BB', J = 9, 4 H, aromatic), 7.35 and 7.75 (AA'BB', J = 9, 4 H, aromatic), 5.54 (m, 1 H, CH=CH$_2$), 4.9 (m, 2 H, CH=CH_2), 4.71 (q, J = 4, 1 H, H-5α), 4.40 (m, 1 H, H-3α), 3.65 (q, J = 4, 1 H, H-1α), 2.47 (s, 6 H, CH_3), 1.95–2.35 (m, 5 H, H-2β, H-4, and CH_2CH=CH$_2$). IR: 2600 (s), 1350 (s), 1185 (s), 1170 (s), 1090 (s), 820 (s). Mass spectrum: m/z 466 (M^+, 10%), 294 (M – $CH_3C_6H_4SO_3H$, 40%), 155 ($CH_3C_6H_4SO_2$, 50%), 122 (62%), 91 (C_7H_7, 100%), 80 (55%), 79 (44%), 65 (43%), 55 (35%), 41 (CH_2=CHCH_2, 46%).

Anal. Calcd for $C_{22}H_{30}O_7S_2$: C, 56.63; H, 5.62; S, 13.74. Found: C, 56.57; H, 5.78; S, 13.81.

A solution of 4.4 g (9.52 mmol) of the unsaturated alcohol in 150 mL of absolute ethanol plus 50 mL of ethyl acetate was hydrogenated with 0.25 g of 5% Pd/C at atmospheric pressure for 9 h at 22 °C. Removal of the catalyst and concentration gave the reduction product **14** as an oil. Crystallization from 8:1 ether/hexane yielded 4.108 g (92%) of the ditosylate as white crystals, mp 79–80.5 °C. ^{1}H NMR: δ 7.36 and 7.79 (AA'BB', J = 8, 4 H, aromatic), 7.33 and 7.74 (AA'BB', J = 8, 4 H, aromatic), 4.71 (q, J = 4.5, 1 H, H-5α), 4.39 (m, 1 H, H-3α), 3.61 (q, J = 4, 1 H, H-1α), 2.48 (s, 3 H, CH_3), 2.08–2.30 (m, 3 H, H-2β, H-4α, and OH), 2.03 (dt, J_{gem} = 15, $J_{3\alpha,4\beta} = J_{4\beta,5\alpha}$ = 4, 1 H, H-4β), 1.07–1.37 (m, 4 H, C$H_2CH_2CH_3$), 0.76 (t, J = 7, 3 H, CH_2CH_3). IR: 3560 (s), 1350 (s), 1190 (s), 1175 (s), 1090 (m), 815 (s). Mass spectrum: m/z 468 (M^+, 1%), 172 (37%), 155 ($CH_3C_6H_4SO_2$, 52%), 141 (66%), 124 (38%), 91 (C_7H_7, 100%), 65 (44%).

Anal. Calcd for $C_{22}H_{28}O_7S_2$: C, 56.39; H, 6.02; S, 13.69. Found: C, 56.25; H, 6.07; S, 13.42.

(1*RS*,2*RS*,3*SR*,5*RS*)-3,5-Dimercapto-2-propyl-1-cyclopentanol (8). A solution of 539.3 mg (4.72 mmol) of potassium thioacetate and 1.0206 g (2.18 mmol) of the ditosylate **14** in 20 mL of dimethylformamide under N_2 was placed in an 84 °C oil bath for 36 min. The cloudy yellow solution was cooled and taken up in 150 mL of ether, washed with water and brine, dried over Na_2SO_4, and concentrated to give the crude dithioacetate (0.57 g) as a yellow oil. Reextraction of the aqueous phases gave another 26.2 mg of crude product. The crude product was subjected to chromatography on silica gel, with 1:19 ethyl acetate/hexane and 1:9 ethyl acetate/hexane as the eluents. From the 1:9 elution was isolated 0.29 g of pure crystalline dithioacetate. Some impure product (0.1 g) was isolated from subsequent fractions and was purified by TLC to give an additional 0.06 g of product. The total yield of pure crystalline dithioacetate was 0.35 g (58%). An analytical sample, mp 58.5–60 °C, was prepared by recrystallization from 1:4 ether/hexane. ^{1}H NMR: δ 4.09 (m, 1 H, H-3β), 3.78 (dd, $J_{1\alpha,2\beta}$ = 8.5, $J_{1\alpha,5\beta}$ = 5.5, 1 H, H-1α), 3.64 dt, $J_{4\beta,5\beta}$ = 10.2, $J_{4\alpha,5\beta}$ = 5, 1 H, H-5β), 3.57 (br s, 1 H, OH), 2.81 (m, 1 H, H-4β), 2.15 (p, J = 6, 1 H, H-2β), 1.69 (dt, J_{gem} = 15, $J_{3\beta,4\alpha} = J_{4\alpha,5\beta}$ = 5, 1 H, H-4α), 1.28–1.61 (m, 4 H, C$H_2CH_2CH_3$), 0.90 (t, J = 6.5, 3 H, CH_2CH_3). IR: 3800 (m), 1690 (s), 1100 (s). Mass spectrum: m/z 276 (M^+, 1%), 233 (M – CH_3CO, 23%), 191 (26%), 173 (34%), 125 (41%), 124 (45%), 43 (CH_3CO, 100%).

Anal. Calcd for $C_{12}H_{20}O_3S_2$: C, 52.14; H, 7.29; S, 23.20. Found: C, 52.40; H, 7.09; S, 22.86.

A solution of 0.29 g (1.05 mmol) of the dithioacetate in 50 mL of 4.6% methanolic HCl (prepared by adding acetyl chloride to methanol) under N_2 was heated in a 55 °C oil bath for 4 h. The solution was concentrated to give the dithiol **8**, which was immediately converted to the dithioacetal **9** in the subsequent reaction. ^{1}H NMR: δ 3.77 (t, J = 7, 1 H, H-1α), 3.63 (p, J = 6, 1 H, H-5β), 2.94 (m, 2 H, H-3β and H-4β), 2.58 (br s, 1 H, OH), 1.28–3.0 (m, 8 H, H-2β, H-4α, $CH_2CH_2CH_3$, and SH), 0.99 (t, J = 6, 3 H, CH_2CH_3).

(1*SR*,3*SR*,5*RS*,6*RS*,7*RS*)-6-Hydroxy-3-(4-methoxyphenyl)-7-propyl-2,4-dithiabicyclo[3.2.1]octane (9). To a solution of 0.20 g (1 mmol) of the dithiol **8** in 50 mL of $CHCl_3$ under N_2 was added 6.8 mL (1.18 mmol) of a solution of 200 μL of *p*-anisaldehyde in 10 mL of $CHCl_3$ and 13.5 mL (1.32 mmol) of a solution of 0.3 mL of BF_3·OEt_2 in 25 mL of $CHCl_3$. After 2 h at 22 °C, the reaction was stopped by adding 30 mL of saturated $NaHCO_3$ and stirring overnight. After separation of the layers, the organic phase was washed with 50 mL of brine, dried over Na_2SO_4, and concentrated to give a yellow oil. Preparative TLC on 2-mm silica gel plates yielded 235.8 mg (74%) of the desired dithioacetal **9**. ^{1}H NMR: δ 6.83 and 7.43 (AA'BB', J = 9, 4 H, aromatic), 5.29 (s, 1 H, benzylic), 4.47 (d, $J_{6endo,7exo}$ = 5, 1 H, H-6endo), 3.25 (dd, $J_{1,8anti}$ = 3, $J_{1,7exo}$ = 6, 1 H, H-1), 3.01 (m, 1 H, H-5), 2.78 (br s, 1 H, OH), 2.39 (t, distorted 2 H, H-8), 2.18 (p, J = 6, 1 H, H-7exo), 1.80 (q, J = 7.5, 2 H, $CH_2CH_2CH_3$), 1.45 (m, 2 H, CH_2CH_3), 1.00 (t, J = 7, 3 H, and CH_2CH_3). IR: 3400 (s), 1250 (s), 1030 (s), 840 (s). Mass spectrum: m/z 310 (M^+, 36%), 153 (72%), 152 (65%), 151 (60%), 137 (15%), 121 ($CH_3OC_7H_6$, 100%). High-resolution mass spectrum, calcd for $C_{16}H_{22}O_2S_2$: 310.1059. Found: 310.1077.

(1*SR*,3*SR*,5*RS*,6*RS*,7*RS*)-6-[(Methanesulfonyl)oxy]-3-(4-methoxyphenyl)-7-propyl-2,4-dithiabicyclo[3.2.1]octane (19a). To a solution of 53.7 mg (0.53 mmol) of triethylamine in 1.75 mL of CH_2Cl_2 was added at 0 °C 54.4 mg (0.175 mmol) of the alcohol **9** under N_2. To this solution was added 44.6 mg (0.40 mmol) of methanesulfonyl chloride in 0.92 mL of CH_2Cl_2. After the solution was stirred for 30 min at 0 °C, it was taken up in 20 mL of brine, dried over Na_2SO_4, and concentrated to give the mesylate **19a** as a yellow oil weighing 75.4 mg (quantitative). ^{1}H NMR: δ 6.84 and 7.44 (AA'BB', J = 9, 4 H, aromatic), 5.34 (s, 1 H, benzylic), 5.28 (d, $J_{6endo,7exo}$ = 5, 1 H, H-6endo), 3.78 (s, 3 H, OCH_3), 3.39 (d, $J_{5,8anti}$ = 6, 1 H, H-5), 3.32 (t, $J_{1,7exo}$ = $J_{1,8anti}$ = 5.5, 1 H, H-1), 2.50 (m, 2 H, H-7exo and H-8syn), 2.38 (dt, J_{gem} = 13, 1 H, H-8anti), 1.90 (m, 2 H, $CH_2CH_2CH_3$), 1.43 (m, 2 H, CH_2CH_3), 1.02 (t, J = 7, 3 H, CH_2CH_3).

(1*SR*,3*SR*,5*RS*,6*RS*,7*SR*)-6-Bromo-3-(4-methoxyphenyl)-7-propyl-2,4-dithiabicyclo[3.2.1]octane (19c) and (1*RS*,3*RS*,5*RS*,6*RS*,8*RS*)-6-Bromo-3-(4-methoxyphenyl)-8-propyl-2,4-dithiabicyclo[3.2.1]octane (20). A solution of 12.8 mg (0.027 mmol) of the mesylate **19a** and 24 mg (0.28 mmol) of LiBr in 0.75 mL of dimethoxyethane under N_2 was placed in an oil bath at 62 °C for 30 min, whereupon 1.5 mL of saturated $NaHCO_3$ was added. The solution was taken up in 20 mL of ethyl acetate, washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated to give 7.5 mg (60%) of the bromide **19c**. A ^{1}H NMR spectrum indicated that the product was pure. Upon standing in chloroform-*d* for 5 days at −20 °C, the pure bromide was partially converted to the rearranged bromide **20** (20%). By comparison of the ^{1}H NMR spectrum of this mixture with the spectrum of the unrearranged bromide **19c**, most of the proton absorptions of the rearranged bromide **20** could be assigned. ^{1}H NMR **19c**: δ 6.85 and 7.43 (AA'BB', J = 8, 4 H, aromatic), 5.38 (s, 1 H, benzylic), 4.50 (d, $J_{6endo,7exo}$ = 6, 1 H, H-6endo), 3.79 (s, 3 H, OCH_3), 3.53 (d, $J_{5,8anti}$ = 6, 1 H, H-5), 3.23 (t, $J_{1,7exo}$ = 6, 1 H, H-1), 2.83 (p, J = 7, 1 H, H-7exo), 2.55 (m, 2 H, H-8), 1.87 (m, 2 H, $CH_2CH_2CH_3$), 1.5 (m, 2 H, CH_2CH_3), 1.01 (t, J = 7, 3 H, CH_2CH_3). Mass spectrum: m/z 374 (M^+ + 2, 3%), 372 (M^+, 3%), 293 (25%), 285 (23%), 153 (28%), 152 (33%), 151 (40%), 121 ($CH_3C_7H_6$, 100%). ^{1}H NMR **20**: δ 6.85 and 7.45 (AA'BB', J = 8, 4 H, aromatic), 5.44 (s, 1 H, benzylic), 5.10 (dd, $J_{6endo,7exo}$ = 3, $J_{6endo,7endo}$ = 8, 1 H, H-6endo), 3.79 (s, 3 H, OCH_3), 3.33 (m, 2 H, H-1 and H-5), 3.24 (dd, J_{gem} = 15, 1 H, H-7endo), 3.00 (ddd, $J_{1,7exo}$ = 8, 1 H, H-7exo), 1.06 (t, J = 7, 3 H, CH_2CH_3).

(1*RS*,3*SR*,4*SR*,5*SR*)-5-[4-[(*tert*-Butyldimethylsilyl)oxy]-1-(4-methoxyphenyl)non-2-ynylthio]-4-propyl-2-thiabicyclo[3.1.0]hexane (21). To a solution of 450 μL (378.5 mg, 1.57 mmol) of (*S*)-3-[(*tert*-butyldimethylsilyl)oxy]-1-octyne in 2.5 mL of hexane was added under N_2 at 0 °C 0.91 mL (1.69 M, 1.54 mmol) of *n*-butyllithium. After 1 h, the solution was transferred quantitatively with 1 mL of hexane under N_2 to 55 mg of $AlCl_3$ (0.42 mmol), which was weighed out in a dry box, at 0 °C. After the mixture was stirred for 0.5 h, all the $AlCl_3$ had dissolved, resulting in a yellow solution. Volatiles were removed at 22 °C (1 torr), the resulting light brown oil was cooled in an ice/water bath, and 68.1 mg (0.175 mmol) of the mesylate **19a** was added in 3 mL of dry 1,2-dichloroethane. The reaction was allowed to proceed for 50 min. The solution was taken up in 30 mL of hexane, washed with two 20-mL portions of 10% HCl followed by 20 mL of saturated $NaHCO_3$, dried over Na_2SO_4, and concentrated in vacuo. Preparative thin-layer chromatography of the crude product (152.5 mg) eluting with 0.5% pyridine in 1:9 ethyl acetate/hexane afforded 52.5 mg of the acetylene **21** as a 6:4 mixture of two diastereomers. Rechromatography gave 21.2 mg of pure acetylene **21** (23%). ^{1}H NMR: δ 6.83 and 7.36 (AA'BB', J = 8, 4 H, aromatic), 4.61 (s, 0.4 H, benzylic), 4.58 (s, 0.6 H, benzylic), 4.45 (m, 1 H, CHOSi), 3.79 (s, 3 H, OCH_3), 3.14 (m, 3 H, H-1, H-3, and H-5exo), 1.2–1.65 (m, 15 H), 0.95 (m, 15 H, CH_3), 0.11 (s, 6 H, $SiCH_3$). IR: 1250 (s). Mass spectrum: m/z 532 (M^+, 3%), 359 (benzylic fragment, 2%), 173 (thiyl fragment, 100%), 121 ($CH_3OC_7H_6$, 25%), 75 (65%), 73 (100%).

Anal. Calcd for $C_{30}H_{48}O_2S_2Si$: C, 67.61; H, 9.08; S, 12.03; Si, 5.27. Found: C, 67.34; H, 8.89; S, 11.79; Si, 5.01.

(*Z*)-(1*RS*,2*SR*,3*RS*,5*SR*)-2-(5-Carboxy-2-hexenyl)-3,5-bis(phenylmethoxy)-1-cyclopentanol (23). A solution of 222.1 mg (0.66 mmol) of olefin **11** in 5 mL of CH_2Cl_2 and 5 mL of methanol was ozonized at −78 °C and then 1 mL of dimethyl sulfide was added. After 30 min, the solution was warmed to −20 °C for 1 h with stirring, which was continued at 0 °C for 1 h and at 22 °C for 1 h under a stream of N_2 to leave a residue, which was taken up in 30 mL of CH_2Cl_2, washed with 20 mL of water and 30 mL of brine, dried over Na_2SO_4, and concentrated to give the aldehyde as a yellow oil weighing 239.4 mg (quantitative). Preparative thin-layer chromatography was performed only for analysis; otherwise, the crude product was used directly in the subsequent Wittig reaction. ^{1}H NMR: δ 9.75 (t, J = 2, 1 H, CHO), 7.23–7.42 (m, 10 H, aromatic), 4.39 and 4.67 (AB, J = 11, 2 H, benzylic), 4.51 (t, J = 10.5, 2 H, benzylic), 3.85 (m, 1 H, H-5α), 3.49–3.67 (m, 2 H, H-3α and H-1α), 2.79 (d, J = 9, 1 H, OH), 2.4–2.66 (m, 2 H, CH_2CHO), 2.21 (m, 1 H, H-4α), 1.90 (ddd, J_{gem} = 14, $J_{3\alpha,4\beta}$ = 6, $J_{4\beta,5\alpha}$ = 3, 1 H, H-4β). IR: 3450 (s), 1725 (s). Mass spectrum: m/z 249 (M − C_7H_7, 1%), 143 (22%), 125 (17%), 107 (18%), 92 (33%), 91 (C_7H_7, 100%).

Anal. Calcd for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11. Found: C, 74.00; H, 6.96.

A 50% dispersion of 623.4 mg of NaH was washed under N_2 with hexane and thoroughly dried. Freshly distilled dimethyl sulfoxide (10 mL) was added and the flask heated in a 75 °C oil bath for 50 min. To a solution of 1.9545 g (4.4 mmol) of (4-carboxybutyl)triphenylphosphonium bromide in 11 mL of dimethyl sulfoxide was then added 5.93 mL (7.7 mmol) of the dimsyl sodium solution. After 5 min, a solution of 354 mg (1.04 mmol) of the aldehyde in 11 mL of Me_2SO was introduced. After 1.5 h at 22 °C, the reaction was quenched with 50 mL of 10% HCl and the mixture extracted with two 30-mL portions of ether. The organic layer was washed with 10% HCl and three 30-mL portions of saturated Na_2CO_3. The combined carbonate washes were acidified with concentrated HCl and then extracted with two 30-mL portions of ether. The ether extracts were combined, washed with 30 mL of 10% HCl followed by 30 mL of brine containing a trace of HCl, dried over Na_2SO_4, and concentrated to give the acid **23** as a yellow oil weighing 475.6 mg (quantitative). The product was generally used in the next reaction in this crude form. For characterization, preparative thin-layer chromatography was performed, eluting with 20:20:1 ethyl acetate/hexane/acetic acid, R_f 0.35. ^{1}H NMR: δ 7.22–7.40 (m, 10 H, aromatic), 5.34–5.56 (m, 2 H, CH=CH), 4.42 and 4.62 (AB, J = 12, 2 H, benzylic), 4.52 (q, J = 6, 2 H, benzylic), 3.80 (q, $J_{4\alpha,5\alpha}$ = $J_{4\beta,5\alpha}$ = $J_{1\alpha,5\alpha}$ = 5.5, 1 H, H-5α), 3.67 (t, $J_{1\alpha,2\beta}$ = 5, 1 H, H-1α), 3.53 (q, J = 5, 1 H, H-3α), 2.30 (t, J = 7.5, 2 H, CH_2CO_2H), 2.0–2.26 (m, 6 H, H-2β, H-4α, and CH_2CH=$CHCH_2$), 1.94 (dt, J_{gem} = 14, $J_{3\alpha,4\beta}$ = 5, 1 H, H-4β),

1.65 (p, J = 7.5, 2 H, CH_2CH$_2$CO$_2$H). IR: 3200 (s), 1725 (s). Mass spectrum: m/z 91 (C_7H_7, 100%).

(*Z*)-(1*SR*,2*RS*,3*SR*,4*RS*)-1,4-Bis(phenylmethoxy)-2-(2-oxapropyloxy)-3-(8,10-dioxa-2-undecenyl)cyclopentane (24). A solution of 411 mg (0.968 mmol) of the crude acid **23** in 25 mL of dry ether under N_2 was treated at 0 °C with 106.9 mg (2.8 mmol) of lithium aluminum hydride and allowed to remain for 18 h at 22 °C. The reaction was quenched with sodium sulfate decahydrate. The mixture was filtered and the filtrate concentrated to give the diol as a clear oil weighing 162.4 mg. The filter cake was treated with concentrated HCl and extracted with ether, and the ether extract was washed with 10% HCl and brine, dried over Na_2SO_4, and concentrated to give additional diol weighing 126.3 mg. The total yield of product was 288 mg (68%). The crude diol was used in the subsequent reaction without further purification. For analysis, preparative thin-layer chromatography was performed. ^{1}H NMR: δ 7.23–7.39 (m, 10 H, aromatic), 5.44 (m, 2 H, CH=CH), 4.43 and 4.62 (AB, J = 12, 2 H, benzylic), 4.50 and 4.54 (AB, J = 9, 2 H, benzylic), 3.81 (q, J = 5, 1 H, H-5α), 3.66 (t, J = 5, 1 H, H-1α), 3.57 (t, J = 6, 3 H, H-3α and CH_2OH), 1.91–2.28 (m, 7 H, H-2β, H-4α, and CHCH=CHCH_2), 1.94 (dt, J_{gem} = 14, $J_{3\alpha,4\beta}$ = $J_{4\beta,5\alpha}$ = 5, 1 H, H-4β), 1.53 (p, J = 6.5, 2 H, CH_2CH$_2$OH), 1.38 (p, J = 6.5, 2 H, CH_2CH$_2$CH$_2$OH). IR: 3400 (s). Mass spectrum: m/z 91 (C_7H_7, 100%).

Anal. Calcd for $C_{26}H_{34}O_4$: C, 76.06; H, 8.35. Found: C, 75.70; H, 8.19.

A solution of 352 mg (0.858 mmol) of the diol in 6 mL of CH_2Cl_2 under N_2 was treated with 0.98 mL (6.14 mmol) of diethylaniline and 0.43 mL (5.66 mmol) of chloromethyl methyl ether for 24 h at 22 °C. Thin-layer chromatography indicated some monoprotected intermediate present, R_f 0.09 in 2:8 ethyl acetate/hexane. The R_f of the bis ether was 0.15. An additional 0.33 mL (2.07 mmol) of diethylaniline and 0.14 mL (1.84 mmol) of chloromethyl methyl ether were added. After 24 h, 10 mL of saturated $NaHCO_3$ was added, and the mixture was stirred for 0.5 h, taken up in 40 mL of ether, washed with $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated to yield the bis methoxymethyl ether **24** as a clear oil weighing 430 mg (quantitative). The product was generally used in the subsequent reaction without purification. For characterization, preparative thin-layer chromatography was performed. ^{1}H NMR: δ 7.23–7.4 (m, 10 H, aromatic), 5.45 (t, J = 5, CH=CH), 4.4–4.72 (m, 8 H, OCH$_2$O and benzylic), 3.80 (q, J = 6, 1 H, H-1α), 3.65 (dd, $J_{2\alpha,3\beta}$ = 6.6, $J_{1\alpha,2\alpha}$ = 4.5, 1 H, H-2α), 3.53 (m, 1 H, H-3α), 3.51 (t, J = 6, 2 H, CH_2OCH$_2$OCH$_3$), 3.38 (s, 3 H, OCH$_3$), 3.34 (s, 3 H, OCH$_3$), 2.39 (p, J = 6, 1 H, H-3β), 2.0–2.33 (m, 6 H, H-5 and CH_2CH=CHCH_2), 1.59 (p, J = 7, 2 H, CH=CHCH$_2$CH$_2$CH_2), 1.42 (p, J = 7, 2 H, CH=CHCH$_2$CH_2). IR: 735 (s), 700 (s). Mass spectrum: m/z 421 (3%), 407 (M – $C_6H_5CH_2$, 1%), 91 (C_7H_7, 100%), 45 (CH_3OCH_2, 100%).

Anal. Calcd for $C_{30}H_{42}O_6$: C, 72.26; H, 8.49. Found: C, 72.52; H, 8.31.

(*Z*)-(1*SR*,2*RS*,3*RS*,4*RS*)-2-(2-Oxapropyloxy)-3-(8,10-dioxa-2-undecenyl)-1,4-bis[(*p*-toluenesulfonyl)oxy]cyclopentane (25). A solution of 420.6 mg (0.843 mmol) of the dibenzyl ether **24** in 10 mL of dry THF under N_2 was cooled in a dry ice/acetone bath and 0.3 mL (5.14 mmol) of ethanol added. Approximately 50 mg of ammonia, dried over Na, was distilled into the solution, and 120.9 mg (5.26 mmol) of Na was added in portions. The solution turned blue and then faded, so an additional 30 mg of Na was added. After 1.5 h, the reaction was quenched with 4 g of NH_4Cl and ammonia was allowed to evaporate overnight. The residue was taken up in 25 mL of ether and 25 mL of water. The layers were separated, and the aqueous phase was saturated with NaCl and then extracted with two 25-mL portions of ether. The combined ether layers were dried over Na_2SO_4 and concentrated to yield the diol as a clear oil weighing 266.7 mg (99%). This crude product was used in the subsequent tosylation reaction without further purification. For characterization, preparative thin-layer chromatography was performed. ^{1}H NMR: δ 5.49 (m, 2 H, CH=CH), 4.71 (q, J = 6, 2 H, OCH$_2$O), 4.62 (s, 2 H, OCH$_2$O), 4.18 (m, 1 H, H-1α), 3.82 (m, 1 H, H-4α), 3.54 (m, 3 H, H-2α and CH_2OCH$_2$OCH$_3$), 3.43 (s, 3 H, OCH$_3$), 3.37 (s, 3 H, OCH$_3$), 3.27 (br s, 2 H, OH), 1.89–2.37 (m, 6 H, H-5 and CH_2CH=CHCH_2), 1.61 (m, 2 H, CH=CHCH$_2$CH$_2$CH_2), 1.45 (m, 2 H, CH=CHCH$_2$CH_2). IR: 3450 (s). Mass spectrum: m/z 45 (CH_3OCH_2, 100%).

Anal. Calcd for $C_{16}H_{30}O_6$: C, 60.35; H, 9.50. Found: C, 60.59; H, 9.24.

A solution of 209.3 mg (0.657 mmol) of the above diol in 6 mL of dry pyridine under N_2 was treated at 0 °C with 0.74 g (3.88 mmol) of *p*-toluenesulfonyl chloride for 4 days at 0 °C, whereupon 1 mL of cold water was added and the solution stirred for 0.5 h. The solution was then transferred quantitatively with 2 mL of pyridine to a separatory funnel containing 30 mL of ice/water and shaken for 0.5 h. Water was then added and the aqueous phase extracted with 50 mL of ether. The organic phase was washed with three 20-mL portions of 10% HCl, 20 mL of saturated $NaHCO_3$, and 20 mL of brine, dried over Na_2SO_4, and concentrated to a yellow oil weighing 393.6 mg. Column chromatography was performed over 15 g of silica gel eluting with 5:7 ethyl acetate/hexane plus one drop of pyridine per 125 mL of eluent. A total of 373.9 mg (91%) of the ditosylate **25** was obtained as a clear oil. ^{1}H NMR: δ 7.39 and 7.78 (AA′BB′, J = 8, 4 H, aromatic), 5.35 (m, 1 H, CH=CHCH$_2$CH$_2$), 5.14 (m, 1 H, CH=CHCH$_2$CH$_2$), 4.84 (q, J = 4, 1 H, H-1α), 4.62 (s, 2 H, OCH$_2$O), 4.51 (AB, J = 7, 2 H, OCH$_2$O), 4.45 (m, 1 H, H-4α), 3.58 (dd, $J_{1\alpha,2\alpha}$ = 4, $J_{2\alpha,3\beta}$ = 9, 1 H, H-2α), 3.51 (t, J = 6.5, 2 H, CH_2OCH$_2$OCH$_3$), 3.36 (s, 3 H, OCH$_3$), 3.34 (s, 3 H, OCH$_3$), 2.46 (s, 6 H, CH$_3$), 1.91–2.26 (m, 7 H, H-3β, H-5, and CH_2CH=CHCH_2), 1.56 (m, 2 H, CH=CHCH$_2$CH$_2$CH_2), 1.38 (m, 3 H, CH=CHCH$_2$CH_2). IR: 1350 (s). Mass spectrum: m/z 91 (C_7H_7, 18%), 75 (59%), 45 (CH_3OCH_2, 100%).

Anal. Calcd for $C_{30}H_{42}O_{10}S_2$: C, 57.49; H, 6.75; S, 10.23. Found: C, 57.23; H, 6.66; S, 10.46.

(*Z*)-(1*RS*,2*RS*,3*RS*,4*SR*)-2-Hydroxy-3-(7-hydroxy-2-heptenyl)cyclopentane-1,4-dithiol (22). A solution of 43.8 mg (0.69 mmol) of the ditosylate **25** and 388 mg (3.4 mmol) of potassium thioacetate in 4.9 mL of freshly distilled and degassed dimethylformamide was heated in a 64 °C oil bath for 2.5 h. The resulting dark brown solution was taken up in 50 mL of ether and washed with 50 mL of water. The aqueous phase was extracted with two 30-mL portions of ether, and the ether layers were combined, dried over Na_2SO_4, and concentrated to give the dithioacetate as a brown oil (302 mg, quantitative yield). The compound was used directly for the subsequent hydrolysis reaction. ^{1}H NMR: δ 5.44 (m, 1 H, CH=CHCH$_2$CH$_2$), 5.33 (m, 1 H, CH=CHCH$_2$CH$_2$), 4.59 and 4.73 (AB, J = 7, 2 H, OCH$_2$O), 4.63 (s, 2 H, OCH$_2$O), 4.11 (q, J = 6.5, 1 H, H-4β), 3.81 (m, 2 H, H-1β and H-2β), 3.53 (t, J = 6.5, 2 H, CH_2OCH$_2$OCH$_3$), 3.38 (s, 6 H, OCH$_3$), 2.83 (dt, $J_{4\beta,5\beta}$ = $J_{1\beta,5\beta}$ = 6.5, J_{gem} = 13, 1 H, H-5β), 2.36 (s, 3 H, SCOCH$_3$), 2.35 (s, 3 H, SCOCH$_3$), 2.26 (m, 1 H, H-3β), 2.01–2.16 (m, 4 H, CH_2CH=CHCH_2), 1.70 (m, 1 H, H-5α), 1.62 (p, J = 6.5, 2 H, CH=CHCH$_2$CH$_2$CH_2), 1.44 (p, J = 6.5, 2 H, CH=CHCH$_2$CH_2). IR: 1690 (s). Mass spectrum: m/z 391 (M – CH$_3$CO, 1%), 359 (M – CH$_3$COS, 1%), 45 (CH_3OCH_2, 100%), 43 (CH$_3$CO, 100%).

Anal. Calcd for $C_{20}H_{34}O_6S_2$: C, 55.27; H, 7.89; S, 14.75. Found: C, 55.44; H, 7.86; S, 14.39.

A solution of 302 mg (0.69 mmol) of the above dithioacetate and 5 mg of EDTA in 30 mL of 4.8% methanolic HCl under N_2 was heated in an oil bath at 53 °C for 4 h. The solution was concentrated to yield the unpleasantly smelling dithiol **22**, which was used immediately in the subsequent reaction without characterization.

(*Z*)-(1*SR*,3*SR*,5*RS*,6*RS*,7*SR*)-6-Hydroxy-7-(7-hydroxy-2-heptenyl)-3-(4-methoxyphenyl)-2,4-dithiabicyclo[3.2.1]octane (26a). A solution of 182.1 mg (0.69 mmol) of the crude dithiol **22** in 28 mL of chloroform under N_2 was treated with 104.7 mg (0.77 mmol) of *p*-anisaldehyde in 4.7 mL of $CHCl_3$ for 1.5 h at 22 °C, whereupon 25 mL of saturated $NaHCO_3$ was added. After 3 h of vigorous stirring, the layers were separated. The organic phase was washed with 30 mL of brine, dried over Na_2SO_4, and concentrated to a brown oil weighing 319 mg. The crude product was chromatographed over 10 g of silica gel eluting with 1:1 ethyl acetate/hexane with 0.5% pyridine. A total of 146 mg (55% from ditosylate **25**) of the desired dithioacetal **26a** was obtained as an oil. ^{1}H NMR: δ 6.85 and 7.43 (AA′BB′, J = 8.5, 4 H, aromatic), 5.52 (m, 2 H, CH=CH), 5.31 (s, 1 H, benzylic), 4.50 (d, $J_{6endo,7exo}$ = 8, 1 H, H-6endo), 3.79 (s, 3 H, OCH$_3$), 3.63 (t, J = 6, 2 H, CH_2OH), 3.27 (m, 1 H, H-1), 3.04 (m, 1 H, H-5), 2.69 (p, J = 6.5, 1 H, CHHCH=CHCH$_2$CH$_2$), 2.4 (m, 3 H, H-8 and CHHCH=CHCH$_2$CH$_2$), 2.21 (m, 3 H, H-7exo and CHHCH=CHCH_2CH$_2$),

1.59 (p, J = 6.5, 2 H, CH_2CH_2OH), 1.46 (p, J = 6.5, 2 H, $CH_2CH_2CH_2OH$). IR: 3400 (s), 1250 (s), 840 (s). Mass spectrum: m/z 380 (M^+, 23%), 347 (21%), 259 (43%), 153 (87%), 152 ($CH_3OC_6H_4CHS$, 35%), 151 (31%), 121 ($CH_3OC_7H_6$, 100%).

Anal. Calcd for $C_{20}H_{28}O_3S_2$: C, 63.12; H, 7.42; S, 16.85. Found: C, 62.85; H, 7.22; S, 16.51.

(*Z*)-(1*SR*,3*SR*,5*RS*,6*RS*,7*SR*)-7-(7-Hydroxy-2-heptenyl)-6-[(methanesulfonyl)oxy]-3-(4-methoxyphenyl)-2,4-dithiabicyclo[3.2.1]octane (26b). The alcohol **26a** (13.3 mg, 0.031 mmol) was treated under N_2 with 21.2 mg (0.21 mmol) of triethylamine in 0.69 mL of CH_2Cl_2 and 18.4 mg (0.16 mmol) of methanesulfonyl chloride in 0.38 mL of CH_2Cl_2 for 40 min at 0 °C. The solution was taken up in 20 mL of CH_2Cl_2, washed with 15 mL of water and then 15 mL of brine, dried over Na_2SO_4, and concentrated to yield the mesylate **26b** as a yellow oil weighing 18.6 mg (quantitative). ^1H NMR: δ 6.86 and 7.44 (AA'BB', J = 8.5, 4 H, aromatic), 5.46 (m, 2 H, CH=CH), 5.34 (s, 1 H, benzylic), 5.28 (d, $J_{6endo,7exo}$ = 5, 1 H, H-6endo), 4.05 (t, J = 7, 2 H, CH_2OAc), 3.80 (s, 3 H, OCH_3), 3.41 (d, $J_{5,8anti}$ = 6, 1 H, H-5), 3.36 (t, $J_{1,7exo}$ = $J_{1,8anti}$ = 5, 1 H, H-1), 3.16 (s, 3 H, SO_2CH_3), 2.13–2.84 (m, 7 H, H-7exo, H-8, and CH_2CH=$CHCH_2$), 2.06 (s, 3 H, $COCH_3$), 1.67 (p, J = 7, 2 H, CH_2CH_2OAc), 1.47 (p, J = 7, 2 H, $CH_2CH_2CH_2OAc$).

(*Z*)-(1*RS*,3*SR*,4*SR*,5*SR*)-4-[7-[(Methanesulfonyl)oxy]-2-heptenyl]-5-[1-(4-methoxyphenyl)non-2-ynylthio]-2-thiabicyclo[3.1.0]hexane (27). A solution of 255 μL (1.73 mmol) of 1-octyne in 3 mL of hexane was treated under N_2 at 0 °C with 1.6 mL (1.07 M, 1.7 mmol) of n-butyllithium for 1 h. The reaction mixture was warmed to 22 °C and transferred under N_2 with two 1.5-mL washes of hexane to 57.4 mg (0.43 mmol) of $AlCl_3$ held at 0 °C. The heterogeneous mixture was stirred for 1 h and then concentrated to a white solid. To this solid was added at 0 °C a solution of 72.8 mg (0.136 mmol) of the mesylate **26b** in 3.5 mL of ethylene dichloride under N_2. After 1 h, the solution was taken up in 25 mL of hexane, washed with 10% HCl and saturated $NaHCO_3$, dried over Na_2SO_4, and concentrated to give the alkyne **27** as an oil weighing 62.4 mg (84%). The crude product was used in the subsequent reaction without purification. Preparative thin-layer chromatography afforded a pure analytical sample. ^1H NMR (270 MHz): δ 6.82 and 7.36 (AA'BB', J = 8, 4 H, aromatic), 5.5 (m, 2 H, vinyl), 4.56 (s, 0.5 H, benzylic), 4.53 (s, 0.5 H, benzylic), 4.23 (m, 2 H, CH_2OMs), 3.80 (s, 3 H, OCH_3), 3.28 (m, 3 H, CHS), 3.00 (s, 3 H, CH_3SO_2), 1.0–2.9 (m). IR: 1350 (s), 1250 (s). Mass spectrum: m/z 321 (episulfide fragment, 1%), 229 (benzylic fragment, 2%), 135 (40%), 121 ($CH_3OC_7H_6$, 40%), 79 (100%), 43 (100%). High-resolution mass spectrum, calcd for benzylic fragment, $C_{16}H_{21}O$: 229.1592. Found: 229.1599. Calcd for episulfide fragment, $C_{13}H_{21}O_3S_3$: 321.0651. Found: 321.0667.

(*Z*)-(1*RS*,3*SR*,4*SR*,5*SR*)-4-(7-Hydroxy-2-heptenyl)-5-[1-(4-methoxyphenyl)non-2-ynylthio]-2-thiabicyclo[3.1.0]hexane (28). To 62.4 mg (0.113 mmol) of the crude mesylate **27** in 2 mL of dimethylformamide was added ca. 30 mg of tetra-n-butylammonium formate under N_2. The resulting solution was heated for 2 h at 60 °C, taken up in 25 mL of ether, washed with three 20-mL portions of water and 15 mL of brine, dried over Na_2SO_4, and concentrated to give 60.1 mg of the formate (quantitative). The crude product was used in the next reaction without purification. ^1H NMR: δ 8.09 (s, 1 H, formate), 6.85 and 7.39 (AA'BB', J = 8, 4 H, aromatic), 5.5 (m, 2 H, vinyl), 4.58 (s, 0.5 H, benzylic), 4.55 (s, 0.5 H, benzylic), 4.20 (t, J = 6, 2 H, CH_2OCHO), 3.81 (s, 3 H, OCH_3), 3.3 (m, 3 H, CHS), 1.2–3.2 (m), 0.95 (t, J = 6, 3 H, CH_3). IR: 1730 (s), 1250 (s). Mass spectrum: m/z 271 (thiyl fragment, 10%), 229 (benzylic fragment, 2%), 135 (30%), 121 ($CH_3OC_7H_6$, 34%), 43 (100%). High-resolution mass spectrum, calcd for benzylic fragment, $C_{16}H_{21}O$: 229.1592. Found: 229.1611. Calcd for thiyl fragment, $C_{13}H_{19}O_2S_2$: 271.0825. Found: 271.0832.

A solution of 56.7 mg (0.113 mmol) of the above formate in 2 mL of methanol was treated under N_2 with 200 mg of $NaHCO_3$ for 45 min at 22 °C. The solution was then taken up in 20 mL of ether, washed with three portions of water and with brine, dried over Na_2SO_4, and concentrated to a yellow oil weighing 52.6 mg. Preparative thin-layer chromatography eluting with 1:1 ethyl acetate/hexane plus a trace of pyridine gave 19.6 mg (37%) of the alcohol **28** as a mixture of two isomers. ^1H NMR: 6.85 and 7.39 (AA'BB', J = 8, 4 H, aromatic), 5.5 (m, 2 H, vinyl), 4.58 (s, 0.5 H, benzylic), 4.56 (s, 0.5 H, benzylic), 3.81 (s, 3 H, OCH_3), 3.68 (m, 2 H, CH_2OH), 3.30 (m, 3 H, CHS), 1.2–2.8 (m), 0.93 (t, J = 6, 3 H, CH_3). IR: 3400 (s), 1250 (s). Mass spectrum: m/z 243 (thiyl fragment, 20%), 229 (benzylic fragment, 5%), 211 (20%), 176 (30%), 161 (100%), 121 ($CH_3OC_7H_6$, 55%). High-resolution mass spectrum, calcd for benzylic fragment, $C_{16}H_{21}O$: 229.1592. Found: 229.1589. Calcd for thiyl fragment, $C_{12}H_{19}OS_2$: 243.0876. Found: 243.0891.

Reduction of Alcohol 28 with Sodium in Ammonia to (*E*)-1-(4-Methoxyphenyl)-2-nonene (29). A solution of 10.8 mg (0.023 mmol) of alcohol **28** and 125 μL (2.14 mmol) of ethanol in 2 mL of ether was cooled in a dry ice/acetone bath, and 10 mL of ammonia, which had been dried over Na, was distilled into the solution. After addition of Na (64 mg, 2.78 mmol) over 30 min the solution remained blue. The reaction was quenched with 0.5 g of NH_4Cl, and the ammonia evaporated under N_2 over 2 h. The residue was taken up in ether and water. The organic phase was dried over Na_2SO_4 and blown down under a stream of N_2. Approximately one-third of this crude product was subjected to preparative thin-layer chromatography eluting with 2:8 ethyl acetate/hexane to give 1.3 mg of the olefin **29**, R_f 0.5. The GC retention time of 6.1 min on a 1.5% OV 1 column was the same as that for the olefin prepared by an independent route. The mass and ^1H NMR spectra were also identical for the two preparations.

(*E*)-1-(4-Methoxyphenyl)-2-nonene (29). A solution of 0.3 mL (density 0.7497, 2.0 mmol) of 1-octyne in 10 mL of dry ether under N_2 was cooled in an ice/water bath and treated with 1.24 mL (1.57 M, 1.95 mmol) of n-butyllithium for 0.5 h, whereupon 0.243 mL (density, 1.119, 20 mmol) of p-methoxybenzaldehyde was added. The solution was allowed to warm to 22 °C and stirred for 2 h. The reaction was then quenched with 1 g of NH_4Cl and the solution taken up in ether. The ether solution was washed with two portions of water and with brine, dried over Na_2SO_4, and concentrated to yield the benzylic alcohol as a yellow oil weighing 459.5 mg (96%). This material was pure by ^1H NMR and was used in the subsequent reduction reaction without purification. For characterization, preparative thin-layer chromatography was performed. ^1H NMR: δ 6.88 and 7.46 (AA'BB', J = 8, 4 H, aromatic), 5.4 (s, 1 H, benzylic), 3.80 (s, 3 H, OCH_3), 2.27 (t, J = 7, 2 H, C≡CCH_2CH_2), 2.22 (br s, 1 H, OH), 1.54 (p, J = 7, 2 H, C≡CCH_2CH_2), 1.24–1.47 (m, 6 H, methylenes), 0.90 (t, J = 7, 3 H, CH_3). IR: 3400 (s), 1250 (s). Mass spectrum: m/z 246 (M^+, 1%), 244 (3%), 135 ($CH_3OC_6H_4CO$, 100%).

Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 77.99; H, 8.78.

A solution of 61.9 mg (0.25 mmol) of the above alcohol in 2 mL of dry ether was cooled under N_2 in a dry ice/acetone bath, and 125 μL (2.1 mmol) of ethanol and 10 mL of dry ammonia were added. This was followed by addition of 68 mg (3 mmol) of Na. After 0.5 h, the blue solution was quenched with 1 g of NH_4Cl and the ammonia allowed to evaporate. The residue was taken up in ether and water. The ether phase was washed with brine, dried over Na_2SO_4, and concentrated to a colorless oil weighing 54.7 mg (94%), whose ^1H NMR spectrum showed it to be the desired olefin **29**. Preparative thin-layer chromatography of the crude product gave 35.1 mg of purified olefin. ^1H NMR: δ 6.83 and 7.09 (AA'BB', J = 8, 4 H, aromatic), 5.50 (tt, J = 5 and 17, 2 H, CH=CH), 3.78 (s, 3 H, OCH_3), 3.27 (d, J = 5, 2 H, benzylic), 2.01 (q, J = 6, 2 H, CH=$CHCH_2$), 1.22–1.50 (m, 8 H, methylenes), 0.88 (t, J = 6, 3 H, CH_3). IR: 1250 (s), 960 (s). Mass spectrum: m/z 232 (M^+, 5%), 147 ($CH_3OC_6H_4CH_2CH$=CH, 100%), 121 ($CH_3OC_7H_6$, 85%). High-resolution mass spectrum, calcd for $C_{16}H_{24}O$: 232.1827. Found: 232.1821.

(1*SR*,3*SR*,5*RS*,6*RS*,7*RS*)-6-Hydroxy-3-phenyl-7-propyl-2,4-dithiabicyclo[3.2.1]octane (30a), (1*SR*,3*RS*,5*RS*,6*RS*,7*RS*)-6-Hydroxy-3-phenyl-7-propyl-2,4-dithiabicyclo[3.2.1]-octane (31a) and (1*RS*,3*SR*,5*RS*,6*RS*,8*RS*)-6-Chloro-3-phenyl-8-propyl-2,4-dithiabicyclo[3.2.1]octane (32). To a solution of 58.6 mg (0.551 mmol) of benzaldehyde and 84.9 mg (0.442 mmol, assuming quantitative conversion from ditosylate 14) of the dithiol 8 in 2.8 mL of $CHCl_3$ was added 2.2 mL (0.356 mmol) of a solution of 200 μL of BF_3·OEt_2 in 10 mL of $CHCl_3$ at 23 °C under N_2. The reaction was allowed to proceed for 1 h, and then the mixture was taken up in 20 mL of $CHCl_3$, washed with 20 mL of saturated $NaHCO_3$ and 20 mL of brine, dried over Na_2SO_4, and concentrated to an oil weighing 121.3 mg. Prepa-

rative thin-layer chromatography eluting with 40% ethyl acetate in hexane afforded 26 mg (21% from the ditosylate **14**) of the exo alcohol **30a**, R_f 0.51, 20.6 mg (16%) of the endo alcohol **31a**, R_f 0.45, and 27.9 mg (22.5%) of the rearranged chloride **32**, R_f 0.71. A noteworthy feature in the extraction process was the ease of oxidation of the exo alcohol **30a** to the S-4 sulfoxide when the elution was performed without the exclusion of air. Use of degassed solvents effectively prevented this oxidation and afforded pure **30a**. ^{1}H NMR **30a**: δ 7.50 (m, 2 H, aromatic), 7.30 (m, 3 H, aromatic), 5.28 (s, 1 H, benzylic), 4.48 (d, $J_{6endo,7exo}$ = 6, 1 H, H-6endo), 3.24 (m, 1 H, H-1), 3.01 (m, 1 H, H-5), 2.39 (m, 2 H, H-8), 2.17 (p, 1 H, H-7exo), 1.79 (q, 2 H, $CH_2CH_2CH_3$), 1.43 (m, 2 H, $CH_2CH_2CH_3$), 0.98 (t, J = 7.5, 3 H, CH_2CH_3). Mass spectrum **30a**: m/z 280 (M^+, 30%), 263 (3%), 242 (6%), 123 (100%). ^{1}H NMR **31a**: δ 7.52 (m, 2 H, aromatic), 7.31 (m, 3 H, aromatic), 5.28 (s, 1 H, benzylic), 4.22 (d, $J_{6endo,7exo}$ = 4.5, 1 H, H-6endo), 3.56 (t, 1 H, H-1), 3.16 (d, $J_{5,8anti}$ = 6, 1 H, H-5), 2.64 (d, J_{gem} = 15, 1 H, H-8syn), 2.44 (m, 1 H, H-8anti), 1.78 (m, 3 H), 1.24 (m, 2 H, CH_2CH_3), 0.89 (t, J = 7.5, 3 H, CH_2CH_3). Mass spectrum **31a**: m/z 280 (M^+, 45%), 247 (10%), 123 (100%). ^{1}H NMR **32**: δ 7.51 (m, 2 H, aromatic), 7.32 (m, 3 H, aromatic), 5.29 (s, 1 H, benzylic), 4.00 (dd, $J_{6endo,7endo}$ = 9, $J_{6endo,7exo}$ = 3, 1 H, H-6endo), 3.31 (t, 1 H, H-1), 3.20 (d, $J_{5,8anti}$ = 5, 1 H, H-5), 3.09 (dd, J_{gem} = 16.5, 1 H, H-7endo), 2.74 (ddd, $J_{7exo,1}$ = 7.5, 1 H, H-7exo), 2.25 (q, 1 H, H-8anti), 2.10 (p, 2 H, $CH_2CH_2CH_3$), 1.39 (m, 2 H, CH_2CH_3), 1.00 (t, J = 8, 3 H, CH_2CH_3). Mass spectrum **32**: m/z 300 (M + 2, 6%), 298 (M^+, 18%), 263 (2%), 229 (10%), 153 (55%), 121 (85%). ^{1}H NMR **30a sulfoxide**: δ 7.47 (m, 2 H, aromatic), 7.38 (m, 3 H, aromatic), 4.54 (d, $J_{6endo,7exo}$ = 7, 1 H, H-6endo), 4.40 (s, 1 H, benzylic), 3.50 (d, $J_{5,8anti}$ = 9, 1 H, H-5), 3.17 (t, 1 H, H-1).

(1*SR*,3*SR*,5*RS*,6*RS*,7*RS*)-6-[(Methanesulfonyl)oxy]-3-phenyl-7-propyl-2,4-dithiabicyclo[3.2.1]octane (30b). A solution of 12.2 mg (0.11 mmol) of triethylamine and 5.3 mg (0.02 mmol) of the exo alcohol **30a** in 0.4 mL of CH_2Cl_2 under N_2 was cooled in an ice/water bath, and a solution of 7.2 mg (0.063 mmol) of methanesulfonyl chloride in 0.15 mL of CH_2Cl_2 was added. After the solution was stirred for 0.5 h, it was taken up in 20 mL of hexane, washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated to give the mesylate **30b** as an oil weighing 6.6 mg (quantitative), pure by its ^{1}H NMR spectrum. ^{1}H NMR: δ 7.50 (m, 2 H, aromatic), 7.32 (m, 3 H, aromatic), 5.33 (s, 1 H, benzylic), 5.24 (d, $J_{6endo,7exo}$ = 5, 1 H, H-6endo), 3.39 (d, $J_{5,8anti}$ = 6, 1 H, H-5), 3.31 (t, 1 H, H-1), 3.06 (s, 3 H, OSO_2CH_3), 2.49 (m, 2 H, H-7exo and H-8syn), 2.38 (m, 1 H, H-8anti), 1.87 (m, 2 H, $CH_2CH_2CH_3$), 1.43 (m, 2 H, $CH_2CH_2CH_3$), 1.00 (t, J = 7, 3 H, CH_2CH_3). Mass spectrum: m/z 358 (M^+, 3%), 263 (M - SO_3CH_3, 15%), 197 (53%), 153 (55%).

(1*SR*,3*RS*,5*RS*,6*RS*,7*RS*)-6-Chloro-3-phenyl-7-propyl-2,4-dithiabicyclo[3.2.1]octane (31b). A solution of 12.2 mg (0.11 mmol) of triethylamine and 4 mg (0.014 mmol) of the endo alcohol **31a** in 0.4 mL of CH_2Cl_2 under N_2 was cooled in an ice/water bath, and a solution of 7.2 mg (0.06 mmol) of methanesulfonyl chloride in 0.15 mL of CH_2Cl_2 was added. Upon workup as for **30b**, 4 mg (quantitative) of the chloride **31b** was obtained, pure by its ^{1}H NMR spectrum. ^{1}H NMR: δ 7.50 (m, 2 H, aromatic), 7.31 (m, 3 H, aromatic), 5.34 (s, 1 H, benzylic), 4.31 (d, $J_{6endo,7exo}$ = 6, 1 H, H-6endo), 3.70 (t, 1 H, H-1), 3.61 (d, $J_{5,8anti}$ = 6, 1 H, H-5), 2.78 (d, J_{gem} = 15, 1 H, H-8syn), 2.64 (m, 1 H, H-8anti), 2.32 (q, 1 H, H-7exo), 1.91 (q, 2 H, $CH_2CH_2CH_3$), 1.39 (m, 2 H, $CH_2CH_2CH_3$), 1.00 (t, J = 7.5, 3 H, $CH_2CH_2CH_3$). Mass spectrum: m/z 300 (M + 2, 10%), 298 (M^+, 30%), 263 (M - Cl, 1%), 197 (33%), 121 (100%).

(1*SR*,2*SR*,3*SR*,5*RS*)-3-[[4-[(*tert*-Butyldimethylsilyl)oxy]-1-phenylnon-2-ynyl]thio]-2-propyl-1,5-epithiocyclopentane (33) and *rac*-15-[(*tert*-Butyldimethylsilyl)oxy]-9-mercapto-11-sulfinyl-1,2,3,4-tetranorprost-13-yne 9,11-(*S*,*S*-*exo*-Phenylmethylene acetal) (34b). A solution of 251.3 mg (1.047 mmol) of (*S*)-3-[(*tert*-butyldimethylsilyl)oxy]-1-octyne in 1.5 mL of dry hexane under N_2 was cooled in an ice/water bath, and 0.65 mL (1.6 M, 1.04 mmol) of *n*-butyllithium was added. After the solution was stirred for 1 h, it was transferred via syringe, with a 1-mL hexane wash, to a nitrogen-purged flask containing 34.4 mg (0.258 mmol) of $AlCl_3$ under N_2 at 0 °C. The reaction was allowed to proceed for 1 h, after which the volatiles were removed at 22 °C (20 torr). The resulting brown oil was cooled in an ice/water bath, and a solution of 21.4 mg (0.06 mmol) of the mesylate **30b** in 3 mL of 1,2-dichloroethane was added. After 1.25 h, the solution was taken up in 25 mL of hexane, washed with 10% HCl, saturated $NaHCO_3$, and brine, dried over Na_2SO_4, and concentrated to dryness in vacuo at 1 torr for 18 h to give a crude product weighing 78.8 mg. Preparative TLC eluting with 1:4 ethyl acetate/hexane afforded a two-component mixture weighing 38.1 mg, R_f 0.65–0.70. Multiple elutions with various solvent systems failed to separate the two compounds. Separation could be achieved after the silica gel containing the two compounds was stirred in oxygenated ethyl acetate for 3 days, followed by extraction, concentration, and a second preparative thin-layer chromatography with 1:4 ethyl acetate/hexane to yield 20.3 mg (58%) of **33**, R_f 0.62, and 4 mg (12%) of the sulfoxide **34b**, R_f 0.33. ^{1}H NMR **33**: δ 7.82 (d, J = 9, 2 H, aromatic), 7.27 (m, 3 H, aromatic), 4.81 (s, 1 H, benzylic), 4.22 (t, 1 H, C*H*OSi), 3.16 (m, 2 H, H-1, H-5), 3.06 (m, 1 H, H-3), 1.00 (t, J = 7.5, 3 H, $CH_2CH_2CH_3$), 0.84 (12 H, *t*-Bu, $(CH_2)_4CH_3$), 0.04 (d, 6 H, Si$(CH_3)_2$). Mass spectrum **33**: m/z 502 (M^+ <1%), 445 (M - *t*-Bu, 1.5%), 411 (1%), 323 (3%). ^{1}H NMR **34b** δ 7.47 (m, 2 H, aromatic), 7.38 (m, 3 H, aromatic), 4.38 (s, 1 H, benzylic), 3.7 (d, $J_{11,10\beta}$ = 7.5, 1 H, H-11), 3.23 (d, $J_{12\alpha,8\beta}$ = 7, 1 H, H-12), 3.14 (t, 1 H, H-9), 2.5–2.80 (m, 2 H, H-10, H-8), 1.02 (t, J = 7.5, 3 H, CH_2CH_3), 0.93 (s, 12 H, *t*-Bu, $(CH_2)_4CH_3$), 0.11 (d, Si$(CH_3)_2$). Mass spectrum **34b**: m/z 518 (M^+, 1%), 461 (M - *t*-Bu, 1%), 427 (M - C_7H_7, 1%), 149 (50%), 105 (100%).

***rac*-15-*tert*-Butoxy-9,11-dimercapto-1,2,3,4-tetranorprost-13-yne 9,11-(*S*,*S*-*endo*-Phenylmethylene acetal) (35).** A solution of 131.1 mg (0.719 mmol) of (*S*)-3-*tert*-butoxy-1-octyne in 0.2 mL of toluene under N_2 was cooled in an ice/water bath, and 260 μL (2.76 M, 0.718 mmol) of *n*-butyllithium was added. After the reaction mixture was stirred for 6 min, 395 μL (1 M, 0.395 mmol) of dimethylchloroalane was added and the reaction was allowed to proceed for 50 min. A solution of 25.9 mg (0.075 mmol) of the chloride **31b** in 1.2 mL of toluene was then added by syringe, and the solution was stirred for 1.25 h. The reaction was quenched by dropwise addition of 0.5 mL of saturated Na_2SO_4, and the reaction mixture was taken up in 15 mL of ether, vortexed, and centrifuged and the supernatant withdrawn by pipette. This process was repeated with three 15-mL portions of ether, the supernatants were combined, dried over Na_2SO_4, and evaporated to dryness, and the residue was subjected to high vacuum, 1 torr, for 18 h to give an oil weighing 86.1 mg. Preparative TLC with 15% ethyl acetate in hexane afforded 2.7 mg (5%) of the episulfide **33** and an inseparable mixture of the desired alkynylated product **35** and rearranged chloride **32** weighing 5.1 mg (~16%), R_f 0.46. The ^{1}H NMR spectrum of the mixture indicated that the chloride was the minor component. ^{1}H NMR **35**: δ 7.52 (m, 2 H, aromatic), 7.30 (m, 3 H, aromatic), 5.35 (s, 1 H, benzylic), 4.11 (dt, 1 H, C*H*O-*t*-Bu), 3.66 (t, 1 H, H-9), 3.44 (d, $J_{11,10\beta}$ = 7.5, 1 H, H-11), 3.14 (d, $J_{12,8\beta}$ = 7.5, 1 H, H-12), 2.70 (d, J_{gem} = 15, 1 H, H-10α), 2.41 (m, 1 H, H-10β), 2.06 (m, 1 H, H-8β), 1.30 (s, 9 H, *t*-Bu), 0.95 (t, J = 7.5, 3 H, $CH_2CH_2CH_3$), 0.92 (t, 3 H, $(CH_2)_4CH_3$). Mass spectrum: m/z 444 (M^+, 1%), 387 (M - *t*-Bu, 1%), 195 (10%), 121 (60%), 91 (60%).

Preparation of (*Z*)-(1*SR*,3*RS*,5*RS*,6*RS*,7*RS*)- and (*Z*)-(1*SR*,3*SR*,5*RS*,6*RS*,7*RS*)-6-Hydroxy-7-(7-hydroxy-2-heptenyl)-3-phenyl-2,4-dithiabicyclo[3.2.1]octane (36a and 37a) and (*Z*)-(1*RS*,3*SR*,5*RS*,6*RS*,8*RS*)-6-Chloro-8-(7-hydroxy-2-heptenyl)-3-phenyl-2,4-dithiabicyclo[3.2.1]octane (38). A solution of 138 mg (0.527 mmol, assuming quantitative conversion from ditosylate **25**) of dithiol **22** and 69 mg (0.651 mmol) of benzaldehyde in 3.3 mL of chloroform under argon was treated with a solution of 50.7 mg (0.357 mmol) of BF_3-OEt_2 in 2.2 mL of chloroform for 1.25 h at 23 °C. The solution was then taken up in 30 mL of chloroform, washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated to an oil weighing 150 mg. Preparative TLC with 50% ethyl acetate in hexane afforded 65 mg (35%) of an inseparable mixture of epimeric alcohols **36a** and **37a**, R_f 0.10, and 14 mg (7.5%) of the rearranged chloride **38**, R_f 0.33. ^{1}H NMR **37a**: δ 7.49 (m, 2 H, aromatic), 7.31 (m, 3 H, aromatic), 5.5 (m, 2 H, olefinic), 5.33 (s, 1 H, benzylic), 4.53 (d, $J_{6endo,7exo}$ = 6, 1 H, H-6endo), 3.64 (t, 2 H, CH_2OH), 3.30 (m, 1 H, H-1), 3.07 (br d, 1 H, H-5), 2.69 (m, 1 H), 2.53 (m, 1 H), 2.44 (m, 2 H), 2.22 (m, 3 H), 1.67 (m, 2 H, $CH_2CH_2CH_2OH$), 1.47 (m, 2 H, CH_2CH_2OH). Mass spectrum **37a**: m/z 350 (M^+, 3%), 332 (M - H_2O, 1%), 259 (M - C_7H_7, 10%). ^{1}H NMR **36a**:

δ 7.52 (m, 2 H, aromatic), 7.31 (m, 3 H, aromatic), 5.44 (m, 2 H, olefinic), 5.37 (s, 1 H, benzylic), 4.36 (d, $J_{6endo,7exo}$ = 6, 1 H, H-6endo), 3.62 (t, 3 H, CH_2OH and H-1), 3.24 (d, $J_{5,anti}$ = 5, 1 H, H-5), 2.73 (m, 2 H), 2.64 (m, 1 H), 2.57 (m, 1 H), 2.22 (q, 2 H), 1.91 (m, 1 H), 1.62 (q, 2 H, $CH_2CH_2CH_2OH$), 1.46 (q, 2 H, $CH_2CH_2CH_2OH$). Mass spectrum **36a**: m/z 350 (M^+, 2%), 259 (M − C_7H_7, 10%). High-resolution mass spectrum of **36a** and **37a** (mixture), calcd for $C_{19}H_{26}O_2S_2$: 350.1374. Found: 350.1380. ^1H NMR **38**: δ 7.51 (m, 2 H, aromatic), 7.32 (m, 3 H, aromatic), 4.47 (m, 2 H, olefinic), 4.33 (s, 1 H, benzylic), 4.03 (dd, $J_{6endo,7endo}$ = 9, $J_{6endo,7exo}$ = 3, 1 H, H-6endo), 3.66 (t, J = 6, 2 H, CH_2CH_2OH), 3.36 (t, 1 H, H-1), 3.26 (d, $J_{5,8}$ = 5, H-5), 3.16 (dd, J_{gem} = 16.5, H-7endo), 2.96 (m, 2 H), 2.81 (ddd, $J_{7exo,1}$ = 9, 1 H, H-7exo), 2.30 (m, 3 H), 2.63 (m, 3 H), 1.49 (m, 2 H, $CH_2CH_2CH_2OH$)). Mass spectrum **38**: m/z 371 (M + 3, 3%), 370 (M + 2, 6%), 369 (M^+ + 1, 21%), 333 (M − Cl, 2%), 277 (M − C_7H_7, 10%), 211 (30%).

(*Z*)-(1*SR*,3*RS*,5*RS*,6*RS*,7*RS*)- and (*Z*)-(1*SR*,3*SR*,5*RS*,6*RS*,7*RS*)-6-Hydroxy-7-[7-(triphenylmethoxy)-2-heptenyl]-3-phenyl-2,4-dithiabicyclo[3.2.1]octane (36b and 37b). A solution of 36.7 mg (0.105 mmol) of a mixture of alcohols **36a** and **37a** and 59 mg (0.212 mmol) of triphenylmethyl chloride in 0.5 mL of pyridine was stirred under argon for 18 h at 23 °C. The solution was then taken up in 30 mL of chloroform, washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated to an oil weighing 104 mg. Preparative thin-layer chromatography with 50% ethyl acetate in hexane furnished 6 mg (9.7%) of the endo alcohol **36b**, R_f 0.41, and 47 mg (76%) of the exo alcohol **37b**, R_f 0.48. ^1H NMR **37b**: δ 7.29–7.59 (20 H, aromatic), 5.51 (m, 2 H, olefinic), 5.33 (s, 1 H, benzylic), 4.52 ($J_{6endo,7exo}$ = 5, 1 H, H-6endo), 3.28 (t, 1 H, H-1), 3.06 (t, 3 H, H-5 and CH_2CH_2OTr), 2.64 (p, 1 H), 2.48 (m, 1 H), 2.41 (m, 1 H), 2.24 (m, 1 H), 2.14 (m, 2 H), 1.64 (m, 2 H, $CH_2CH_2CH_2OTr$), 1.50 (m, 2 H, $CH_2CH_2CH_2OTr$). Mass spectrum **37b**: m/z 592 (M^+, 1%), 349 (M − trityl, 3%). ^1H NMR **36b**: δ 7.16–7.55 (20 H, aromatic), 5.41 (m, 2 H, olefinic), 5.38 (s, 1 H, benzylic), 4.33 (d, $J_{6endo,7exo}$ = 5, 1 H, H-6endo), 3.60 (t, 1 H, H-1), 3.23 (d, $J_{5,8anti}$ = 5.5, 1 H, H-5), 3.54 (t, J = 4.5, 2 H, CH_2CH_2OTr), 1.69 (d, J_{gem} = 15, 1 H, H-8syn), 1.63 (m, 1 H), 1.50 (m, 2 H), 2.10 (q, 2 H), 1.80 (m, 1 H), 1.61 (q, 2 H, CH_2CH_2OTr), 1.44 (q, 2 H, $CH_2CH_2CH_2OTr$). Mass spectrum **36b**: m/z 349 (M − $C(C_6H_5)_3$, 2%).

Isomerization of 37b to 36b by Treatment with *n*-Butyllithium. A solution of 10.9 mg (0.018 mmol) of the exo alcohol **37b** in 0.2 mL of dry tetrahydrofuran under N_2 was treated with 100 μL (2.25 M, 0.225 mmol) of *n*-butyllithium at −30 °C with the development of a pale red color of the solution. The solution was allowed to warm to −20 °C and stirred for 1.25 h. After warming to 0 °C, 0.4 mL of a cold 0.1 N HCl solution was quickly added and the solution was vigorously stirred for 5 min. The solution was then taken up in 25 mL of chloroform, washed with brine, dried over Na_2SO_4, and concentrated to an oil weighing 9 mg, whose ^1H NMR spectrum indicated 95% conversion to the endo isomer **36b**.

Acid-Catalyzed Epimerization of the Acetate of 36b to the Acetate of 37b by Treatment with 10% Anisole in Trifluoroacetic Acid. To 4 mg (0.006 mmol) of the acetate of **36b** under N_2 was added 100 μL of 10% anisole in trifluoroacetic acid solution at 0 °C. The solution developed a red color and after 0.5 h was concentrated under a stream of argon and then subjected to high vacuum at 1 torr for 0.25 h. This product was treated with 100 μL of acetic anhydride and 150 μL of pyridine for 18 h at 23 °C under argon, and the solution was subsequently taken up in 20 mL of hexane, washed with brine, dried over Na_2SO_4, and concentrated to an oil. Preparative TLC eluting with 50% ethyl acetate in hexane afforded 2 mg (50%) of the acetate of the exo isomer **37b**, R_f 0.53. ^1H NMR of **acetate of 36b**: δ 7.19–7.53 (20 H, aromatic), 5.40 (m, 1 H, olefinic), 5.36 (s, 1 H, benzylic), 5.27 (m, 1 H, olefinic), 5.14 (d, $J_{6endo,7exo}$ = 4.5, 1 H, H-6endo), 3.61 (t, 1 H, H-1), 3.30 (d, $J_{5,8anti}$ = 5.5, H-5), 3.02 (t, 2 H, CH_2CH_2OTr), 2.73 (d, J_{gem} = 15, 1 H, H-8syn), 2.02 (s, 3 H, $COCH_3$), 1.61 (q, 2 H, $CH_2CH_2CH_2CH_2OTr$), 1.43 (q, 2 H, $CH_2CH_2CH_2OTr$). ^1H NMR of **acetate of 37b**: δ 7.16–7.50 (20 H, aromatic), 5.30 (m, 4 H, olefinic, H-6endo and benzylic), 3.30 (t, 1 H, H-1), 3.10 (d, $J_{5,8anti}$ = 6, 1 H, H-5), 3.00 (t, 2 H, CH_2CH_2OTr), 2.46 (d, J_{gem} = 15, 1 H, H-8syn), 2.03 (s, 3 H, $COCH_3$), 1.60 (m, 2 H, $CH_2CH_2CH_2OTr$), 1.41 (q, 2 H, $CH_2CH_2CH_2OTr$).

(*Z*)-(1*SR*,3*RS*,5*RS*,6*RS*,7*RS*)-6-Chloro-7-[7-(triphenylmethoxy)-2-heptenyl]-3-phenyl-2,4-dithiabicyclo[3.2.1]octane (Chloride of 36b). A solution of 6 mg (0.01 mmol) of the endo alcohol **36b** and 8.27 mg (0.07 mmol) of triethylamine in 0.27 mL of CH_2Cl_2 under N_2 was cooled in an ice/water bath, and 0.12 mL (5.82 mg, 0.05 mmol) of a solution of 0.165 mL of methanesulfonyl chloride in 5 mL of CH_2Cl_2 was added. After 0.5 h, the solution was taken up in 20 mL of hexane, washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated to give the chloride as an oil weighing 6.1 mg (quantitative). ^1H NMR of chloride: δ 7.19–7.53 (20 H, aromatic), 5.42 (m, 1 H, olefinic), 5.33 (m, 1 H, olefinic), 5.30 (s, 1 H, benzylic), 4.30 (d, $J_{6endo,7exo}$ = 4.5, 1 H, H-6endo), 3.63 (t, 1 H, H-1), 3.57 (d, $J_{5,8anti}$ = 4.5, 1 H, H-5), 3.13 (m, 1 H), 3.03 (t, 2 H, CH_2OTr), 2.68 (d, J_{gem} = 15, 1 H, H-8syn), 2.61 (m, 2 H), 2.30 (m, 1 H), 2.10 (q, 2 H), 1.63 (m, 2 H, $CH_2CH_2CH_2CH_2OTr$), 1.43 (q, 2 H, $CH_2CH_2CH_2OTr$).

(*Z*)-(1*SR*,3*SR*,5*RS*,6*RS*,7*RS*)-6-[(Methanesulfonyl)oxy]-7-[7-(triphenylmethoxy)-2-heptenyl]-3-phenyl-2,4-dithiabicyclo[3.2.1]octane (Mesylate of 37b). A solution of 7.6 mg (0.013 mmol) of the exo alcohol **37b** and 12.26 mg (0.112 mmol) of triethylamine in 0.4 mL of CH_2Cl_2 under N_2 was cooled in an ice/water bath, and 0.15 mL (7.27 mg, 0.06 mmol) of a solution of 165 mL of methanesulfonyl chloride in 5 mL of CH_2Cl_2 was added. After 0.5 h, the solution was taken up in 25 mL of hexane, washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated to give the mesylate of **37b** as an oil weighing 7.8 mg (quantitative). ^1H NMR of mesylate: δ 7.20–7.59 (20 H, aromatic), 5.48 (m, 2 H, olefinic), 5.37 (s, 1 H, benzylic), 5.28 (d, $J_{6endo,7exo}$ = 5, 1 H, H-6endo), 3.42 (d, $J_{5,8anti}$ = 6, 1 H, H-5), 3.36 (t, 1 H, H-1), 3.06 (5 H, CH_2CH_2OTr, OSO_2CH_3), 1.64 (m, 2 H, $CH_2CH_2CH_2OTr$), 1.50 (m, 2 H, $CH_2CH_2CH_2OTr$).

(*Z*)-(1*SR*,2*SR*,3*SR*,5*RS*)-3-[[4(*S*)-Hydroxy-1-phenylnon-2-ynyl]thio]-2-(7-triphenylmethoxy-2-heptenyl)-1,5-epithiocyclopentane (39), (*Z*)-(1*RS*,3*RS*,5*RS*,6*SR*,8*RS*)-6-[3(*S*)-Hydroxy-1-octynyl]-3-phenyl-8-(7-triphenylmethoxy-2-heptenyl)dithiabicyclo[3.2.1]octane (40), and (*Z*)-9,11-Dimercapto-15(*S*)-hydroxy-1-trityloxyprost-5-en-13-yne 9,11-(*S*,*S*-*exo*-Phenylmethylene acetal) and 15*S*-*ent* Compound (41). A solution of 478 mg (1.99 mmol) of (*S*)-3-[(*tert*-butyldimethylsilyl)oxy]-1-octyne in 1.6 mL of dry toluene under N_2 was cooled in an ice/water bath, and 0.72 mL (2.77 M, 1.99 mmol) of *n*-butyllithium was added. The solution was stirred for 6 min, and then 0.762 mL (1.4 M, 1.067 mmol) of dimethylaluminum chloride was syringed in. After 50 min, a solution of 73 mg (0.11 mmol) of the mesylate of **37b** in 5.5 mL of toluene was introduced, and the solution was stirred for 1.25 h. The reaction was quenched by adding 0.7 mL of saturated Na_2SO_4, and the slurry was filtered through a C sintered-glass funnel. The precipitate was washed with 500 mL of ether and the ether layer washed with brine and dried over Na_2SO_4, and the solvent was recovered in vacuo to afford an oil weighing 103 mg. Preparative TLC eluting with 30% ethyl acetate in hexane afforded an inseparable mixture of alkynylated silyl ethers weighing 88 mg.

A solution of the above mixture in 0.55 mL of dry tetrahydrofuran under N_2 was cooled in an ice/water bath, and 0.55 mL (1 M, 0.55 mmol) of a solution of tetra-*n*-butyl ammonium fluoride was added. After the solution was stirred for 35 min, it was warmed to 0 °C and stirred for an additional 15 min. The solution was taken up in 50 mL of hexane and washed with water, and the hexane layer was dried over Na_2SO_4 and concentrated to an oil weighing 75 mg. Three passes in preparative thin-layer chromatography eluting with 30% ethyl acetate in hexane afforded 10 mg (12.4%) of **39**, R_f 0.45, 28.2 mg (36%) of **40**, R_f 0.40, and 29 mg (37%) of **41**, R_f 0.42. Characterization of **40** and **41** were carried out on their acetates. ^1H NMR **39**: δ 7.97 (d, J = 4.5, 2 H, aromatic), 7.26–7.57 (18 H, aromatic), 5.40 (m, 2 H, olefinic), 4.74 (s, 1 H, benzylic), 4.23 (m, 1 H, CHOH), 3.19 (m, 1 H), 3.11 (m, 1 H), 3.06 (m, 3 H), 2.81 (m, 2 H), 2.73 (m, 2 H), 2.41 (dd, 1 H), 0.85 (t, J = 4.5, 3 H, CH_2CH_3). Mass spectrum of **acetate of 39**: m/z 742 (M^+, 3%), 499 (M − trityl, 10%), 439 (M − trityl − CH_3CO_2H, 10%), 243 (trityl, 100%). High-resolution mass spectrum of the **acetate of 39**, calcd for $C_{48}H_{54}O_3S_2$: 742.3515. Found: 742.3482.

(*Z*)-(1*RS*,3*RS*,5*RS*,6*SR*,8*RS*)-6-[3(*S*)-Acetoxy-1-octynyl]-3-phenyl-8-[7-(triphenylmethoxy)-2-heptenyl]dithiabicyclo[3.2.1]heptane (Acetate of 40). A solution of 28.2 mg

(0.04 mmol) of **40** in 0.35 mL of dry pyridine was treated with 0.3 mL of acetic anhydride under N_2 for 18 h at 23 °C, which yielded 30 mg (quantitative) of the acetate. ^{1}H NMR: δ 7.17–7.52 (20 H, aromatic), 5.45 (m, 2 H, olefinic), 5.40 (s, 1 H, benzylic), 5.36 (t, 1 H, C*H*OAc), 3.66 (dd, 1 H, H-6endo), 3.28 (t, 1 H, H-1), 3.19 (d, $J_{5,8}$ = 4.5, 1 H, H-5), 3.08 (t, 2 H, C*H*$_2$OTr), 2.83–3.00 (m, 3 H), 2.52 (m, 1 H), 2.26 (q, 1 H), 2.07 (s, 3 H, COC*H*$_3$), 0.90 (t, 3 H, CH$_2$C*H*$_3$). Mass spectrum: m/z 742 (M$^+$, 10%), 651 (M – C_7H_7, 2%), 499 (M – trityl, 3%), 243 (trityl, 100%). High-resolution mass spectrum, calcd for $C_{48}H_{54}O_3S_2$: 742.3515. Found: 742.3437.

(*Z*)-15(*S*)-Acetoxy-9,11-dimercapto-1-trityloxyprost-5-en-13-yne 9,11-(*S,S-exo*-Phenylmethylene acetal) and 15*S-ent* Compound (Acetate of 41). Acetylation of 21 mg (0.03 mmol) of the alcohol **41** gave 22 mg (quantitative) of the acetate. ^{1}H NMR (500 MHz): δ 7.18–7.50 (20 H, aromatic), 5.48 (m, 2 H, olefinic), 5.44 (s, 1 H, benzylic), 5.39 (t, 1 H, C*H*OAc), 3.40 (d, $J_{11,10\beta}$ = 4.5, 1 H, H-11), 3.20 (t, 1 H, H-9), 3.06 (m, 3 H, H-1, H-12), 2.63 (m, 1 H), 2.04 (s, 3 H, COC*H*$_3$), 2.56 (m, 1 H), 2.50 (d, J_{gem} = 15, 1 H, H-10α), 2.37 (m, 1 H), 2.13 (m, 2 H), 2.04 (s, 3 H, COC*H*$_3$), 1.26–1.74 (12 H), 0.90 (t, CH$_2$C*H*$_3$). Mass spectrum: m/z 742 (M$^+$, 1%), 651 (M – C_7H_7, 1%), 499 (M – trityl, 3%), 243 (trityl, 100%).

(*Z*)-15(*S*)-Acetoxy-9,11-dimercaptoprost-5-en-13-yn-1-ol 9,11-(*S,S-exo*-Phenylmethylene acetal) and 15*S-ent* Compound (42). To 21 mg (0.028 mmol) of the acetate of **41** was added 1.2 mL of a 9:1 acetate acid/water solution under N_2. After 14 h, the solution was taken up in 25 mL of hexane, washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated to give 24 mg of product. Preparative TLC eluting with 30% ethyl acetate in hexane afforded 14 mg (quantitative) of the alcohol **42**, R_f 0.18. ^{1}H NMR: δ 7.49 (m, 2 H, aromatic), 7.31 (m, 3 H, aromatic), 5.48 (m, 2 H, olefinic), 5.46 (s, 1 H, benzylic), 5.37 (dt, 1 H, C*H*OAc), 3.68 (t, J = 6, 2 H, CH$_2$C*H*$_2$OH), 3.44 (d, $J_{11,10\beta}$ = 4.5, 1 H, H-11), 3.27 (t, 1 H, H-9), 3.11 (br d, $J_{12,8exo}$ = 6, $J_{12,15}$ = 1.5, 1 H, H-12), 2.11 (s, 3 H, COC*H*$_3$), 0.93 (t, J = 6, 3 H, CH$_2$C*H*$_3$). Mass spectrum: m/z 500 (M$^+$, <1%), 409 (M – C_7H_7, 3%), 349 (M – $C_7H_7OCH_3CO_2H$, 1%). High-resolution mass spectrum, calcd for $C_{29}H_{40}O_3S_2$: 500.2419. Found: 500.2426.

(*Z*)-15(*S*)-Acetoxy-9,11-dimercaptoprost-5-en-13-ynoic Acid *S,S-exo*-Phenylmethylene Acetal Methyl Ester and 15*S-ent* Compound (43a) and (*Z*)-15(*S*)-Acetoxy-9-mercapto-11-sulfinylprost-5-en-13-ynoic Acid *S,S-exo*-Phenylmethylene Acetal Methyl Ester and 15*S-ent* Compound (43b). A solution of 5.3 mg (0.04 mmol) of oxalyl chloride in 150 μL of CH_2Cl_2 under N_2 was cooled in a dry ice/acetone bath, 18.7 μL (6.97 mg, 0.089 mmol) of a solution of 339 μL of dimethyl sulfoxide/mL of CH_2Cl_2 was added, and the reaction mixture was stirred for 10 min. A solution of 14 mg (0.028 mmol) of **42** in 550 μL of CH_2Cl_2 was then added, and the solution was stirred for 15 min. This was followed by addition of 50 μL of triethylamine, with stirring for 5 min and warming of the solution to 23 °C, whereupon 100 μL of water was added and the biphasic mixture was vigorously stirred for 10 min. Water and methylene chloride were added, and the CH_2Cl_2 layer was dried over Na_2SO_4 and concentrated to an oil weighing 12.1 mg.

The crude aldehyde from the above reaction was treated with 0.7 mL (0.3 M, 0.2 mmol) of pyridinium dichromate in dimethylformamide for 7 h under N_2 at 23 °C. The solution was taken up in 7 mL of water and extracted with four 15-mL portions of ether. The ether extracts were combined, dried over Na_2SO_4, and concentrated to an oil weighing 11.6 mg. The oil was dissolved in 3 mL of 2:1 ether/methanol and cooled in an ice/water bath. An ethereal diazomethane solution was added dropwise until the solution remained yellow. Removal of the solvents under N_2 and in high vacuum gave a yellow oil weighing 11.6 mg. Preparative TLC eluting with 30% ethyl acetate in hexane afforded 5 mg (36%) of the methyl ester **43a**, R_f 0.44, and 1.3 mg (10%) of the sulfoxide methyl ester **43b**, R_f 0.14. ^{1}H NMR **43a**: δ 7.52 (m, 2 H, aromatic), 7.31 (m, 3 H, aromatic), 5.45–5.55 (3 H, olefinic and benzylic), 5.37 (t, 1 H, H-15), 3.63 (s, 3 H, OC*H*$_3$), 3.39 (d, $J_{11,10\beta}$ = 4.5, 1 H, H-11), 3.22 (t, 1 H, H-9), 3.10 (d, $J_{12,8exo}$ = 6, 1 H, H-12), 2.50 (d, J_{gem} = 12.5, 1 H, H-10α), 2.01 (s, 3 H, OCOC*H*$_3$), 0.91 (t, 3 H, CH$_2$C*H*$_3$). Mass spectrum **43a**: 528 (M$^+$, <1%), 468 (M – CH_3CO_2H, 1%), 437 (M – C_7H_7, 2%), 377 (M – CH_3CO_2H – C_7H_7, 2%). High-resolution mass spectrum, calcd for $C_{30}H_{40}O_4S_2$: 528.2338. Found: 528.2351. ^{1}H NMR **43b**: δ 7.48 (m, 2 H, aromatic), 7.38 (m, 3 H, aromatic), 5.45–5.58 (2 H, olefinic), 5.34 (t, 1 H, H-15), 4.39 (s, 1 H, benzylic), 3.71 (d, $J_{11,10\beta}$ = 6, 1 H, H-11), 3.65 (s, 3 H, OC*H*$_3$), 3.26 (d, $J_{12,8exo}$ = 6, 1 H, H-12), 3.12 (t, 1 H, H-9), 2.57 (d, J_{gem} = 12.5, 1 H, H-10α), 2.05 (s, 3 H, OCOC*H*$_3$), 0.93 (t, 3 H, CH$_2$C*H*$_3$). Mass spectrum **43b**: m/z 544 (M$^+$, 1%), 484 (M – CH_3CO_2H, <1%).

2-Phenyl-1,3-dithiane. To 200 μL (208 mg, 1.97 mmol) of benzaldehyde and 197 μL (212 mg, 1.97 mmol) of 1,3-propanedithiol in a N_2-purged test tube was added 169 μL (195 mg, 1.38 mmol) of BF_3·OEt, and the solution was stirred at 23 °C for 3 h. After workup, 380 mg (quantitative) of 2-phenyl-1,3-dithiane, pure by its ^{1}H NMR spectrum, was obtained. ^{1}H NMR: δ 7.48 (m, 2 H, aromatic), 7.33 (m, 3 H, aromatic), 5.20 (s, 1 H, benzylic), 3.10 (dt, 2 H, J = 12 and 1.5, H-4ax and H-6ax), 1.95 (td, 2 H, J = 12 and 3, H-4eq and H-6eq), 2.19 (m, 1 H, H-5eq), 2.04 (m, 1 H, H-5ax). Mass spectrum: m/z 196 (M$^+$, 35%), 121 (100%).

***trans*-2-Phenyl-1-oxo-1,3-dithiane (44).** A solution of 74 mg (0.377 mmol) of 2-phenyl-1,3-dithiane in 1 mL of CH_2Cl_2 under N_2 was cooled in a dry ice/acetone bath, and a solution of 72.5 mg (0.41 mmol) of *m*-chlorobenzoic acid in 2.5 mL of CH_2Cl_2 was added. After the solution was stirred for 20 min, it was taken up in 30 mL of CH_2Cl_2 and washed with saturated Na_2SO_3, $NaHCO_3$, and brine, dried over Na_2SO_4, and concentrated to yield the crude sulfoxide **44** weighing 80 mg. Preparative TLC eluting with 2:1 ethyl acetate/hexane afforded 72 mg (89%) of the sulfoxide **44**, R_f 0.05. ^{1}H NMR: δ 7.37 (m, 5 H, aromatic), 4.56 (s, 1 H, benzylic), 3.57 (br d, J-11.5, 1 H, H-5eq), 2.34–2.93 (m, 5 H, H-4, H-5, H-6ax). Mass spectrum: m/z 212 (M$^+$, 25%), 163 (7%), 121 (85%), 90 (100%).

Low-Temperature ^{1}H NMR Study of the Reaction of Trifluoroacetic Anhydride and the Sulfoxide 44. A solution of 17.2 mg (0.081 mmol) of the sulfoxide **44** in 700 μL of $CDCl_3$ was cooled to –50 °C (acetonitrile/dry ice bath), and 12 μL (17 mg, 0.085 mmol) of trifluoroacetic anhydride was added with stirring. After 20 min, 500 μL of the solution was transferred to an argon-purged NMR tube fitted with a rubber septum cooled to –50 °C. The NMR spectrum was recorded at –50 °C. The spectrum indicated formation of 1,2-dithiacyclopentane, benzaldehyde, and some impurity. No essential change was observed after 40 min and after warming the probe to 0 °C. The spectrum showed few changes, but particulate matter had formed and the solution had turned brown. ^{1}H NMR of reaction mixture: δ 9.95 (s, 1 H, C*H*O), 7.96 (d, 2 H, aromatic), 7.76 (t, 1 H, aromatic), 7.60 (t, 2 H, aromatic), 3.22 (t, J = 6, 4 H, SC*H*$_2$), 2.37 (q, J = 6, 2 H, CH$_2$C*H*$_2$CH$_2$).

Peracid Oxidation of the Methyl Ester Acetate 43a to the Sulfoxide Methyl Ester Acetate 43b. A solution of 5 mg (0.0095 mmol) of **43a** in 300 μL of CH_2Cl_2 was cooled in a dry ice/acetone bath under N_2, and a solution of 1.79 mg (0.011 mmol) of *m*-chloroperbenzoic acid in 64 μL of CH_2Cl_2 was added. The solution was stirred for 15 min and then taken up in 25 mL of CH_2Cl_2, washed with 18 mL of brine containing Na_2SO_3 and $NaHCO_3$, dried over Na_2SO_4, and concentrated to 4.1 mg (80%) of the sulfoxide **43b**, R_f 0.5, as the only product on a diagnostic TLC plate (eluting with 50% ethyl acetate in hexane).

Reaction of the Sulfoxide Ester 43b with Trifluoroacetic Anhydride/Trifluoroacetic Acid. A solution of 4 mg (0.0074 mmol) of **43a** in 200 μL of CH_2Cl_2 was cooled to –40 °C under N_2, and a solution of 10.4 mg (0.05 mmol) of trifluoroacetic anhydride in 100 μL of $CHCl_3$, and 10 μL (14.8 mg, 0.12 mmol) of trifluoroacetic acid were added. After 10 min, the mixture was warmed to 23 °C and blown down under N_2 and then subjected to high vacuum at 1 torr for 20 min. Preparative TLC afforded the ester **43a** weighing 1.8 mg (46%).

Exchange Reaction of the Alkynyl Diacetate 45 with 1,3-Propanedithiol and BF_3·OEt_2. To 3 mg (0.006 mmol) of the alkynyldiacetate **45** under argon were added 100 μL of propanedithiol and a solution of 7.35 mg (0.05 mmol, 0.2 M overall concentration) of BF_3·OEt_2 in 100 μL of $CHCl_3$, and the solution was stirred for 24 h at 24 °C. The solution was blown down under a stream of argon and subjected to high vacuum (1 torr) for 1.5 h. The resulting brown oil was treated with 350 μL of pyridine and 300 μL of acetic anhydride for 15 h under argon, taken up in 30 mL of hexane, washed with brine, dried over Na_2SO_4, and concentrated to dryness to yield 23 mg. Preparative TLC eluting

with 30% ethyl acetate in hexane afforded 2 mg (66%) of the tetraacetate **46**, R_f 0.37. ^{1}H NMR **46**: 5.36 (m, 3 H, H-5, H-6, and H-15), 4.07 (t, 3 H, H-1 and H-11β), 3.80 (m, 1 H, H-9β), 2.91 (m, 1 H, H-10β), 2.40 (m, 1 H, H-8β), 2.32 (6 H, 2 s for SCOCH_3), 2.24 (m, 1 H, H-12α), 2.07 (s, 3 H, OCOCH_3), 2.06 (s, 3 H, OCOCH_3), 1.76 (m, 1 H, H-10α), 0.89 (t, 3 H, CH_2CH_3). IR: 1690, 1730 cm^{-1}. Mass spectrum: m/z 538 (M^+, <1%), 495 (M - CH_3CO, 3%), 435 (M - CH_3CO_2H - CH_3CO, 3%), 292 (M - 2CH_3CO - CH_3CO_2H, 3%), 359 (M - CH_3CO_2H - CH_3COSH - CH_3CO, 3%). High-resolution mass spectrum, calcd for $C_{26}H_{39}O_5S_2$ (M - CH_3CO): 495.2239. Found: 495.2250. Calcd for $C_{24}H_{35}O_3S_2$ (M - CH_3CO_2H - CH_3CO): 435.2028. Found: 435.2029.

(*Z*)-1,15-Dihydroxy-9,11-epidithioprost-5-en-13-yne and 15*S*-*ent* Compound (47a). To a solution of 2 mg (0.004 mmol) of **46** in 0.5 mL of methanol was added 15 mg (0.11 mmol) of K_2CO_3, and the mixture was stirred at 25 °C for 0.5 h. The reaction was stopped by dropwise addition of 3 mL of 1 N HCl, and the aqueous layer was extracted with two 15-mL portions of ether. The ether layers were dried over Na_2SO_4 and concentrated to give the diol **47a**, weighing 1.5 mg (quantitative), with a small amount of impurity, R_f 0.07. ^{1}H NMR: δ 5.37 (m, 2 H, H-5 and H-6), 4.33 (t, 1 H, H-15), 3.81 (br s, 1 H, H-11), 3.64 (m, 3 H, H-1 and H-9), 2.90 (distorted d, 1 H, J_{gem} = 12.5, 1 H, H-10β), 2.60 (d, 1 H, $J_{12,8exo}$ = 4.5, H-12), 2.48 (m, 1 H, H-8exo), 2.26 (d, J_{gem} = 12.5, H-10α), 0.91 (t, 3 H, CH_2CH_3).

(*Z*)-1,15(*S*)-Diacetoxy-9,11-epidithioprost-5-en-13-yne and 15*S*-*ent* Compound (47b). To 1.5 mg (0.004 mmol) of the diol **47a** was added 150 μL of pyridine and 100 μL of acetic anhydride. The reaction mixture was stirred under argon for 12 h, and the solution was taken up in 20 mL of hexane, washed with brine, dried over Na_2SO_4, and concentrated to an oil **47b** weighing 1.5 mg (assumed to be quantitative), R_f 0.44, as the only product. ^{1}H NMR **47b** (500 MHz): δ 5.32 (m, 3 H, H-5, H-6, and H-15), 4.06 (t, 2 H, H-1), 3.79 (br s, 1 H, H-11), 3.67 (distorted t, 1 H, H-9), 2.90 (d, 1 H, H-10β), 2.61 (d, 1 H, H-12), 2.49 (m, 1 H, H-8exo), 2.27 (d, 1 H, H-10α), 2.06 (s, 3 H, OCOCH_3), 2.03 (s, 3 H, OCOCH_3), 0.91 (t, 3 H, CH_2CH_3). Mass spectrum: m/z 452 (M^+, 10%), 392 (M - CH_3CO_2H, <1%). High-resolution mass spectrum, calcd for $C_{26}H_{36}O_4S_2$: 452.2055. Found: 452.2042.

(*Z*)-9,11-Epidithio-15(*S*)-hydroxyprost-5-en-13-ynoic Acid Methyl Ester and 15*S*-*ent* Compound (2). To 2.6 mg (0.0049 mmol) of the methyl ester **43a** was added 62 μL (0.62 mmol) of 1,3-propanedithiol and a solution of 4.89 mg (0.0344 mmol, 0.1 M overall concentration) of BF_3·OEt_2 in 248 μL of degassed $CHCl_3$ at 24 °C, and the reaction was allowed to proceed under argon for 14 h. The solution was blown down under a stream of argon and then subjected to high vacuum (1 torr) for 1 h. The resulting brown oil was treated with 250 μL of pyridine and 200 μL of acetic anhydride for 24 h under argon, and then the solution was taken up in 20 mL of hexane and washed with 7 mL of brine. The aqueous layer was extracted with three 10-mL portions of hexane, and the combined hexane layers were dried over Na_2SO_4 and concentrated to an oil weighing 3 mg. Preparative thin-layer chromatography eluting with 30% ethyl acetate in hexane afforded 0.5 mg (20%) of the triacetate methyl ester, R_f 0.49. ^{1}H NMR: 5.39 (m, 3 H, H-5, H-6, and H-15), 4.07 (m, 1 H, H-11), 3.80 (m, 1 H, H-9β), 3.68 (s, 3 H, CO_2CH_3), 2.38 (6 H, 2 s for SCOCH_3), 2.07 (s, 3 H, COCH_3), 0.91 (distorted t, CH_2CH_3). Mass spectrum: m/z 481 (M - CH_3CO, <1%), 421 (M - CH_3CO_2H - CH_3CO, 1%), 345 (M - CH_3CO_2H - CH_3COSH - CH_3CO, 1%), 312 (M - CH_3CO_2H - 2CH_3COSH, 2%).

To a solution of 0.5 mg (0.001 mmol) of the triacetate methyl ester in 0.5 mL of methanol was added 8 mg (0.06 mmol) of potassium carbonate, and the reaction was allowed to proceed at 25 °C under argon for 50 min. The solution was acidified with 3 mL of 1 N HCl and extracted with several portions of ether. The ether layers were washed with water and dried over Na_2SO_4, and the solvent was removed in vacuo. After drying in high vacuum (1 torr) for 16 h, 0.45 mg of the endodisulfide analogue **2** was obtained. ^{1}H NMR (500 MHz): 5.38 (m, 2 H, H-5 and H-6), 4.34 (distorted t, 1 H, H-15), 3.80 (br s, 1 H, H-11), 3.65 (s, 4 H, H-9 and CO_2CH_3), 2.90 (distorted d, 1 H, J_{gem} = 12.5, H-10β), 2.62 (d, 1 H, $J_{12,8exo}$ = 4.5, H-12), 2.48 (m, 1 H, H-8exo), 2.30 (d, 1 H, J_{gem} = 12.5, H-10α), 0.91 (CH_2CH_3). Mass spectrum: 397 (M + 1), 396 (M^+, 1%), 365 (M - OCH_3, <1%).

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