Silicon in Synthesis. 21. Reagents for Thiophenyl-Functionalized Cyclopentenone Annulations and the Total Synthesis of (±)-Hirsutene

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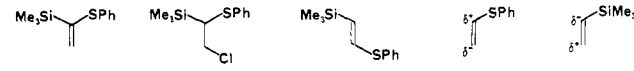
1-(Trimethylsilyl)-1-(phenylthio)ethylene (1) reacts with cyclic α,β-unsaturated acid chlorides to give β-mercaptophenyl-substituted cyclopentenones, whereas 1-(trimethylsilyl)-2-(phenylthio)ethylene (2) under similar conditions results in thiophenyl migration to give rearranged cyclopentenones. The former annulation reaction has been used to synthesize (±)-hirsutene (25) where the key steps utilize organosilicon chemistry.

The synthetic utility of vinylsilanes[1] and vinyl sulfides[2] has increased enormously during the past several years. Here we describe a combination of their respective electronic effects in the form of 1-(trimethylsilyl)-1-(phenylthio)ethylene (1) and 1-(trimethylsilyl)-2-(phenylthio)-ethylene (2) as reagents for thiophenyl-functionalized cyclopentenone annulations via the so-called Nazarov cyclization.[3]

Vinyltrimethylsilanes undergo regiospecific electrophilic substitution reactions.[4] This is a direct manifestation of the β-effect, where the buildup of electrophilic character β to the C–Si bond is stabilized, provided the developing electrophilic $2p_z$ orbital is in the same plane as the C–Si σ-bond. This stabilization is a delicate effect that can be readily perturbed by relatively small steric and electronic changes. Soft polarizable heteroatoms in conjugation with a trimethylsilyl group are predicted to dominate the ensuing electrophilic chemistry. These views have been expressed by us before as a valid caution in using the β-effect as a dominant driving force in the electrophilic additions of vinylsilanes.[7]

The polarization of vinyl sulfides directs electrophiles β to the sulfur substituent 3, opposite to the situation for vinyltrialkylsilanes 4.[5] Consequently, the combination of vinyltrialkylsilane and vinyl sulfide functional groups, with their opposed polarizations, should produce unusual functionalized cyclopentenone annulation reactions. Here we report the full details of the reactions of the reagents 1 and 2 with α,β-unsaturated acid chlorides and the total synthesis of (±)-hirsutene (25).[6]



1 1a 2 3 4

Results

The reagent 1 is readily available on a multigram scale by two routes. Addition of phenylsulfenyl chloride to vinyltrimethylsilane gave the adduct 1a which, on dehydrodehalogenation with DBU, provides 1. Treatment of 3 with LDA at −78 °C, followed by $ClSiMe_3$, also gave 1. The full details of these procedures have previously been reported.[7]

Cyclopentenoyl chloride 5 (R = H) in CH_2Cl_2/$ClCH_2CH_2Cl$ was treated with $AgBF_4$ at −50 °C, followed by the reagent 1. After warming the mixture to 20 °C, the bicyclo[3.3.0]oct-3-en-2-one 7 (R = H) was isolated in 35% yield. Using other Lewis acids, such as $SnCl_4$, $TiCl_4$, BF_3OEt_2, and $AlCl_3$, gave none of the required enone 7 (R = H) and only the thioester 9 (R = H). The blank reaction using the same conditions that gave 7, except that 5 was replaced by phenyl vinyl sulfide (3), gave none of the enone 7, thus demonstrating the necessity for the Me_3Si group. By way of contrast, the classical Nazarov cyclization, mediated by vinyltrimethylsilane, gave the enone isomer 10. Consequently, the thiophenyl substituent in effect transposes the enone double bond to the less substituted side of the newly formed cyclopentanone ring. The structure of 7 was confirmed by treatment with MeLi, followed by mercuric ion assisted hydrolysis ($HgCl_2$/

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(2) Oshima, K.; Shimoji, K.; Takahashi, H.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1973**, *95*, 2694. Vlattas, I.; Veechia, L. D.; Lee, A. D. *Ibid.* **1976**, *98*, 2008. Cookson, R. C.; Parsons, P. J. *J. Chem. Soc., Chem. Commun.* **1976**, 990. Cohen, T.; Mura, A. J., Jr.; Skull, W.; Fogel, E. R.; Ruffner, R. J.; Falck, J. R. *J. Org. Chem.* **1976**, *41*, 3218. Trost, B. M.; Crimmin, M. J.; Butler, D. *Ibid.* **1978**, *43*, 4549. Cookson, R. C.; Parson, P. J. *J. Chem. Soc., Chem. Commun.* **1978**, 821. Harirchian, B.; Magnus, P. *Ibid.* **1977**, 522. Posner, G. H.; Tang, P-W. *J. Org. Chem.* **1978**, *43*, 4131. Hopkins, P. B.; Fuchs, P. L. *J. Org. Chem.* **1978**, *43*, 1208. Grinderman, K. D.; Holtmann, P. *Angew. Chem., Int. Ed. Engl.* **1966**, *7*, 668. Verboom, W.; Meijer, J.; Brandsma, L. *Synthesis* **1978**, 577.

(3) Nazarov, N. I.; Zaretskaya, I. I. *Zh. Obshch. Khim.* **1957**, 27, 693. Woodward, R. B.; Hoffmann, R. "The Conservation of Orbital Symmetry"; Verlag Chemie: Weinheim/Bergstr, Germany, 1970. Sorenson, T. S. *J. Am. Chem. Soc.* **1967**, *89*, 3784. Deno, N. C.; Pittman, C. V.; Turner, J. O. *Ibid.* **1965**, *87*, 2153. Ohloff, G.; Schulte, K. H.; Demole, E. *Helv. Chim. Acta* **1971**, *54*, 2813. For a recent example of a silicon-directed Nazarov cyclization see: Denmark, S. E.; Jones, T. K. *J. Am. Chem. Soc.* **1982**, *104*, 2642. Marino, J. P.; Linderman, R. J. *J. Org. Chem.* **1981**, *46*, 3696.

(4) For leading references to the electrophilic chemistry of vinylsilanes see: ref 1. Fleming, I.; Pearce, A., *J. Chem. Soc., Chem.Commun.* **1975**, 633. Chan, T. H.; Lau, P. W. K.; Mychajlowskij *Tetrahedron Lett.* **1977**, 3317. Fristad, W. E.; Dime, D. S.; Bailey, T. R.; Paquette, L. A. *Tetrahedron Lett.* **1979**, 1999; *J. Org. Chem.* **1980**, *45*, 3017. Hudrlick, P. F.; Hudrlick, A. M.; Rona, R. J.; Misra, R. N.; Withers, G. P. *J. Am. Chem. Soc.* **1977**, *99*, 1993.

(5) For a leading and authoritative description of the synthetic chemistry of vinylsulfides see: Trost, B. M.; Lavoie, A. C. *J. Am. Chem. Soc.* **1983**, *105*, 5075 and references therein. Hopskins, P. B.; Fuchs, P. L. *J. Org. Chem.* **1978**, *43*, 1208. Oshima, K.; Shimojii, K.; Takashi, H.; Yamamoto, H.; Nozaki, H. *J. Am. Chem. Soc.* **1973**, *95*, 2694. Vlattas, I.; Veechia, L. D.; Lee, A. D. *J. Am. Chem. Soc.* **1976**, *98*, 2008. Cookson, R. C.; Parsons, P. J. *J. Chem. Soc, Chem. Commun.* **1976**, 990. Cohen, T.; Mura, A. J.; Skull, D. W.; Fogel, E. R.; Ruffner, R. J.; Falck, J. R. *J. Org. Chem.* **1976**, *41*, 3218. Trost, B. M.; Crimmin, M. J.; Butler, D. *J. Org. Chem.* **1978**, *43*, 4549. Harirchian, B.; Magnus, P. *J. Chem. Soc., Chem. Commun.* **1977**, 522. Posner, G. H.; Tang, P-W. *J. Org. Chem.* **1978**, *43*, 4131.

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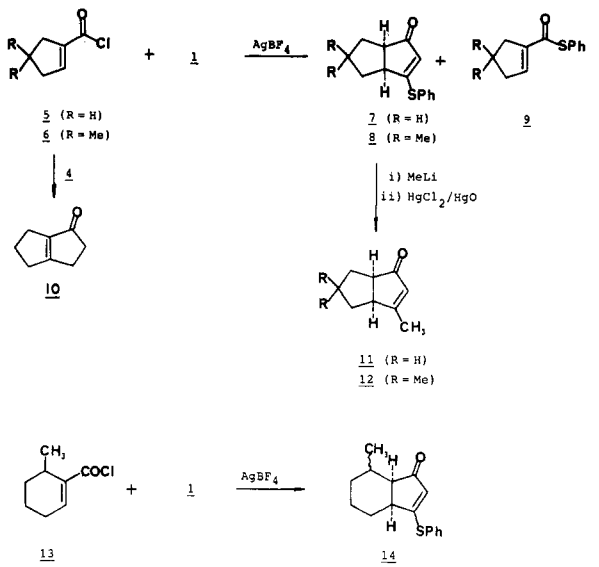
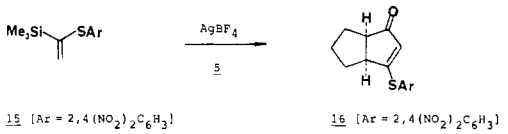
(7) Cooke, F.; Moerck, R.; Schwinderman, J.; Magnus, P. *J. Org. Chem.* **1980**, *45*, 1046. (a) Ager, D. *Tetrahedron Lett.* **1982**, 23, 1945. Hase, T. A.; Lahtinen, L. *Ibid.* **1981**, *22*, 3285.

0022-3263/85/1950-1621$01.50/0

$HgO/THF/H_3O^+$) to give 4-methylbicyclo[3.3.0]oct-3-en-2-one (11) (R = H) in 90% yield. While the yield in the thiophenyl-substituted Nazarov reaction is modest (35%), it is only marginally less (ca. 10%) than the typical yield described for the unsubstituted Nazarov reaction.[7] Overall, the route to 11 (R = H) is only two steps and conducted with readily available starting materials.

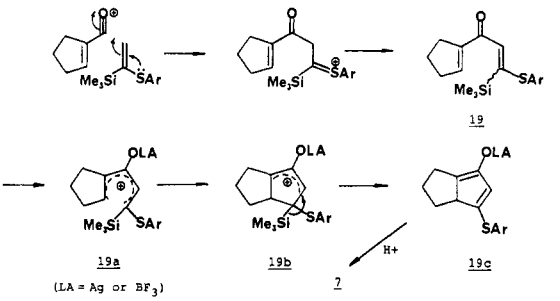


Similarly, treatment of the acid chloride **13** with **1** in the presence of $AgBF_4$ gave the bicyclo[4.3.0]nonenone **14** as a mixture of epimers at the secondary methyl group in 42% yield. In an effort to improve the yields of these cyclopentenone annulations we examined other derivatives of **1**. While the (methylthio)- and (*tert*-butylthio)-1-(trimethylsilyl)ethylenes gave no useful results, we reasoned that a substituent attached to sulfur, that would decrease the availability of electron density on sulfur and consequently suppress the formation of thioester byproducts, was needed. To test this hypothesis, the reagent 1-(trimethylsilyl)-1-[(2,4-dinitrophenyl)thio]ethylene (**15**) was treated with **5** (R = H) by using the standard set of experimental conditions ($AgBF_4/CH_2Cl_2/ClCH_2CH_2Cl$) to give **16** in 58% yield. This substantial increase in yield (23%) appears to justify the idea that suppression of the availability of the sulfur lone pairs of electrons would minimize the formation of undesired byproducts. Unfortunately, we were unable to add MeLi, MeMgBr, or Me_2CuLi to **16**, or carry out any mercuric ion assisted hydrolysis to give a β-diketone. The reagent 1-(trimethylsilyl)-1-[(4-chlorophenyl)thio]ethylene (**17**) gave the bicyclic enone **18** in only 15% yield.

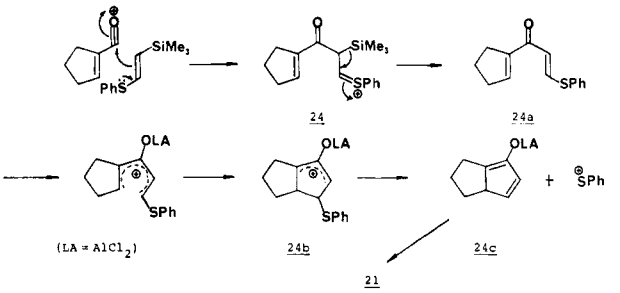


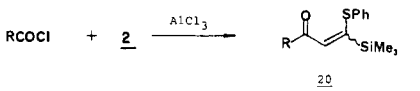
A plausible mechanistic interpretation of these thiophenyl substituted cyclopentenone annulations is outlined in Scheme I. The first phase of the reaction is dominated by the nucleophilicity of the thioenol ether functionality, leading to the cross-conjugated dienone **19**. This is consistent with the observation that saturated acid chlorides, on treatment with **1** in the presence of $AlCl_3$, gave the adducts **20**.[7a] Conrotary cyclization (Nazarov reaction) via the pentadienyl cation **19a** to the oxyallyl cation **19b** places the trimethylsilyl group in the same plane as the empty $2p_z$ orbital. Consequently, the oxyallyl cation **19b** is stabilized by the trimethylsilyl group (β-effect) and subsequently eliminates the $SiMe_3$ group to give the diene **19c**, which on protonation gives the cis-fused 4-(phenylthio)-cyclopentenone **7**.

Scheme I



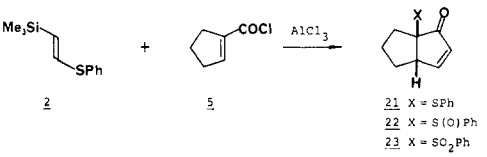
Scheme II





In terms of stabilization of cationic character, the trimethylsilyl group and the arylthio group in the reagent **1** are opposed to one another and are not in electronic concert. Consequently, a reagent based upon Si and S substituents that work together (both stabilize the buildup of electrophilic character) should accomplish the annulation reaction in Scheme I.

(Trimethylsilyl)acetylene and thiophenol (1:1) were irradiated with a 450-W UV lamp to give 1-(trimethylsilyl)-2-(phenylthio)ethylene (**2**) in 98.8% yield.[8] Treatment of **5** with **2** in the presence of $AlCl_3/ClCH_2CH_2Cl$ at 50 °C gave, unexpectedly, the bicyclo[3.3.0]octenone **21** (55%). The structure of **21** was established by successive oxidations, first to the sulfoxide **22** (mixture of diastereomers) by using $NaIO_4$/MeOH, and subsequently treatment of **22** with MCPBA gave the crystalline sulfone **23**, whose structure was determined by single-crystal X-ray crystallography.[9] This remarkable phenylthio group rearrangement may be rationalized in the following way, Scheme II. Acylation of **2** with **5** parallels Scheme I in that the nucleophilicity of the thioenol ether functionality dominates the first step to give the sulfonium ion **24**. Since the $SiMe_3$ group is β to a sulfonium ion, it can be lost at



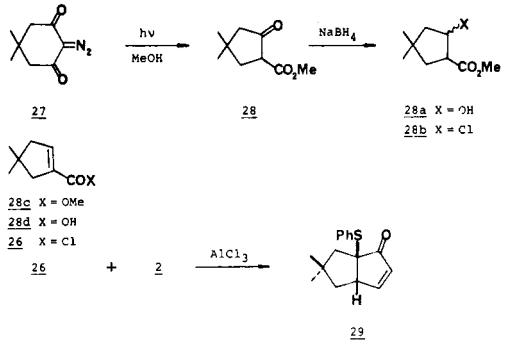
(8) Komarov, N. V.; Torosh, O. G., *Izv. Akad. Nauk SSR Ser. Khim.* **1967**, *3*, 690.

(9) The X-ray crystallographic details (see also ref 6) are available in the supplementary material.

this stage to give the cross-conjugated dienone **24a**. Conrotatory cyclization of **24a** leads to the oxyallyl cation **24b**, which can lose PhS^+ to give the kinetic enolate **24c**. Sulfenylation of **24c** with the in situ generated PhS^+ gives **21**.[10] Rather than compilate an extensive list of examples of these annulations we proceeded directly to apply this chemistry to the total synthesis of racemic hirsutene **25**.[11]

A substantial number of sesquiterpene natural products, having the linearly fused cis,anti,cis-tricyclo[6.3.0.$0^{2,6}$]undecanoid carbon skeleton, have been isolated.[12] More recently, the antitumor substance coriolin and hirsutic acid have become the successful targets of many diverse synthetic approaches aimed at developing the methods available for making five-membered rings.[12]

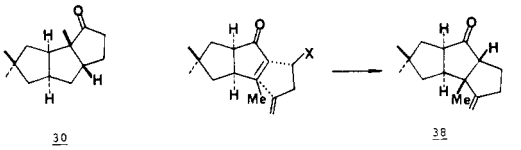
The first requirement of a synthesis of hirsutene (**25**), dependent upon the 1-(trimethylsilyl)-1-(phenylthio)-ethylene annulation strategy, is a convenient synthesis of 4,4-dimethylcyclopentenoyl chloride **26**. The known diazo dione **27** was irradiated in methanol to give the β-keto ester **28** (82%).[13] Reduction of **28** with $NaBH_4$/MeOH gave the alcohol **28a** as a mixture of cis and trans isomers (3:1). Treatment of **28a** with $SOCl_2$/pyridine gave the β-chloride **28b** (72%), which on exposure to DBU/CH_2Cl_2 gave the α,β-unsaturated ester **28c** (94%). Standard base hydrolysis of **28c** gave the acid **28d** (96%), mp 57–59 °C, which was converted into the acid chloride **26** (68%) by treatment with oxalyl chloride in benzene.



With the α,β-unsaturated acid chloride **26**, we examined its annulation with **1** and **2**. Treatment of **26** with **2** in the presence of $AlCl_3$/$ClCH_2CH_2Cl$ gave **29** (40%), and similarly, when **26** was treated with **1** in the presence of $AgBF_4$/CH_2Cl_2/$ClCH_2CH_2Cl$ at −20 °C, the required bicyclic enone **8** (38%) was isolated.

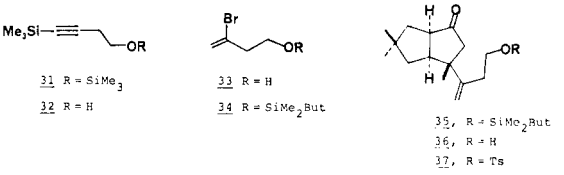
The β-thiophenyl enone **8** was treated with MeLi/Et_2O at −78 °C, followed by workup with H_3O^+/$HgCl_2$/HgO to give the known enone **12** (93%).[14] This sequence provides a convenient synthesis of **12** and confirms the structure of **8**.

Scheme III



Most of the previous syntheses of hirsutene proceed through the known degradation product, namely the ketone **30**, and convert this ketone, using the Wittig reaction, into hirsutene **25**.[11] Our specific objective was to add the requisite four-carbon unit to **12** with the *exo*-methylene group intact, and thus avoid correlation with **30** and proceed directly to hirsutene (**25**). This strategy is outlined in Scheme III. We required a four-carbon unit capable of fulfilling the role outlined in Scheme III. Semmelhack[15] has described a similar strategy, and more recently Piers[16] has reported a general solution to this type of *exo*-methylenecyclopentane annulation using organostannane chemistry.

3-Bromo-3-buten-1-ol (**33**) was made by using a procedure developed by Boeckman.[17] 3-Butyn-1-ol was treated with *n*-BuLi followed by $ClSiMe_3$ to give 1-[(trimethylsilyl)oxy]-4-(trimethylsilyl)-3-butyne (**31**). When **31** was exposed to HBr gas at 0 °C, with careful monitoring by gas chromotography, selective desilylation of the protected primary alcohol took place to give **32**. Further exposure to the above conditions gave the vinyl bromide **33** (65%) which was protected as its *tert*-butyldimethylsilyl ether **34** (89%).



After considerable experimentation we found that treatment of the vinyl bromide **34** with *t*-BuLi in ether at −120 °C gave the vinyllithium compound (as judged by quenching with 2-adamantanone).[18] The so generated vinyllithium compound was treated with CuI/HMPT, following a procedure described by Semmelhack[15] and Noyori and Hooz.[19] The resulting mixture, at −78 °C, was treated with BF_3OEt_2[20] followed by the enone **12**. In this way we were able to isolate the conjugate addition adduct **35** in 60% yield. The 1,4-addition was completely stereospecific, no evidence could be found for any of the β-stereoisomer. Desilylation of the protected primary alcohol **35** with $BzEt_3N^+Cl^-$/KF, $2H_2O$/CH_3CN[21] gave **36** (84%), which was converted into its *p*-toluenesulfonate

(10) Gerber, U.; Widmer, U.; Schmid, R. *Helv. Chim. Acta* **1978**, *83*, 61. Kozikowski, A. P.; Huie, E.; Springer, J. P. *J. Am. Chem. Soc.* **1982**, *104*, 2059 and reference cited therein. Browbridge, P.; Warren, S. *J. Chem. Soc., Perkin Trans. 1* **1976**, 2125.

(11) The isolation, structure, and first synthesis of hirsutene was reported by Nozoe in 1976: Nozoe, S.; Furukawa, J.; Sankawa, U.; Shibata, S. *Tetrahedron Lett.* **1976**, 195. Ohfune, Y.; Shirahama, H.; Matsumoto, T., *Tetrahedron Lett.* **1978**, 1991. Tatsuta, K.; Akimoto, K.; Kinoshita, M. *J. Am. Chem. Soc.* **1979**, *101*, 6116. Greene, A. E. *Tetrahedron Lett* **1980**, 3059. Hudlicky, T.; Kutchan, T.; Wilson, S. R.; Mao, D. T. *J. Am. Chem. Soc.* **1980**, *102*, 6351. Little, R. D.; Muller, G. W. *J. Am. Chem. Soc.* **1981**, *103*, 2744. Mehta, G.; Reddy, A. V. *J. Chem. Soc., Chem. Commun.* **1981**, 756. Wender, P. A.; Howbert, J. J. *Tetrahedron Lett.* **1982**, 3983. Hayano, K.; Ohfune, Y.; Shirahama, H.; Matsumoto, T. *Helv. Chim. Acta* **1981**, *64*, 1347. Ley, S. V.; Murray, P. J. *J. Chem. Soc., Chem. Commun.* **1982**, 1252. Little, R. D.; Higby, R. G.; Moeller, K. D. *J. Org. Chem.* **1983**, *48*, 3139. Dawson, B. A.; Ghosh, A. K.; Jurlina, J. L.; Stothers, J. B. *J. Chem. Soc., Chem. Commun.* **1983**, 204.

(12) For a recent review of polyquinane chemistry see: Paquette, L. A. "Recent Synthetic Developments in Polyquinane Chemistry"; Springer-Verlag: Berlin, 1984.

(13) Capiano, L.; Kirn, R. H.; Zander, R. *Chem. Ber.* **1976**, *109*, 2456. Froberg, J.; Magnusson, G. *J. Am. Chem. Soc.* **1978**, *100*, 6728.

(14) 4,7,7-Trimethyl-*cis*-bicyclo[3.3.0]oct-3-en-2-one is a well-known compound that has been prepared by a variety of routes: Fex, T.; Froberg, J.; Magnusson, G.; Thorén, S. *J. Org. Chem.* **1976**, *41*, 3518. (This is a very convenient method, especially on a large scale.) Ohfune, Y.; Shirahama, H.; Matsumoto, T. *Tetrahedron Lett.* **1975**, 4377. Miyano, K.; Ohfune, Y.; Azuma, S.; Matsumoto, T. *Tetrahedron Lett.* **1974**, 1545. Paquette, L.; Farkas, E.; Galemmo, R. *J. Org. Chem.* **1981**, *46*, 5434.

(15) Semmelhack, M. F.; Yamashita, A.; Tomesch, J. C.; Hirotsu, K. *J. Am. Chem. Soc.* **1978**, *100*, 5565.

(16) Piers, E.; Karunaratne, V. *J. Chem. Soc., Chem. Commun.* **1983**, 935.

(17) Boeckman, R. K., Jr.; Blum, D. M. *J. Org. Chem.* **1974**, *39*, 3307.

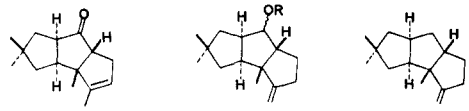
(18) Seebach, D.; Newman, H. *Ber. Dtsch. Chem. Ges.* **1974**, *107*, 847.

(19) Suzuki, M.; Suzuki, T.; Kawagishi, T.; Noyori, R. *Tetrahedron Lett.* **1980**, 1247. Hooz, J.; Layton, R. B. *Can. J. Chem.* **1970**, *48*, 1626.

(20) Smith, A. B.; Jerris, P. *J. Am. Chem. Soc.* **1981**, *103*, 194.

(21) Carpino, L. A. *J. Chem. Soc., Chem. Commun.* **1979**, 514.

ester **37** (94%) by standard methods. Since **37** is a homoallylic tosylate, it was quite probable that elimination to a diene could readily take place. Fortunately, when **37** was exposed to lithium bis(trimethylsilyl)amide at −78 °C followed by warming to −30 °C, the tricyclic ketone **38** (75%), mp 20–25 °C, was formed. The only remaining step needed to synthesize hirsutene (**25**) is removal of the 8-keto function. This is not a trivial task, since the 8-keto group is very sterically hindered. Indeed, the literature shows that reduction of **41** with the Wolff–Kishner method gave *endo*-hirsutene in only 8% yield.[22] Consequently, **38** was treated with $NaBH_4$/MeOH to give the alcohol **39** as a mixture of epimers, which were directly converted into their corresponding xanthate derivatives **40** by treatment with CS_2/NaH/MeI/THF.[23] The epimeric mixture of xanthates **40** was treated with *n*-Bu_3SnH/benzene/AIBN (catalytic)[24] to give (±)-hirsutene (**25**) (70%). The number of steps from **26** to **25** is nine and proceeds in an overall yield of 7%. The thiophenyl-substituted cyclopentenone annulations should be of general use in synthesis, the illustration provided here for the synthesis of hirsutene being exemplary.



41 39 R = H; 40 R = CS_2Me 25

Experimental Section

Infrared spectra were determined on a Perkin Elmer 267 or 298 grating spectrometer, as thin films for liquids, and solutions in $CHCl_3$ for solids. ^1H NMR spectra were taken on the following instruments: Varian EM 360(60MHz), EM 390(90MHz), HR-220 (220 MHz), and Nicolet NT-360(360MHz) spectrometers. ^{13}C NMR spectra were taken on a Bruker WP-80(80MHz) or a Nicolet NT-360 spectrometer. Mass spectra were obtained on either an AEI MS-9 double focussing mass spectrometer, or a Hewlett-Packard 5990 GC/MS unit. Melting points were measured on a Thomas-Hoover capillary apparatus and are uncorrected. Microanalyses were performed by Midwest Microlabs, Inc., Indianapolis, IN.

Gas chromatographs were carried out with a Perkin Elmer 3920 B instrument, employing either a 10% SE-30 or 10% OV-1 stationary phase on WHP support in a 6 ft × $^1/_8$ in. column. Thin-layer chromatography was conducted with Merck silica gel 60F-25F sheets, which were visualized with either shortwave UV light, I_2–H_2SO_4, or 7% phosphomolybdic acid in ethanol. Preparative-layer chromatography was performed with Merck precoated 60F-254 plates (0.5 mm). Column chromatography was conducted with EM silica gel 60 (70–230 mesh). Flash column chromatography was carried out with EM silica gel 60H.

All solvents were purified prior to use by standard methods. Reactions were run under an atmosphere of argon with magnetic stirring, unless otherwise stated.

1-Cyclopentenoyl Chloride 5 (R = H). Prepared from cyclopentanone via 1-cyano-1-cyclopentanol, 1-cyano-1-cyclopentene, and cyclopentene-1-carboxylic acid, mp 120–121 °C.[25]

4-(Phenylthio)-*cis*-bicyclo[3.3.0]oct-3-en-2-one (7) (R = H). To a solution of $AgBF_4$ (2.50 g, 0.012 mol) in dry 1,2-dichloroethane (9 mL) and dry dichloromethane (6 mL), cooled to −50 °C, was added 1-(trimethylsilyl)-1-(phenylthio)ethylene (**1**) (1.70 g, 0.008 mol), followed immediately by 1-cyclopentenoyl chloride (1.20 g, 0.010 mol) via a syringe. A precipitate was formed and the mixture turned red-brown. After 20 h, at 20 °C the above mixture was filtered through Celite and quenched with 10% aqueous $NaHCO_3$ (25 mL). The heterogeneous mixture was extracted with dichloromethane (2 × 25 mL) and the combined organic phases were washed with water (2 × 40 mL), dried (Na_2SO_4), and evaporated in vacuo. The residue was purified by chromatography over silica gel eluting with EtOAc–hexane (1/4) to give **7** (R = H) as a light yellow oil (0.64 g, 35%): IR 3050, 2950, 1690, 1550, 1270 and 750 cm^{-1}; NMR (CCl_4, 60MHz) δ 7.50–7.05 (5 H, m), 5.10 (1 H, s), 3.28–2.90 (1 H, m), 2.82–2.90 (1 H, m), 2.82–2.33 (1 H, m), and 1.94–1.05 (6 H, m); ^{13}C NMR ($CDCl_3$, 80 MHz) ppm 207.158, 183.794, 134.517, 129.844, 129.662, 129.358, 125.535, 52.287, 48,646, 30,622, 28.923 and 24.007; MS, calcd for $C_{14}H_{14}OS$ *m/e* 230.0765, obsd 230.0759. Anal. Calcd for $C_{14}H_{14}OS$: C, 73.04; H, 6.09. Found: C, 72.79; H, 6.16.

4-Methylbicyclo[3.3.0]oct-3-en-2-one (11) (R = H). To a solution of **7** (R = H) (0.10 g, 0.44 mmol) in dry ether (4 mL) at −78 °C, was added methyllithium (0.66 mmol, 0.44 mL of a 1.5 M solution in ether). After 1 h methanol (1 mL) was added, followed by water (1 mL). The mixture was evaporated and THF (3 mL)/H_2SO_4 (2 mL of a 4 N solution) added, followed by $HgCl_2$ (0.08 g) and HgO (0.01 g). After 4 h at 20 °C saturated aqueous $NaHCO_3$ was added and the mixture extracted with dichloromethane (3 × 10 mL). The combined organic phases were washed with water (3 × 10 mL), dried (Na_2SO_4) and evaporated. The residue was dissolved in hexane and chromatographed over silica gel eluting with EtOAc–hexane (4/1) to give **11** (R = H) (0.05 g, 90%): IR 3050, 2955, 2865, 1695, 1620, 1260 and 810 cm^{-1}; NMR (CCl_4, 60 MHz) δ 5.60 (1 H, bs), 3.00–2.65 (1 H, m), 2.60–2.25 (1 H, m), 1.90 (3 H, s) and 1.90–1.00 (6 H, m); MS calcd for $C_9H_{12}O$ *m/e* 136.0888, obsd 136.0891.

9-Methyl-4-(phenylthio)-*cis*-bicyclo[4.3.0]non-3-en-2-one (14). To a solution of $AgBF_4$ (1.60 g, 0.008 mol) in dry 1,2-dichloroethane (8 mL) and dry dichloromethane (5 mL) at −50 °C was added 1-(trimethylsilyl)-1-(phenylthio)ethylene (0.85 g, 0.004 mol), followed by 6-methyl-1-cyclohexenoyl chloride (0.95 g, 0.006 mol). Workup as for the previous example of the type of reaction gave two stereoisomers. **14** (0.43 g, 42%): IR 3050, 2945, 1690, 1580 and 760 cm^{-1}; MS, calcd for $C_{16}H_{18}OS$ *m/e* 258.1078, obsd 258.1085. The first stereoisomer: R_f 0.55 (EtOAc–hexane 1:4); NMR (CCl_4, 60 MHz) δ 7.57–7.13 (3 H, m), 7.13–6.87 (2 H, m), 5.20 (1 H, bs), 3.13–1.17 (9 H, m) and 0.98 (3 H, d, *J* = 7 Hz). The second stereoisomer: R_f 0.50; NMR (CCl_4, 60 MHz) δ 7.56–7.06 (3 H, m), 7.06–6.76 (2 H, m), 5.10 (1 H, s), 2.95–1.20 (9 H, m) and 1.00 (3 H, d, *J* = 7 Hz).

1-(Trimethylsilyl)-1-[(2,4-dinitrophenyl)thio]ethylene (15). To a solution of 2,4-dinitrobenzenesulfenyl chloride (7.04 g, 0.03 mol) in dry dichloromethane (50 mL) at −78 °C was added vinyltrimethylsilane (3.0 g, 0.03 mol). The mixture was warmed to 20 °C and after 12 h filtered and concentrated in vacuo to leave an orange residue. The residue, in dry dichloromethane (65 mL) at 0 °C was treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (9.2 g, 0.06 mol) and warmed to 20 °C. After 12 h the mixture was washed with 5% aqueous HCl (3 × 60 mL) and brine (60 mL), dried (Na_2SO_4), and evaporated. The residue was purified by chromatography over silica gel eluting with EtOAc–hexane (1:1) to give **15** (7.24 g, 81%): mp 63–65 °C (from hexane); IR (Nujol mull) 3090, 2940, 1580, 1500, 1330, 1290, 840 and 730 cm^{-1}; NMR ($CDCl_3$, 60 MHz) δ 9.07 (1 H, d, *J* = 2.5 Hz), 8.28 (1 H, dd, *J* = 2.5 Hz and 9 Hz), 7.60 (1 H, d, *J* = 9 Hz), 6.53 (2 H, s) and 0.18 (9 H, s). Anal. Calcd for $C_{11}H_{14}N_2O_4SSi$: C, 33.17; H, 3.52; N, 7.04; S, 8.04. Found: C, 33.04; H, 3.42; N, 6.78; S, 7.84.

4-[(2,4-Dinitrophenyl)thio]-*cis*-bicyclo[3.3.0]oct-3-en-2-one (16). To a solution of $AgBF_4$ (0.24 g, 1.2 mmol) in dry 1,2-dichloroethane (3 mL) and dry dichloromethane (3 mL) at −25 °C was added **15** (0.36 g, 1.2 mmol) followed immediately by 1-cyclopentenoyl chloride (0.125 g, 1 mmol). After 4 h at 20 °C the mixture was worked up in the usual way to give **16** (0.186 g, 58%): mp 124–125 °C (from EtOAc–hexane); IR (Nujol mull) 3095, 2950, 2860, 1690, 1590, 1525, 1340, 1265, 835, 745 and 735 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 8.83 (1 H, d, *J* = 2.5 Hz), 8.40 (1 H, dd, *J* = 2.5 Hz and 8 Hz), 7.88 (1 H, d, *J* =8 Hz), 5.85 (1 H, s), 3.57–3.33 (1 H, m), 3.05–2.83 (1 H, m) and 2.00–1.13 (6 H, b); MS, calcd for $C_{14}H_{12}N_2O_5S$ *m/e* 320.0467, obsd 320.0474. Anal. Calcd for

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$C_{14}H_{12}N_2O_5S$: C, 52.50; H, 3.75. Found: C, 52.80; H, 3.87.

4-[(4-Chlorophenyl)thio]-*cis*-bicyclo[3.3.0]oct-3-en-2-one (18). To a solution of $AgBF_4$ (0.605 g, 3.1 mmol) in dry 1,2-dichloroethane (7 mL) and dry dichloromethane (7 mL) at −50 °C was added **17** (0.97 g, 4 mmol) followed immediately by 1-cyclopentenoyl chloride (0.37 g, 3 mmol). After 16 h at 20 °C the mixture was worked up in the usual way to give **18** (0.150 g, 15%): IR (thin film) 3050, 2950, 2880, 1685, 1550, 1270, 750 and 690 cm^{-1}; NMR (CCl_4, 90 MHz) 7.37 (4 H, s), 5.32 (1 H, s), 3.40–3.13 (1 H, m), 2.90–2.63 (1 H, m) and 2.0–1.0 (6 H, b); MS, calcd for $C_{14}H_{13}OSCl$ m/e 264.0376, obsd 264.0362.

(*E*)-1-(Trimethylsilyl)-2-(phenylthio)ethylene (2). Thiophenol (3.0 g, 0.027 mol) and (trimethylsilyl)acetylene (3.9 g, 0.040 mol) were irradiated with a 450-W UV lamp for 0.5 h. Distillation afforded **2** (5.56 g, 98.8%): bp 76–78 °C (0.2 torr); IR 3060, 2950, 2890, 1540, 1475, 1245, 950 and 850 cm^{-1}; NMR (CCl_4, 60 MHz) δ 7.05–7.37 (5 H, m), 6.60 (1 H, d, J = 18 Hz), 5.70 (1 H, d, J = 18 Hz) and 0.10 (9 H, s).

1-(Phenylthio)-*cis*-bicyclo[3.3.0]oct-3-en-2-one (21). To a mixture of $AlCl_3$ (0.33 g) in dry 1,2-dichloroethane (10 mL) at 20 °C was added (*E*)-1-(trimethylsilyl)-2-(phenylthio)ethylene (**2**) (0.60 g, 3 mmol), followed by 1-cyclopentenoyl chloride (0.25 g, 2 mmol). After 1 h at 20 °C, the mixture was heated at 80 °C for 18 h. Workup in the usual way gave **21** (0.25 g, 55%) as a yellow oil: IR 3050, 2940, 1705, 1585, 750 and 690 cm^{-1}; NMR (CCl_4, 60 MHz) δ 7.58–7.12 (6 H, m), 5.97 (1 H, dd, J = 2 Hz and 7 Hz), 3.26 (1 H, m) and 1.1–2.3 (6 H, m); MS, calcd for $C_{14}H_{14}OS$ m/e 230.0765, obsd 230.0759.

1-(Phenylsulfinyl)-*cis*-bicyclo[3.3.0]oct-3-en-2-one (22). To a solution of sodium periodate (0.128 g) in water (4 mL) was added **21** (91 mg) in methanol (8 mL). After 2 h, water (8 mL) was added and the mixture extracted with dichloromethane (2 × 25 mL), dried (Na_2SO_4), and evaporated. The residue was purified by PLC eluting with EtOAc–hexane (3:7) to give **22** (63 mg, 64%): mp 99–105 °C (as a mixture of sulfoxide epimers 2:1); IR ($CHCl_3$) 3050, 2940, 1705, 1590, 1050 and 695 cm^{-1}; NMR (CCl_4, 90 MHz) δ 7.37 (5 H, b), 7.10 (1 H, dd, J = 7 Hz and 3 Hz), 6.10 and 5.63 (1 H, dd, J = 7 Hz and 1.5 Hz) in the ratio 1:2, 3.83 and 3.63 and 3.57–3.33, in a ratio of 1:2 (1 H, m) and 2.37–1.00 (6 H, m); MS, calcd for $C_{14}H_{14}O_2S$ m/e 246.0714, obsd 246.0719.

1-(Phenylsulfonyl)-*cis*-bicyclo[3.3.0]oct-3-en-2-one (23). To a solution of **22** (15 mg) in dry dichloromethane (0.35 mL) at 0 °C was added *m*-chloroperoxybenzoic acid (16 mg). After 3 h at 20 °C the mixture was quenched with 10% aqueous $NaHSO_3$ (1 mL) and extracted with dichloromethane (2 × 2 mL). The combined extracts were washed with 25% aqueous $NaHCO_3$ solution (2 × 3 mL), dried (Na_2SO_4), and evaporated to give **23** (13 mg, 83%). Recrystallization from hexane gave colorless cubes suitable for single-crystal X-ray crystallography: mp 155–157 °C; NMR ($CDCl_3$, 220 MHz) δ 7.38–7.44 (6 H, m), 6.08 (1 H, dd, J = 5 Hz and 2 Hz), 4.00 (1 H, br d, J = 9 Hz) and 2.28–1.14 (6 H, m). Anal. Calcd for $C_{14}H_{14}O_3S$: C, 64.12; H, 5.34. Found: C, 64.32; H, 5.17.

2-Diazo-5,5-dimethyl-1,3-cyclohexanedione (27). Prepared according to the procedure of Doering and Depuy from dimedone to give **27** as yellow crystals (75%): mp 106–107 °C lit.[26] mp 106–108 °C).

2-(Methoxycarbonyl)-4,4-dimethylcyclopentanone (28). Prepared according to the procedure of Froberg and Magnusson[13] from **27** to give **28** as a colorless oil (82%): bp 60–62 °C (0.15 torr); NMR (CCl_4, 60 MHz) δ 3.63 (3 H, s), 3.47–3.13 (1 H, t, J = 10 Hz), 2.10 (2 H, s), 2.10–1.95 (2 H, d, J = 10 Hz), 1.17 (3 H, s) and 0.95 (3 H, s).

4,4-Dimethylcyclopent-1-ene-1-carboxylic Acid (28d). To a solution of **28** (5.10 g, 0.03 mol) in methanol (120 mL) at 0 °C was added $NaBH_4$ (2.28 g, 0.06 mol). After 0.5 h the mixture was worked up in the usual way to give **28a** (5.12 g, 100%) as a mixture (3:1) of cis and trans isomers: NMR (CCl_4, 60 MHz) δ 4.53–4.23 (1 H, q, J = 4 Hz), 3.62 (3 H, s), 3.10–2.63 (2 H, m), 2.00–1.40 (4 H, m), 1.17 (3 H, s) and 0.90 (3 H, s) for the cis isomer, 4.64–4.20 (1 H, q, J = 7.5 Hz), 3.63 (3 H, s), 3.17 (1 H, bs), 3.00–2.50 (1 H, dt, J = 7.5 and 3 Hz), 2.10–1.20 (4 H, m), 1.05 (3 H, s) and 0.95 (3 H, s).

A solution of **28a** (5.00 g, 0.029 mol) in dry pyridine (2.8 mL) at 0 °C was treated with thionyl chloride (4.05 g, 0.034 mol). After 3 h at 20 °C the mixture was warmed to 65 °C for 1 h and cooled to 20 °C, ether (40 mL) added, and the mixture filtered. The ether extracts were washed with 5% aqueous HCl (2 × 50 mL) and water (50 mL) and dried ($MgSO_4$). Evaporation and chromotography of the residue over silica gel eluting with EtOAc–hexane (1:4) gave **28b** (4.00 g, 72%).

To a solution of **28b** (4.00 g, 0.021 mol) in dry dichloromethane (100 mL) at 0 °C was added 1,8-diazobicyclo[5.4.0]undec-7-ene (4.85 g, 0.032 mol). The mixture was stirred at 20 °C for 3 h and worked up in the usual way to give **28c** (3.05 g, 94%): IR (thin film) 2950, 2860, 1715, 1630, 1250 and 730 cm^{-1}; NMR (CCl_4, 60 MHz), δ 6.67–6.50 (1 H, b), 3.60 (3 H, s), 2.43–2.10 (4 H, m) and 1.05 (6 H, s).

Standard base hydrolysis of **28c** (3.05 g) gave the required acid **28d** (2.62 g, 96%): mp 57–59 °C (from $CHCl_3$–hexane); IR ($CHCl_3$) 3400–2400, 1685, 1620 cm^{-1}; NMR ($CDCl_3$, 60 MHz) δ 11.90 (1 H, bs, exchanged by D_2O), 6.83–6.66 (1 H, bt), 2.44–2.17 (4 H, m) and 1.05 (6 H, s); MS, calcd for $C_8H_{12}O_2$ m/e 140.0837, obsd 140.0841.

4,4-Dimethyl-1-cyclopentenoyl Chloride (26). To a solution of the acid **28d** (4.00 g, 0.028 mol) in dry benzene (50 mL) at 0 °C was added oxalyl chloride (5.70 g, 0.045 mol). After 0.5 h at 0 °C the mixture was heated to 70 °C for 1 h and evaporated to give **26** (3.00 g, 68%) purified by distillation: mp 90–95 °C (20 torr); IR (thin film) 2950, 1750, 1680, 1240 and 750 cm^{-1}; NMR (CCl_4, 60 MHz) δ 6.97–6.73 (1 H, bt), 2.52–2.25 (4 H, m) and 1.09 (6 H, s).

1-(Phenylthio)-7,7-dimethyl-*cis*-bicyclo[3.3.0]oct-3-en-2-one (29). To a solution of $AlCl_3$ (1.20 g, 9 mmol) in dry 1,2-dichloroethane (20 mL) at 20 °C was added (*E*)-1-(trimethylsilyl)-2-phenylthio)ethylene (1.87 g, 9 mmol), followed by 4,4-dimethyl-1-cyclopentenoyl chloride (**26**) (1.20 g, 7.5 mmol). After 8 h at reflux, workup gave **29** (0.75 g, 40%): IR (thin film) 3050, 2950, 1700, 1580, 750 and 690 cm^{-1}; NMR (CCl_4, 90 MHz) δ 7.45–7.08 (6 H, m), 5.85 (1 H, dd, J = 2 Hz and 7 Hz), 3.30 (1 H, bm), 2.40 (2 H, m), 1.85 (2 H, m), 1.13 (3 H, s), 0.87 (3 H, s). Anal. Calcd for $C_{16}H_{18}OS$: C, 74.42; H, 6.98. Found: C, 74.32; H, 6.78.

4-(Phenylthio)-7,7-dimethyl-*cis*-bicyclo[3.3.0]oct-3-en-2-one (8). To a solution of $AgBF_4$ (4.30 g, 0.022 mol) in dry dichloromethane (10 mL) and dry 1,2-dichloroethane (15 mL) at −50 °C was added **1** (4.58 g, 0.022 mol) followed immediately by 4,4-dimethyl-1-cyclopentenoyl chloride (**26**) (3.00 g, 0.019 mol). After 20 h at 20 °C the mixture was worked up in the usual way to give **8** (1.84 g, 38%): IR (thin film) 3050, 2950, 1685, 1550, 1435, 1270, 1180 and 690 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 7.50–7.10 (5 H, m), 5.17 (1 H, s), 3.50–3.18 (1 H, m), 3.10–2.76 (1 H, m), 1.85–1.00 (4 H, m), 0.88 (3 H, s) and 0.85 (3 H, s); ^{13}C NMR (80 Mhz) ppm 207.401, 184.522, 134.638, 129.965, 129.783, 129.480, 122.986, 52.772, 49.434, 45.126, 43.366, 41.849, 28.498 and 27.891. Anal. Calcd for $C_{16}H_{18}OS$: C, 74.42; H, 6.98. Found: C, 74.73; H, 7.27.

4,7,7-Trimethylbicyclo[3.3.0]oct-3-en-2-one (12). To a solution of **8** (0.80 g) in dry ether (20 mL) at −78 °C was added MeLi (3.0 mL of a 1.5 M solution in ether). After 4 h at −78 °C, the above mixture was quenched with water (1 mL) and evaporated. The residue was dissolved in THF (15 mL) and treated with 4 N H_2SO_4 (10 mL)/$HgCl_2$ (1.63 g)/HgO (catalyst). The mixture was stirred at 20 °C for 14 h, neutralized with aqueous NaOH, and evaporated and the residue extracted with ether (3 × 20 mL). The combined extracts were dried (Na_2SO_4) and evaporated, and the residue was purified by column chromatography eluting with ether–hexane (1:1) to give **12**[14] (0.46 g, 93.5%): IR (thin film) 2945, 2850, 1695, 1620 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 5.67 (1 H, bs), 3.43–3.07 (1 H, m), 3.05–2.70 (1 H, m), 2.00 (3 H, s), 1.92–1.10 (4 H, m), 0.94 (6 H, s).

3-Bromo-3-buten-1-ol (33). 3-Butyn-1-ol (5.76 g, 0.082 mol) in ether (50 mL) at −78 °C was treated with *n*-BuLi (103 mL of a 1.6 M solution in hexane), warmed to −40 °C, and then recooled to −78 °C, and $ClSiMe_3$ (17.90 g, 0.65 mol) added dropwise. The mixture was warmed to 20 °C. After 6 h the reaction was quenched with water (100 mL) and extracted with ether (75 mL). The dried (Na_2SO_4) extract was evaporated and the residue distilled under vacuum to give 1-[(trimethylsilyl)oxy]-4-(trimethylsilyl)-3-butyne (**31**) (11.2 g, 63%): bp 90–92 °C (20 torr); IR (thin film) 2940, 2165, 1250, 1100 cm^{-1}; NMR (CCl_4, 90 MHz)

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δ 3.67 (2 H, t, J = 7 Hz), 0.09 (9 H, s) and 0.06 (9 H, s).

The above bis(trimethylsilyl) adduct **31** (10.0 g) was cooled to 0 °C and HBr gas bubbled through the liquid with continuous monitoring by gas chromotography. After 1 h the mixture was poured into saturated aqueous $NaHCO_3$ (30 mL) and extracted with ether (3 × 30 mL). The combined, dried (Na_2SO_4) ether solution was evaporated and the crude 1-(trimethylsilyl)-1-butyn-4-ol (**32**) used directly in the next stage.

Hydrogen bromide was bubbled through 1-(trimethylsilyl)-1-butyn-4-ol (6.25 g) at 0 °C. After 2 h work up as above gave **33** (4.3 g, 65% from **31**): bp 80–82 °C (30 torr); IR (thin film) 3340, 2950, 1630, 1050, 890 and 840 cm^{-1}; NMR (CCl_4, 90 MHz) δ 5.67 (1 H, d, J = 1.5 Hz), 5.50 (1 H, d, J = 1.5 Hz), 3.77 (2 H, t, J = 7 Hz), 2.77 (1 H, s) and 2.63 (2 H, t, J = 7 Hz). Anal. Calcd for C_4H_7BrO: C, 31.17; H, 4.55; Br, 52.60. Found: C, 30.89; H, 4.45; Br, 52.71.

[(3-Bromo-3-butenyl)oxy]-*tert*-butyldimethylsilane (34). 3-Bromo-3-buten-1-ol (3.8 g, 0.025 mol), Et_3N (5.05 g), p-(dimethylamino)pyridine (0.1 g) in dry dichloromethane (20 mL) at 0 °C was treated with t-$BuMe_2SiCl$ (5.65 g) in dry dichloromethane (10 mL). After 12 h at 20 °C workup gave **34** (5.0 g, 89%): bp 94–97 °C (20 torr); IR (thin film) 2950, 2920, 2850, 1630, 1255, 1100, 835 and 775 cm^{-1}; NMR (CCl_4, 90 MHz) δ 5.60 (1 H, d, J = 1.5 Hz), 5.43 (1 H, d, J = 1.5 Hz), 3.75 (2 H, t, J = 6 Hz), 2.47 (2 H, t, J = 6 Hz), 0.83 (9 H, s), 0.02 (6 H, s).

4,7,7-Trimethyl-4-[1-[2-[(*tert*-butyldimethylsilyl)oxy]-ethyl]vinyl]-*cis*-bicyclo[3.3.0]octan-2-one (35). The vinyl bromide **34** (1.72 g, 6.5 mmol) in dry ether (13 mL) at −120 °C (liquid N_2 in MeOH) was treated with t-BuLi (5.2 mL of a 2.5 M solution in hexane) rapidly in one portion. To this solution was added a freshly prepared solution of CuI (1.24 g)/HMPT (2.45 g) in ether (12 mL) at −120 °C. The mixture was warmed to −78 °C for 1 h and freshly distilled BF_3OEt_2 (1.56 g) added, followed by the dropwise addition of the enone **12** (0.74 g, 4.5 mmol) in dry ether (2 mL). The mixture was warmed to −20 °C and left at this temperature for 8 h. The above solution was poured into aqueous NH_4Cl/6 N HCl (4:1 by volume) and extracted with ether (3 × 25 mL). The combined extracts were washed with 20% aqueous NH_4OH (2 × 60 mL), 2% aqueous HCl (60 mL), and water (60 mL), dried (Na_2SO_4), and evaporated. The residue was purified by flash chromatography eluting with ether–hexane (1:3) to give **35** (0.946 g, 60%; 74% adjusted for 0.102 g of recovered starting enone **12**): IR (thin film) 2950, 2850, 1740, 1470, 1255, 1110, 840 and 785 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 4.78 (1 H, s), 4.73 (1 H, s), 3.68 (2 H, t, J = 8 Hz), 2.33 (2 H, t, J = 8 Hz), 2.20–2.05 (3 H, m), 1.33–1.05 (5 H, m), 1.10 (3 H, s), 1.02 (3 H, s), 0.90 (3 H, s), 0.83 (9 H, s) and 0.01 (6 H, s); MS, $C_{21}H_{38}O_2Si$ (GC) 294 (2.8%), 293 (12.1%), 145 (16.0%), 139 (10.9%), 131 (21.4%), 123 (16.9%) 75 (100%).

(±)-Hirsuten-8-one (38). A mixture of **35** (0.60 g, 1.7 mmol), benzyltriethylammonium chloride (2.05 g, 9 mmol), $KF2H_2O$ (2.27 g, 14 mmol) in acetonitrile (12 mL) was heated at 60 °C for 10 h. The mixture was cooled, quenched with water (15 mL), and extracted with dichloromethane (3 × 10 mL). The combined extracts were washed with 10% brine (2 × 10 mL), dried (Na_2SO_4), and evaporated. The residue was purified by chromatography over florosil with gradient polarity elution from ether/hexane (1:9 to 1:3) to give **36** (0.338 g, 84%): IR (thin film) 3430, 2850, 1735, 1045 and 735 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 4.80 (1 H, s), 4.77 (1 H, s), 3.70 (2 H, m), 3.00–1.20 (16 H, m), 1.08 (3 H, s), 0.97 (3 H, s) and 0.87 (3 H, s).

The alcohol **36** (0.325 g, 1.4 mmol) was converted into its p-toluenesulfonate ester **37** (0.51 g, 94%) in the standard way: IR (thin film) 2950, 2860, 1735, 1465, 1360, 1185, 1170, 960, 900, 810 and 655 cm^{-1}; NMR ($CDCl_3$, 90 MHz) δ 7.73 (2 H, q, J = 8.5 Hz), 7.28 (2 H, q, J = 8.5 Hz), 4.78 (1 H, s), 4.63 (1 H, s), 4.10 (2 H, t, J = 7 Hz), 2.83–2.23 (5 H, m), 2.38 (3 H, s), 1.70–1.17 (5 H, m), 1.03 (3 H, s), 0.98 (3 H, s) and 0.87 (3 H, s).

The tosylate **37** (0.51 g, 1.3 mmol) was added to a solution of LiHMDS (2.6 mmol) in dry ether (10 mL) at −78 °C. After warming to −30 °C over 4 h the mixture was quenched with 1 N HCl (15 mL) and extracted with ether (2 × 15 mL). The extracts were washed with 1 N HCl (35 mL) and water (35 mL), dried (Na_2SO_4), and evaporated. The residue was chromatographed over silica eluting with ether–hexane (1:9) to give **38** (0.212 g, 75%): mp 20–25 °C; IR (thin film) 2950, 2860, 1735 cm^{-1}; NMR ($CDCl_3$, 220 MHz) δ 4.93 (2 H, bs), 2.80–2.70 (1 H, s), 2.60–2.20 (1 H, m), 2.20–1.95 (1 H, m), 1.90–1.50 (5 H, m), 1.12 (3 H, s), 1.02 (3 H, s) and 0.95 (3 H, s). Anal. Calcd for $C_{15}H_{22}O$: C, 82.57; H, 10.09. Found: C, 81.96; H, 10.34.

(±)-Hirsutene (25). To a solution of hirsuten-8-one (**38**) (86 mg, 0.4 mmol) in MeOH (5 mL) at 0 °C was added $NaBH_4$ (30 mg, 0.8 mmol). Workup in the usual way gave a mixture of (±)-hirsuten-8-ol epimers **39** (86.4 mg, 99.6%). To a solution of these epimers (86.4 mg) in THF (3 mL) at 20 °C was added NaH (55 mg, 59% in mineral oil) followed by imidazole (27 mg, 0.4 mmol) and CS_2 (0.122 g, 1.6 mmol). The above mixture was heated at 50 °C for 1 h, followed by addition of MeI (0.227 g, 1.6 mmol). Workup in the usual way, followed by purification by flash chromatography eluting with ether–hexane (2:98) gave **40** (0.114 g, 92%). The epimeric mixture of xanthates **40** (0.114 g, 0.37 mmol) in dry benzene (4 mL) was treated with azobis(isobutyronitrile) (3 mg) and freshly distilled tri-n-butyltin hydride (0.108 g, 0.37 mmol) added. The solution was heated at reflux for 2 h, cooled to room temperature, and evaporated in vacuo. The residue was purified by flash chromatography to give (±)-hirsutene (**25**) (52 mg, 70%): IR (thin film) 2940, 2860, 1645, 1460, 1375, 1360 and 870 cm^{-1}; NMR ($CDCl_3$ 360 MHz) δ 4.82 (1 H, s), 4.78 (1 H, s), 2.47 (3 H, m), 2.18 (1 H, m), 1.73 (1 H, m), 1.65 (1 H, m), 1.43 (6 H, m), 1.22 (1 H, m), 1.06 (3 H, s), 0.96 (3 H, s) and 0.93 (3 H, s); ^{13}C NMR δ 162.76, 103.50, 55.92, 53.43, 49.96, 48.97, 44.25, 41.86 40.86, 38.62, 30.90, 29.73, 27.24, 26.82 and 23.18.

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Supplementary Material Available: the complete details of the single-crystal X-ray crystallographic structure determination of **23** (12 pages), including an ORTEP drawing. Ordering information is given on any current masthead page.