Novel synthesis of a highly functionalized cyclopropane derivative

Stéphane Trudeau and Pierre Deslongchamps

Abstract: A model study was carried out to explore the feasibility of synthesizing fused tricyclic ring structures containing a C_7—C_8 double bond juncture (steroid numbering) by employing an S_N2' cyclization of a silyl enol ether to displace an allylic acetate as the key step. Instead of the anticipated product, highly functionalized cyclopropanes were obtained. These novel cyclopropane structures are the result of the concomitant 1,2-migration of a dithiane thioether moiety and the eventual displacement of the acetate group, followed by the cyclization of the silyl enol ether.

Key words: tricycles, S_N2' cyclization, inductive effect, cyclopropane.

Résumé : Une étude modèle a été réalisée pour vérifier la possibilité de produire des tricycles possédant une double liaison entre les carbones C_7 et C_8 (numérotation des stéroïdes) par une réaction de cyclisation S_N2' entre un éther d'énol silylé et un acétate allylique comme étape clé. Or, une réaction inattendue s'est produite pour conduire à la synthèse de cyclopropanes hautement fonctionnalisés au lieu du produit attendu. Cela étant le résultat d'une cyclisation entre un éther d'énol silylé sur un groupement dithiane où l'un des thioéthers a subi une migration-1,2 tout en déplaçant le groupement acétate partant.

Mots clés : tricycles, cyclisation S_N2', effet inductif, cyclopropane.

Introduction

More than 25 years ago, Nozaki and co-workers (1) studied cationic cyclization of allylic acetates via nucleophilic participation of silyl enol ether. In light of this study, we recently conducted a model study to investigate the possibility of using an S_N2'-type cyclization of a silyl enol ether to displace an allylic acetate to generate C_7–C_8 (steroid numbering) unsaturated fused tricyclic ring structures (cf. **1**, Fig. 1). In model structures containing a sulfone moiety (X = SO_2Ph, Y = H) or a methylene group (X = Y = H) next to the acetate leaving group no cyclization occurred. In contrast, when the model compound was decorated with a dithiane functionality (X, Y = S-$(CH_2)_3$-S) adjacent to the acetate leaving group, instead of obtaining the anticipated product **1** (Fig. 1), the unexpected formation of a highly functionalized cyclopropane was observed (cf. **2**, Fig. 1). The details of this investigation are disclosed herein.

Results and discussion

The use of a sulfone connector for the coupling of rings A and C was explored initially. The intermediate **7** was synthesized starting from the commercially available (*R*)-(–)-carvone. Thus, Michael addition of phenylthiomethyl phenyl sulfone (2, 3) and trapping of the attendant enolate with *tert*-butyldimethylsilyl trifluoromethanesulfonate furnished thioether **4** (Scheme 1). It is noteworthy that the presence of the thioether moiety in the nucleophile was necessary to achieve exclusive 1,4-addition. Thioether **4** was then subjected to *n*-Bu_3SnH–AIBN reduction in refluxing benzene to obtain sulfone **5**. Deprotonation of sulfone **5** with *n*-BuLi, followed by alkylation with the commercially available reagent, 1-cyclohexene-1-carboxaldehyde, afforded the alcohol **6**. The latter product was then acylated with acetic anhydride and catalytic DMAP in pyridine to yield the acetate **7**. All attempts to procure the ABC-fused tricyclic structure, **8**, using the acetate **7** were in vain. For instance, in protic acidic medium, Lewis acid medium, or under anionic conditions, only deprotection of the silyl enol ether was observed. Even with palladium, the formation of the π-allyl palladium species was not observed, and only starting material was recovered instead. It may therefore be concluded that the inductive effect of the sulfonyl group prohibits the solvolysis of the acetate, thus precluding the formation of the π-allyl cation that would have been trapped by the silyl enol ether.

To circumvent the obstacle encountered with the sulfonyl group, alcohol **6** was oxidized with TPAP–NMO in dichloromethane in the presence of 4 Å molecular sieves to produce the ketosulfone **9** (Scheme 2). Subsequent desulfurization with *n*-Bu_3SnH–AIBN in refluxing toluene yielded ketone **10** (4), which was immediately converted to the corresponding alcohol using Luche reduction conditions ($NaBH_4$–$CeCl_3$ in methanol). The alcohol thus obtained was then acylated with acetic anhydride – DMAP (catalytic) in pyridine to obtain the acetate **11**. To our dismay, all efforts directed at effecting cyclization of the precursor acetate **11** to form **12**

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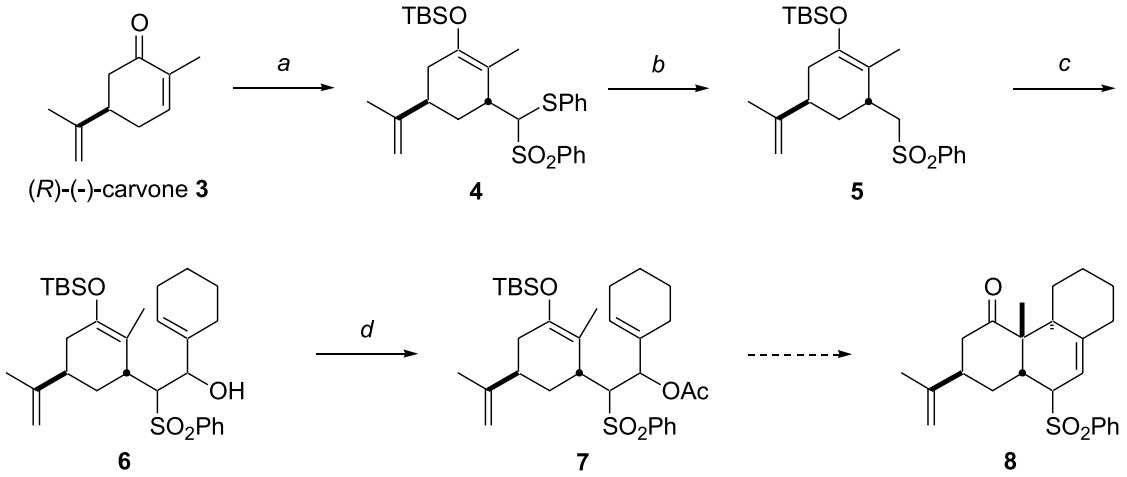
Scheme 1. (*a*) *i.* Phenylsulfonylphenylthiomethane, *n*-BuLi, THF; *ii.* (*R*)-(–)-carvone; *iii.* TBS-OTf, Et_3N (quant.); (*b*) *n*-Bu_3SnH, AIBN, PhH (87%); (*c*) *i. n*-BuLi, THF; *ii.* 1-cyclohexene-1-carboxaldehyde (61%); (*d*) Ac_2O, DMAP, pyridine (92%).



Scheme 2. (*a*) TPAP, NMO, MS 4A, CH_2Cl_2 (60%); (*b*) *n*-Bu_3SnH, AIBN, toluene (quant.); (*c*) $NaBH_4$, $CeCl_3$, MeOH (79%); (*d*) Ac_2O, DMAP, pyridine (86%).

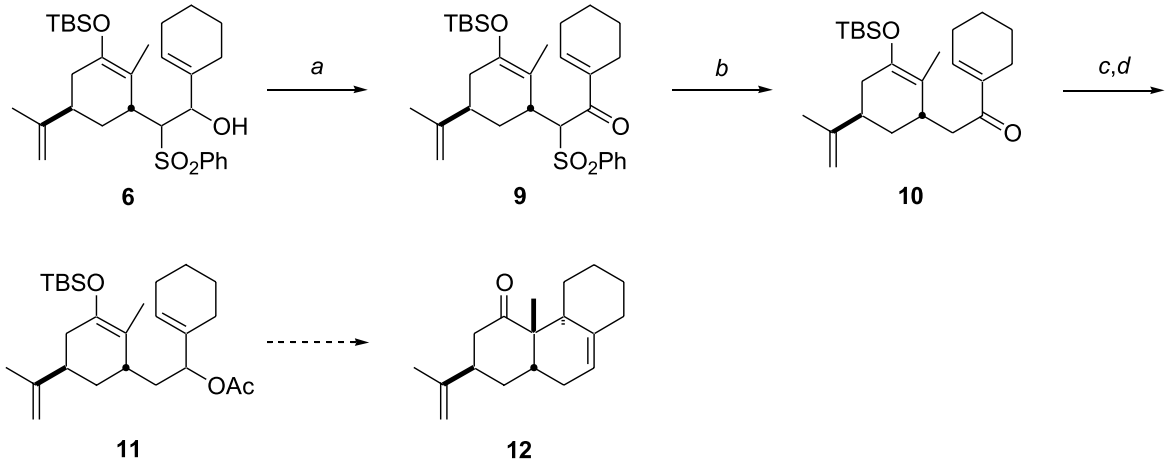
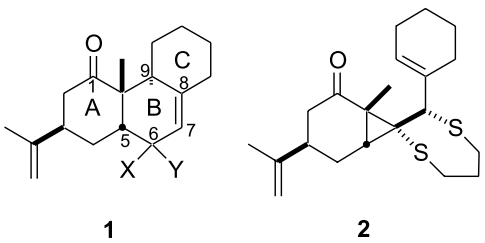


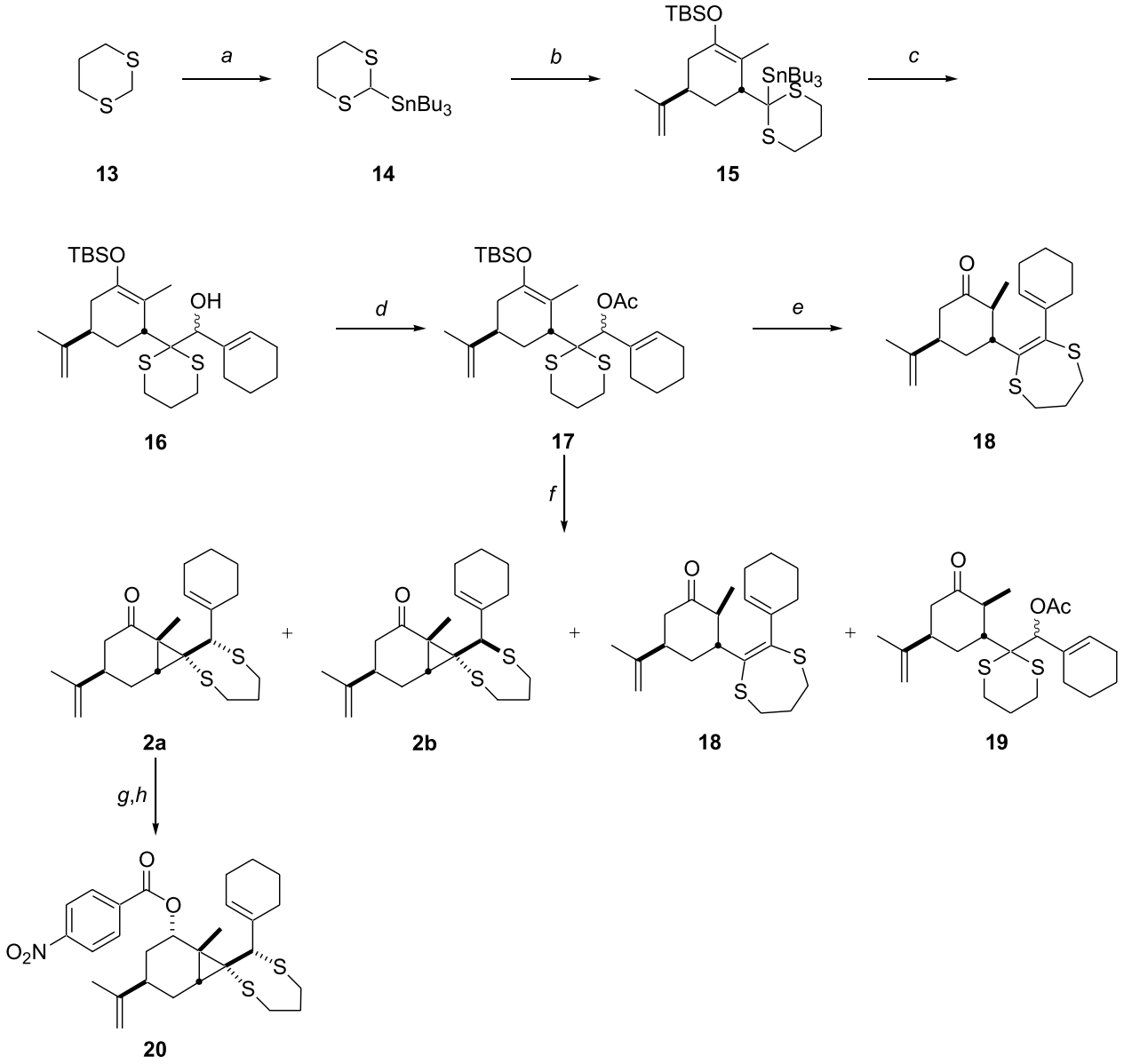
Fig. 1. Target structures.



were unsuccessful. Exclusive deprotection of the silyl enol ether occurred in most cases (acidic medium as well as anionic conditions). With palladium species, only starting material was recovered. On the basis of the above studies, it can be concluded that even in absence of the inductive effect of the sulfonyl group, the acetate group is reluctant to leave and thereby induce cyclization.

Recently, Saigo and co-workers (5) reported that allylic acetates with a thioether as a neighboring group can undergo S_N2' coupling with silyl enol ether in the presence of a Lewis acid. Keeping this in mind, the synthesis of acetate **17** was then undertaken, starting from the commercially available 1,3-dithiane **13** (Scheme 3). Deprotonation of the latter with LDA and trapping of the attendant anion with *n*-Bu_3SnCl furnished stannane **14** in quantitative yield (6). Deprotonation of intermediate **14** with LDA followed by a 1,4-Michael addition with (*R*)-(–)-carvone and trapping of the resultant enolate with *tert*-butyldimethylsilyl trifluoromethanesulfonate in the presence of triethylamine yielded compound **15**. Transmetallation of the stannyl moiety in **15** with *n*-BuLi, followed by alkylation with 1-cyclohexene-1-carboxaldehyde, afforded alcohol **16** in a 3:1 diastereomeric ratio. The alcohol **16** was then acylated with acetic anhydride – DMAP (catalytic) in pyridine to provide the acetate **17** (3:1 diastereomeric mixture). With acetate **17** in hand, a preliminary attempt was made to induce the S_N2' cyclization using *p*-TSA in benzene. The neighboring group participation induced by the dithiane helped the departure of the acetate group, furnishing compound **18** in 64% yield. Thus,

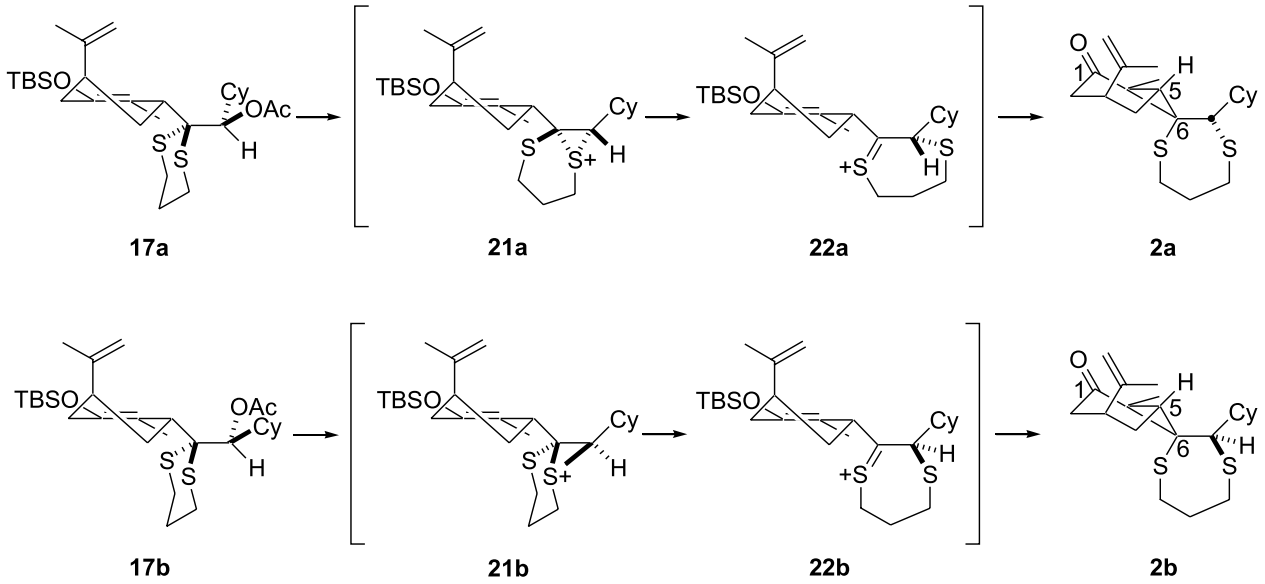
Scheme 3. (*a*) *i.* LDA, THF; *ii.* *n*-Bu_3SnCl (quant.); (*b*) *i.* LDA, THF; *ii.* (*R*)-(–)-carvone, HMPA; *iii.* TBS-OTf, Et_3N (88%); (*c*) *i.* *n*-BuLi, THF *ii.* 1-cyclohexene-1-carboxaldehyde (75%) (ratio of diastereoisomers = 3:1); (*d*) Ac_2O, DMAP, pyridine (79%); (*e*) *p*-TSA, PhH (64%); (*f*) TMS-OTf, CH_2Cl_2 (77%) (ratio **2a**:**2b**:**18**:**19** = 3:1:1.2:1.5); (*g*) $LiAlH_4$, THF (71%) (ratio of diastereoisomers = 7.5:1); (*h*) 4-nitrobenzoyl chloride, DMAP, pyridine, CH_2Cl_2 (40%).



hydrogen abstraction and formation of a double bond induced a net 1,2-migration of a thioether. The structure of compound **18** was assigned by spectral analysis, including DEPT NMR studies. A similar 1,2-migration of a thioether has also been recently reported by Kutateladze and coworkers (7).

We next explored the possibility of effecting the S_N2' cyclization under Lewis acid conditions. To our great surprise, however, when acetate **17** was treated with trimethylsilyl trifluoromethanesulfonate in dichloromethane at –78 °C, cyclopropane **2** was obtained in 46% yield as a separable 3:1 mixture of two diastereoisomers. Compounds **18** and **19** were also isolated from the reaction mixture (14% and 17% yield, respectively). Again, it can be surmised that the dithiane facilitated the departure of the acetate group in compounds **17a** and **17b** to form intermediate **21a** and **21b** as sulfonium cations (Fig. 2). These sulfonium cations could then rearrange to intermediates **22a** and **22b** and, thereby, induce a net 1,2-migration of a thioether moiety. Thus, the silyl enol ether participates in a C—C bond formation at C_6 in a Mukaiyama thio-aldol fashion instead of promoting cyclization at C_9 in an S_N2' manner, contrary to our initial expectations. Moreover, it can be presumed that the Mukaiyama thio-aldol process was stereoselective, as the diastereoisomeric composition in cyclopropane products was identical to that in the acetate starting material. The structure

Fig. 2. Proposed mechanism for formation of cyclopropanes **2a** and **2b**.



of the major diastereoisomer **2a** was assigned by single-crystal X-ray diffraction crystallography of the benzoate **20** (Fig. 3).[2] This product was prepared from compound **2a**, which was reduced with $LiAlH_4$ in THF to give two diastereoisomers (7.5:1) that were readily separable by flash chromatography on silica gel. The major diastereoisomer was subsequently acylated, using 4-nitrobenzoyl chloride – DMAP (catalytic) – pyridine in dichloromethane, to provide **20**.

Experimental

General

All reactions were performed under N_2 atmosphere with flame-dried glassware. Solvents were distilled and dried according to standard procedures. Analytical TLC were performed on precoated glass plates (0.25 mm) with silica gel 60F-250 (Merck). Flash-chromatography was performed with 230–400 mesh gel 60 (Merck). ^1H and ^{13}C NMR spectra were recorded on a Brüker AC-300 and are referenced with respect to the residual signals of the solvent; they are described using standard abbreviations. IR spectra were recorded on a PerkinElmer 1600 FT-IR. Mass spectra were recorded on a ZAB-1F micromass spectrometer.

Thioether (4)

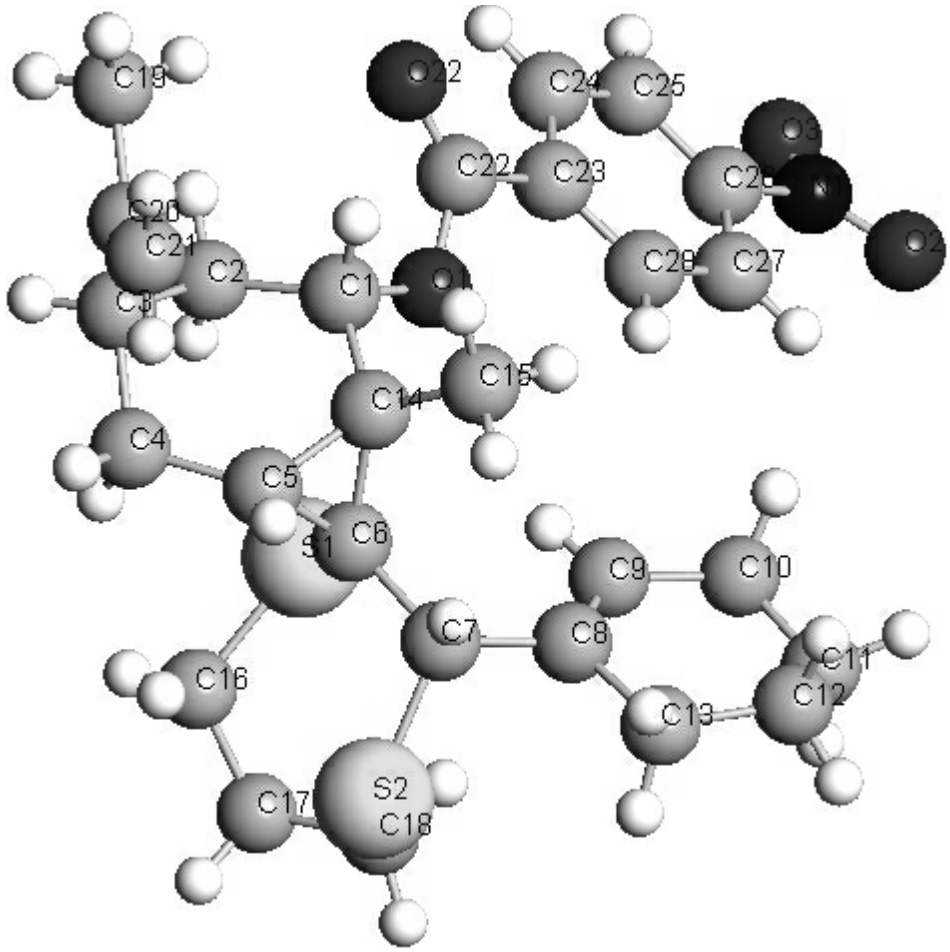
To a solution of phenylthiomethyl phenyl sulfone (2, 3) (0.55 g, 2.1 mmol) in THF (27.0 mL) cooled to –78 °C was added *n*-butyllithium (1.24 mol·L^{-1} in hexane) (1.7 mL, 2.1 mmol). The solution was stirred for 1 h at –78 °C, then (*R*)-(–)-carvone (0.26 g, 1.7 mmol) in THF (6.0 mL) was added. The mixture was stirred for 2 h at –78 °C before *tert*-butyldimethylsilyl trifluoromethanesulfonate (1.2 mL, 5.2 mmol) was added. The mixture was stirred for another 0.75 h, and then triethylamine (1.2 mL, 8.7 mmol) was added. The mixture was warmed to room temperature, stirred for 0.15 h, poured into a saturated aqueous solution of $NaHCO_3$ (30 mL), and extracted with ether (3 × 30 mL). The combined organic phases were washed with brine (100 mL), dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (hexane–ether 8:2) to give the thioether **4** (0.97 g, quantitative) as a pale yellow oil (mixture of diastereoisomers). $[\alpha]_D$ = +63.51° (*c* 1.71, $CHCl_3$). IR (film, cm^{-1}) ν: 3476, 3063, 2955, 2857, 1710, 1583, 1472, 1448, 1307, 1255, 1148, 1083, 836, 741, 688. ^1H NMR (300 MHz, $CDCl_3$, ppm) δ: 7.92 (2H, m, *H* arom. ortho to SO_2R), 7.58 (1H, m, *H* arom. para to SO_2R), 7.46 (2H, m, *H* arom. meta to SO_2R), 7.14 (2H, m, *H* arom. ortho to SR), 7.07 (2H, m, *H* arom. meta to SR), 6.96 (1H, m, *H* arom. para to SR), 4.73 and 4.64 (2H, 2d, *J* = 17.9 and 35.5 Hz, $(CH_3)C=CH_2$), 4.30 (1H, dd, *J* = 37.0 and 2.0 Hz, $PhSO_2$-C*H*-SPh), 3.29 (1H, m), 3.00 (1H, m), 2.38–1.78 (4H, m), 1.77 and 1.63 (3H, 2s, $(CH_3)C=CH_2$), 1.60 and 1.42 (3H, 2s, TBSO-C=C-CH_3), 0.95 (9H, m, $(CH_3)_3$-C-Si), 0.13 (6H, m, $(CH_3)_2$-Si). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ: 148.1, 147.9, 147.1, 138.4, 137.7, 134.3, 133.7, 133.6, 132.3, 131.8, 129.8, 129.4, 129.1, 129.0, 128.8, 127.9, 112.8, 111.0, 109.5, 109.3, 107.8, 105.2, 80.2, 76.4, 39.9, 38.2, 37.8, 37.7, 36.2, 35.4, 34.4, 28.7, 27.2, 26.0, 25.8, 25.8, 25.6, 22.6, 21.2, 20.2, 18.2, 18.0, 16.6, 14.2, –3.5, –3.6. EI-MS: 528 ($[M]^+$). HR-MS ($[M]^+$) calcd. for $C_{29}H_{40}O_3S_2Si$: 528.2188; found: 528.2184.

Sulfone (5)

To a solution of thioether **4** (1.1 g, 2.0 mmol) in benzene (52.0 mL) was added tributyltin hydride (1.1 mL, 4.3 mmol) and AIBN (0.033 g, 0.20 mmol). N_2 was bubbled for 0.1 h

[2] Crystallographic data (excluding structure factors) for the structures in this paper have been deposited. Supplementary data may be purchased from the Depository of Unpublished Data, Document Delivery, CISTI, National Research Council Canada, Ottawa, ON K1A 0S2, Canada (http://www.nrc.ca/cisti/irm/unpub_e.shtml for information on ordering electronically). CCDC 200815 contain the supplementary data for this paper. These data can be obtained, free of charge, via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, U.K.; fax +44 1223 336033; or deposit@ccdc.cam.ac.uk).

Fig. 3. Single-crystal X-ray structure of cyclopropane **20**.



into the solution to exclude O_2. The solution was then heated at reflux for 2 h, cooled to room temperature, and concentrated under reduced pressure. The crude product was purified by flash chromatography (hexane–ether 9:1) to give the sulfone **5** (0.69 g, 87%) as a clear oil. $[\alpha]_D$ = +26.56° (*c* 1.51, $CHCl_3$). IR (film, cm^{-1}) ν: 2930, 2858, 1683, 1472, 1447, 1306, 1253, 1197, 1150, 1087, 1064, 929, 837. ^1H NMR (300 MHz, $CDCl_3$, ppm) δ: 7.93 (2H, m, *H* arom. ortho to SO_2R), 7.61 (3H, *H* arom. meta and para to SO_2R), 4.71 (3H, d, *J* = 17.0 Hz, $(CH_3)C=CH_2$), 3.10 (2H, m, $-CH_2-SO_2Ph$), 2.64 (1H, s), 2.21 (1H, m), 2.00 (3H, m), 1.69 (3H, s, $(CH_3)C=CH_2$), 1.49 (1H, td, *J* = 13.0 and 5.0 Hz), 1.40 (3H, s, TBSO-C=C-CH_3)), 0.91 (9H, s, $(CH_3)_3$-C-Si), 0.08 (6H, s, $(CH_3)_2$-Si). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ: 147.9, 145.7, 139.6, 133.6, 129.3, 128.0, 110.9, 109.7, 105.2, 58.1, 37.0, 35.3, 34.7, 31.3, 25.7, 20.8, 18.2, 14.2, –3.7, –3.8. EI-MS: 420 ($[M]^+$). HR-MS ($[M]^+$) calcd. for $C_{23}H_{36}O_3SSi$: 420.2154; found: 420.2151.

Alcohol (6)

To a solution of sulfone **5** (0.14 g, 0.32 mmol) in THF (2.0 mL) at –78 °C was added *n*-butyllithium (1.24 $mol \cdot L^{-1}$ in hexane) (0.26 mL, 0.32 mmol). The solution was stirred for 1 h at –78 °C and then 1-cyclohexene-1-carboxaldehyde (0.033 mL, 0.29 mmol) was added. The mixture was stirred for 2.5 h and was slowly warmed to –50 °C. It was then poured into a saturated aqueous solution of NH_4Cl (4 mL) and extracted with ether (3 × 5 mL). The combined organic phases were washed with brine (15 mL), dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (hexane–ether 9:1 to 7:3) to give the alcohol **6** (0.095 g, 61%) as a pale yellow oil (mixture of diastereoisomers). $[\alpha]_D$ = +34.76° (*c* 1.03, $CHCl_3$). IR (film, cm^{-1}) ν: 3491, 2931, 2858, 1682, 1447, 1302, 1176, 1140, 1083, 1056, 913, 834, 731. ^1H NMR (300 MHz, $CDCl_3$, ppm) δ: 7.89 (2H, m, *H* arom. ortho to SO_2R), 7.53 (3H, m, *H* arom. meta and para to SO_2R), 5.77 (1H, s, *H*C=C-CH-OH), 4.71 (2H, d, *J* = 33.5 Hz, $(CH_3)C=CH_2$), 4.66 (1H, d, *J* = 12.5 Hz, C*H*-OH), 3.70 (1H, dd, *J* = 8.5 and 3.0 Hz, C*H*-SO_2Ph), 3.00 (1H, d, *J* = 4.5 Hz, CH-O*H*), 2.56 (2H, s), 2.26 (2H, m), 2.00 (4H, m, CH_2-CH=C-CH_2), 1.78 (1H, qu, *J* = 6.5 Hz), 1.71 (3H, s, $(CH_3)C=CH_2$), 1.63 (1H, m), 1.55 (3H, s, TBSO-C=C-CH_3), 1.46 (4H, m, CH_2-CH_2-CH=C-CH_2-CH_2), 0.94 (9H, s, $(CH_3)_3$-C-Si), 0.15 (6H, d, *J* = 10 Hz, $(CH_3)_2$-Si). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ: 147.2, 144.5, 142.9, 136.3, 133.0, 128.6, 128.1, 127.7, 109.6, 109.4, 75.9, 67.9, 37.7, 37.7, 34.2, 28.0, 25.8, 25.1, 22.9, 22.2, 22.1, 21.7, 18.1, 14.5, –3.6. EI-MS: 530 ($[M]^+$). HR-MS ($[M]^+$) calcd. for $C_{30}H_{46}O_4SSi$: 530.2886; found: 530.2894.

Acetate (7)

Acetic anhydride (0.068 mL, 0.72 mmol) and DMAP (0.012 g, 0.10 mmol) were added to a solution of the alcohol

6 (0.26 g, 0.48 mmol) in pyridine (5.0 mL). The solution was stirred for 2 h at room temperature, neutralized with HCl 1 N (5 mL) at 0 °C, and extracted with ethyl acetate (3 × 5 mL). The organic phase was washed with brine (20 mL), dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (hexane–ether 8:2 to 7:3) to yield acetate **7** (0.25 g, 92%) as a clear oil (mixture of diastereoisomers). $[\alpha]_D$ = +13.98° (*c* 1.18, $CHCl_3$). IR (film, cm^{-1}) ν: 2930, 2858, 1747, 1682, 1447, 1306, 1229, 1177, 1144, 913, 832, 730. ^1H NMR (300 MHz, $CDCl_3$, ppm) δ: 7.80 (2H, dd, *J* = 8.0 and 1.2 Hz, *H* arom. ortho to SO_2R), 7.52 (3 H, m, *H* arom. meta and para to SO_2R), 5.91 (1H, s, C*H*=C-(C=O)), 5.74 (1H, d, *J* = 10.1 Hz, C*H*-OAc), 4.72 (2H, d, *J* = 30.5 Hz, $(CH_3)C=CH_2$), 4.00 (1H, dd, *J* = 10.1 and 2.2 Hz, C*H*-SO_2Ph), 2.64 (1H, m), 2.57 (1H, m), 2.42–2.24 (2H, m), 2.00 (4H, m, CH_2-CH_2-CH=C-CH_2-CH_2), 1.85 (1H, m), 1.80 (3H, s, CH-O(C=O)-CH_3), 1.74 (1H, m), 1.71 (3H, s, $(CH_3)C=CH_2$), 1.50 (4H, m, CH_2-CH=C-CH_2), 1.43 (3H, s, TBSO-C=C-CH_3), 0.95 (9H, m, $(CH_3)_3$C-Si), 0.17 (6H, d, *J* = 10.0 Hz, $(CH_3)_2$Si). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ: 168.6, 147.2, 144.0, 143.8, 132.7, 132.1, 131.5, 128.9, 126.9, 109.9, 109.4, 77.8, 64.1, 37.6, 37.1, 34.4, 26.9, 25.9, 25.1, 22.8, 22.1, 21.9, 20.8, 18.1, 14.2, –3.7, –3.8. EI-MS: 572 ($[M]^+$). HR-MS ($[M]^+$) calcd. for $C_{32}H_{48}O_5SSi$: 572.2992; found: 572.3000.

Ketosulfone (9)

To a solution of alcohol **6** (0.49 g, 0.92 mmol) in dichloromethane (9.2 mL) was added 4 Å molecular sieves (0.92 g), 4-methylmorpholine *N*-oxide (0.22 g, 1.9 mmol), and tetrapropylammonium perruthenate (0.032 g, 0.090 mmol). The mixture was stirred for 0.5 h at room temperature, and the solvent was then concentrated under reduced pressure. Ether (10 mL) was added, and the mixture was filtered through a silica gel pad. The pad was rinsed with ether (10 mL), and the combined flitrates were concentrated under reduced pressure. The crude product was purified by flash chromatography (hexane–ether 9:1 to 7:3) to give the ketosulfone **9** (0.30 g, 60%) as a pale yellow oil. $[\alpha]_D$ = +78.64° (*c* 1.03, $CHCl_3$). IR (film, cm^{-1}) ν: 2931, 2859, 1663, 1633, 1448, 1321, 1255, 1196, 1146, 1083, 921, 840. ^1H NMR (300 MHz, $CDCl_3$, ppm) δ: 7.89 (2H, m, *H* arom. ortho to SO_2R), 7.57 (1H, m, *H* arom. para to SO_2R), 7.47 (2H, m, *H* arom. meta to SO_2R), 6.70 (1H, t, *J* = 4.0 Hz, C*H*=C-(C=O)), 4.96 (1H, d, *J* = 10.1 Hz, C*H*-SO_2Ph), 4.79 (2H, m, $(CH_3)C=CH_2$), 3.11 (1H, m), 2.69 (1H, m), 2.61 (1H, d, *J* = 13.6 Hz), 2.12 (6H, m), 1.79 (3H, s, $(CH_3)C=CH_2$), 1.58 (1H, td, *J* = 13.0 and 4.4 Hz), 1.42 (4H, m, CH_2-CH=C-CH_2), 1.25 (3H, s, TBSO-C=C-CH_3), 0.88 (9H, s, $(CH_3)_3$C-Si), 0.04 (6H, d, *J* = 12.6 Hz, $(CH_3)_2$Si). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ: 193.2, 148.2, 147.5, 142.6, 140.5, 138.7, 133.6, 129.9, 128.6, 111.6, 109.6, 70.7, 41.2, 37.0, 35.1, 31.1, 26.3, 25.7, 23.2, 21.5, 21.1, 20.5, 18.1, 17.4, –3.7, –3.8. EI-MS: 528 ($[M]^+$). HR-MS ($[M]^+$) calcd. for $C_{30}H_{44}O_4SSi$: 528.2729; found: 528.2722.

Ketone (10)

To a solution of ketosulfone **9** (0.29 g, 0.54 mmol) in toluene (5.4 mL) was added tributyltin hydride (0.58 mL, 2.16 mmol). N_2 was bubbled for 5 min into the solution to exclude O_2. The solution was then heated at reflux, and AIBN (0.060 g, 0.37 mmol) was added. The solution was heated at reflux 5 min, and then a second portion of AIBN (0.037 g, 0.12 mmol) was added. The solution was heated at reflux another 10 min, cooled to room temperature, and concentrated under reduced pressure. The crude product was purified by flash chromatography (hexane–ether 10:0 to 8:2) to give the enone **10** (0.23 g, quantitative) as a clear liquid. $[\alpha]_D$ = +19.46° (*c* 1.12, $CHCl_3$). IR (film, cm^{-1}) ν: 2929, 2858, 1661, 1463, 1378, 1252, 1174, 1072, 926, 837. ^1H NMR (300 MHz, $CDCl_3$, ppm) δ: 6.89 (1H, m, C*H*=C-(C=O)), 4.71 (2H, m, $(CH_3)C=CH_2$), 2.69 (2H, s, CH_2-(C=O)), 2.32 (1H, m), 2.24 (4H, m), 2.03 (1H, m), 1.70 (3H, s, $(CH_3)C=CH_2$), 1.76–1.24 (8H, m), 1.50 (3H, s, TBSO-C=C-CH_3), 0.95 (9H, m, $(CH_3)_3$C-Si), 0.13 (6H, s, $(CH_3)_2$Si). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ: 201.2, 148.9, 143.9, 139.7, 113.7, 109.0, 40.0, 37.4, 35.8, 35.6, 31.9, 27.8, 26.8, 26.1, 25.8, 23.2, 22.0, 21.5, 17.5, 13.6, –3.7, –3.9. EI-MS: 388 ($[M]^+$). HR-MS ($[M]^+$) calcd. for $C_{24}H_{40}O_2Si$: 388.2797; found: 388.2801.

Acetate (11)

Sodium borohydride (0.012 g, 0.32 mmol) was dissolved in methanol (0.50 mL), and the mixture was cooled to 0 °C. To this mixture was added dropwise a solution of cerium (III) chloride heptahydrate (0.12 g, 0.32 mmol) and ketone **10** (0.11 g, 0.29 mmol) in methanol (0.94 mL). The mixture was stirred for 0.5 h at 0 °C and 0.5 h at room temperature. It was cooled back to 0 °C, and a saturated aqueous solution of NH_4Cl (2 mL) was added. The mixture was extracted with dichloromethane (3 × 3 mL). The combined organic phases were washed with brine (10 mL), dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (hexane–ether 95:5 to 9:1) to give the alcohol (0.089 g, 79%) as a colorless liquid (mixture of diastereoisomers). $[\alpha]_D$ = +14.22° (*c* 1.16, $CHCl_3$). IR (film, cm^{-1}) ν: 3350, 2929, 2858, 1682, 1645, 1448, 1256, 1178, 922, 889, 837, 779, 735. ^1H NMR (300 MHz, $CDCl_3$, ppm) δ: 5.65 (1H, d, *J* = 3.5 Hz, C*H*=C-(C=O)), 4.72 (2H, d, *J* = 0.45 Hz, $(CH_3)C=CH_2$), 4.08–3.97 (1H, m, C*H*-OH), 2.40–1.35 (16H, m), 1.74 (3H, s, $(CH_3)C=CH_2$), 1.59 (3H, s, TBSO-C=C-CH_3), 0.93 (9H, s, $(CH_3)_3$C-Si), 0.10 (6H, d, *J* = 1.1 Hz, $(CH_3)_2$Si). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ: 149.2, 143.3, 143.1, 140.7, 139.2, 124.8, 122.1, 114.8, 114.4, 108.9, 108.8, 76.3, 74.5, 38.1, 37.3, 37.2, 36.9, 36.2, 35.7, 35.7, 35.5, 31.6, 31.4, 30.9, 25.9, 25.1, 24.9, 24.0, 22.6, 22.5, 20.7, 18.2, 15.1, 14.9, –3.7, –3.8, –3.8, –3.9. EI-MS: 390 ($[M]^+$). HR-MS ($[M]^+$) calcd. for $C_{24}H_{42}O_2Si$: 390.2954; found: 390.2951.

Acetic anhydride (0.032 mL, 0.34 mmol) and DMAP (5.5 mg, 0.050 mmol) were added to a solution of the alcohol (0.088 g, 0.23 mmol) of the preceding reaction in pyridine (2.3 mL). The solution was stirred for 3 h at room temperature, neutralized with an aqueous solution of HCl 1 N (5 mL), and extracted with ethyl acetate (3 × 5 mL). The organic phase was washed with brine (15 mL), dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (hexane–ether 97:3) to yield acetate **11** (0.083 g, 86%) as a colorless liquid (mixture of diastereoisomers). $[\alpha]_D$ =

+10.10° (*c* 1.00, $CHCl_3$). IR (film, cm^{-1}) ν: 2927, 1738, 1682, 1645, 1448, 1371, 1236, 1180, 1017, 922, 838, 780, 734. ^1H NMR (300 MHz, $CDCl_3$, ppm) δ: 5.69 (1H, d, *J* = 13.7 Hz, C*H*=C-CH-OAc), 5.15 (1H, m, C*H*-OAc), 4.72 (2H, s, $(CH_3)C=CH_2$), 2.38–2.28 (1H, m), 2.02 (3H, d, *J* = 11.2 Hz, CH-O-(C=O)-CH_3), 1.99–1.34 (15H, m), 1.73 (3H, d, *J* = 5.9 Hz, $(CH_3)C=CH_2$), 1.58 (3H, d, *J* = 5.5 Hz, TBSO-C=C-CH_3), 0.93 (9H, m, $(CH_3)_3C$-Si), 0.10 (6H, m, $(CH_3)_2Si$). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ: 170.5, 170.3, 149.0, 148.9, 143.5, 143.4, 136.4, 135.1, 126.5, 125.9, 124.3, 123.8, 114.2, 114.0, 110.5, 110.4, 109.0, 108.9, 105.2, 78.2, 76.3, 40.0, 39.4, 38.9, 37.3, 37.2, 36.4, 36.1, 35.9, 35.6, 35.6, 34.4, 31.1, 30.9, 25.8, 25.0, 24.9, 24.8, 23.3, 22.4, 21.4, 21.3, 20.8, 20.7, 18.2, 15.0, 14.8, –3.7, –3.9. EI-MS: 432 ($[M]^+$). HR-MS ($[M]^+$) calcd. for $C_{26}H_{44}O_3Si$: 432.3060; found: 432.3063.

Stannane (15)

Tributyl-[1,3]dithian-2-yl-stannane **14** (1.2 g, 2.9 mmol) was dried via azeotropic removal of water with benzene (3 × 3 mL) and was then dissolved in THF (2.5 mL) and cooled to –30 °C. In another flask, diisopropylamine (0.40 mL, 2.9 mmol) was dissolved in THF (2.5 mL), cooled to 0 °C, and a solution of *n*-butyllithium (1.35 $mol \cdot L^{-1}$ in hexane) (2.0 mL, 2.7 mmol) was added dropwise. The solution was stirred for 0.25 h at 0 °C, cooled down to –30 °C, and transferred via canula to the first solution containing the stannane. The mixture was stirred for 3 h at –30 °C and cooled to –78 °C; HMPA (1.0 mL, 5.7 mmol) was added, and the mixture was stirred for another 0.5 h. A solution of (*R*)-(–)-carvone (0.20 g, 1.3 mmol) in THF (1.5 mL) precooled to –78 °C was transferred via canula to the mixture, which was stirred for 1.25 h at –78 °C before *tert*-butyldimethylsilyl trifluoromethanesulfonate (0.60 mL, 2.6 mmol) was added. The mixture was stirred for 0.25 h at –78 °C, triethylamine (0.55 mL, 3.9 mmol) was added, and the mixture was warmed at room temperature and stirred for 0.5 h. Water (10 mL) was added, and the mixture was extracted with ether (3 × 10 mL). The combined organic phases were washed with brine (25 mL), dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (hexane) to give the stananne **15** (0.78 g, 88%) as a colorless oil. $[\alpha]_D$ = +28.14° (*c* 1.13, $CHCl_3$). IR (film, cm^{-1}) ν: 2956, 2856, 1667, 1463, 1252, 1194, 931, 837. ^1H NMR (300 MHz, $CDCl_3$, ppm) δ: 4.74 (2H, s, $(CH_3)C=CH_2$), 3.19 (1H, m), 3.13 (1H, m), 2.90 (1H, m), 2.69 (1H, m), 2.35–1.97 (8H, m), 1.94 (3H, s, TBSO-C=C-CH_3), 1.76 (3H, s, $(CH_3)C=CH_2$), 1.52 (6H, m, Sn-(CH_2-CH_2-CH_2-CH_3)$_3$), 1.33 (6H, m, Sn-(CH_2-CH_2-CH_2-CH_3)$_3$), 1.06 (6H, m, Sn-(CH_2-CH_2-CH_2-CH_3)$_3$), 0.91 (18H, m, $(CH_3)_3C$-Si and Sn-(CH_2-CH_2-CH_2-CH_3)$_3$), 0.14 (6H, s, $(CH_3)_2$-Si). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ: 149.3, 145.4, 114.9, 108.7, 46.8, 36.6, 35.5, 34.0, 29.2, 27.6, 26.5, 25.9, 25.1, 25.0, 20.6, 18.7, 13.7, 10.1, –3.1, –3.3. EI-MS: 617 ($[M - C_4H_9]^+$). HR-MS ($[M - C_4H_9]^+$) calcd. for $C_{28}H_{53}OS_2SiSn$: 617.2329; found: 617.2322.

Alcohol (16)

Stannane **15** (0.61g, 0.91 mmol) was dried via azeotropic removal of water with benzene (3 × 10 mL); it was then dissolved in THF (10.0 mL), cooled to –100 °C, and a solution of *n*-butyllithium (1.35 $mol \cdot L^{-1}$ in hexane) (1.3 mL, 1.8 mmol) was added dropwise. The solution was stirred for 0.5 h at –100 °C, and a solution of 1-cyclohexene-1-carboxaldehyde (0.33 mL, 2.9 mmol) in THF (15.0 mL) was added via canula. The solution was stirred for 1.25 h at –100 °C, brought to 0 °C, neutralized with a saturated aqueous solution of NH_4Cl (20 mL), and extracted with ether (3 × 25 mL). The combined organic phases were washed with brine (50 mL), dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (hexane–ether 100:0 to 95:5) to give alcohol **16** (0.33 g, 75%) as a clear oil (mixture of diastereoisomers, ratio = 3:1). $[\alpha]_D$ = +10.50° (*c* 1.14, $CHCl_3$). IR (film, cm^{-1}) ν: 3444, 2929, 2857, 1667, 1644, 1252, 1192, 927, 837, 780, 734. ^1H NMR (300 MHz, $CDCl_3$, ppm) δ: 6.00 (1H, s, C*H*=C-CH-OH), 4.73 (2H, m, $(CH_3)C=CH_2$), 4.51 (1H, m, C*H*-OH), 3.29–1.34 (15H, m), 1.80 (3H, d, *J* = 9.3 Hz, TBSO-C=C-CH_3), 1.75 (3H, d, *J* = 4.3 Hz, $(CH_3)C=CH_2$), 1.61 (4H, m), 1.40 (1H, tt, *J* = 13.1 and 4.8 Hz), 0.95 (9H, d, *J* = 1.7 Hz, $(CH_3)_3C$-Si), 0.16 (6H, s, $(CH_3)_2Si$). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ: 149.4, 149.3, 148.8, 136.8, 136.4, 127.4, 127.1, 111.9, 111.5, 108.8, 108.7, 78.1, 76.4, 62.1, 61.9, 45.1, 43.0, 38.2, 37.4, 35.3, 35.1, 31.9, 31.8, 28.8, 28.5, 28.5, 27.8, 27.4, 27.2, 25.9, 25.9, 25.5, 24.4, 24.1, 23.1, 23.1, 22.4, 22.1, 20.5, 20.4, 19.5, 18.9, –3.2, –3.3, –3.4. EI-MS: 476 ($[M - H_2O]^+$); 437 ($[M - C_4H_9]^+$). HR-MS ($[M - H_2O]^+$) calcd. for $C_{27}H_{44}OS_2Si$: 476.2603; found: 476.2596.

Acetate (17)

Acetic anhydride (0.27 mL, 2.9 mmol) and DMAP (71.0 mg, 0.58 mmol) were added to a solution of the alcohol **16** (0.79 g, 0.58 mmol) in pyridine (5.8 mL). The solution was stirred for 4 h at room temperature, neutralized with HCl 1 N (5 mL), and extracted with ethyl acetate (3 × 10 mL). The organic phase was washed with brine (15 mL), dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (hexane–ether 95:5) to give acetate **17** (0.24 g, 79%) as a colorless oil (mixture of diastereoisomers, ratio = 3:1). $[\alpha]_D$ = +9.56° (*c* 1.13, $CHCl_3$). IR (film, cm^{-1}) ν: 2929, 2857, 1742, 1667, 1438, 1368, 1230, 1170, 1019, 926, 837, 780, 733. ^1H NMR (300 MHz, $CDCl_3$, ppm) δ: 5.94 (1H, s, C*H*=C-CH-OAc), 5.76 (1H, d, *J* = 19.2 Hz, C*H*-OAc), 4.74 (2H, m, $(CH_3)C=CH_2$), 3.30–3.09 (2H,m), 2.98 (1H, m), 2.76 (1H, m), 2.64–2.46 (1H, m), 2.33–2.12 (3H, m), 2.08 (3H, d, *J* = 2.7 Hz, CH-O-(C=O)-CH_3), 2.03–1.89 (1H, m), 1.84 (3H, d, *J* = 10.5 Hz, TBSO-C=C-CH_3), 1.75 (3H, d, *J* = 3.8 Hz, $(CH_3)C=CH_2$), 1.26 (6H, m), 0.95 (9H, d, *J* = 1.0 Hz, $(CH_3)_3C$-Si), 0.16 (6H, t, *J* = 4.5 Hz, $(CH_3)_2Si$). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ: 169.5, 149.5, 149.4, 148.4, 134.9, 134.6, 129.5, 128.5, 111.7, 111.2, 108.8, 108.6, 82.4, 78.5, 59.7, 59.3, 45.7, 43.5, 37.7, 35.3, 35.1, 31.8, 31.7, 31.6, 28.8, 28.0, 27.7, 27.5, 27.4, 25.9, 25.4, 24.3, 24.2, 22.9, 22.6, 22.0, 22.0, 21.4, 20.5, 20.4, 19.8, 19.2, 18.2, 14.1, –3.3, –3.4. CI-MS: 537 ($[MH]^+$). HR-MS ($[MH]^+$) calcd. for $C_{29}H_{49}O_3S_2Si$: 537.2892; found: 537.2887.

Ketone (18)

Acetate **17** (0.026 g, 0.048 mmol) was dried via azeotropic removal of water with benzene (3 × 1 mL) and

then dissolved in benzene (1.0 mL), and *p*-toluenesulfonic acid monohydrate (2.0 mg, 0.010 mmol) was added. The solution was heated at reflux for 16 h, cooled to room temperature, neutralized with a saturated aqueous solution of $NaHCO_3$ (3 mL), and extracted with ether (3 × 5 mL). The organic phase was dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (hexane–ether 95:5) to give ketone **18** (8.1 mg, 46%) as a yellow oil. $[\alpha]_D$ = –72.35° (*c* 1.15, $CHCl_3$). IR (film, cm^{-1}) ν: 2929, 1708, 1448, 904, 733. ^1H NMR (300 MHz, $CDCl_3$, ppm) δ: 5.39 (1H, m, C*H*=C), 4.84 and 4.61 (2H, 2s, $(CH_3)C=CH_2$), 3.08–2.51 (9H, m), 2.18 (4H, m), 1.97 (2H, m), 1.77 (1H, dd, *J* = 13.7 and 2.7 Hz), 1.70 (3H, d, *J* = 0.6 Hz, $(CH_3)C=CH_2$), 1.63–1.47 (5H, m), 0.94 (3H, d, *J* = 6.5 Hz, (C=O)-C-CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ: 212.6, 146.9, 141.0, 138.1, 137.9, 125.9, 112.4, 47.8, 45.9, 44.6, 41.0, 33.0, 32.4, 31.8, 31.4, 28.3, 25.1, 22.6, 22.5, 21.7, 12.5. EI-MS: 362 ($[M]^+$). HR-MS ($[M]^+$) calcd. for $C_{21}H_{30}OS_2$: 362.1738; found: 362.1729.

Cyclopropanes (2a and 2b)

Acetate **17** (0.35 g, 0.65 mmol) was dried via azeotropic removal of water with benzene (3 × 10 mL) and then dissolved in dichloromethane (33.0 mL) and cooled to –78 °C. Trimethylsilyl trifluoromethanesulfonate (0.12 mL, 0.65 mmol) was added slowly, and the solution was stirred for 5 min before a saturated aqueous solution of $NaHCO_3$ (25 mL) was added. The mixture was extracted with ether (3 × 25 mL). The combined organic phases were washed with brine (50 mL), dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (hexane–ether 95:5) to give compound **19** (0.041 g, 17%), compound **18** (0.033 g, 14%), and the cyclopropane **2** (0.11 g, 46%) as a mixture of two diastereoisomers, which were separated by preparative TLC (eluted 2 times with toluene) to give the major product **2a** (0.033 g) and the minor product **2b** (0.011 g). Major product **2a**: $[\alpha]_D$ = –361.07° (*c* 1.40, $CHCl_3$). IR (film, cm^{-1}) ν: 2923, 1693, 1438, 1407, 1376, 1301, 1103, 894, 755. ^1H NMR (300 MHz, $CDCl_3$, ppm) δ: 6.19 (1H, s, C=C*H*), 4.86 and 4.59 (2H, 2s, $(CH_3)C=CH_2$), 3.25 (1H, m), 3.05 (1H, m), 2.81 (2H, m), 2.63 (3H, m), 2.38 (3H, m), 2.12 (3H, m), 1.95 (2H, m), 1.79 (3H, s, $(CH_3)C=CH_2$), 1.62 (5H, m), 1.27 (1H, dd, *J* = 8.1 and 4.0 Hz), 1.17 (3H, s, (C=O)-C-CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ: 208.9, 147.4, 132.2, 128.1, 111.1, 59.9, 45.0, 43.7, 40.4, 39.5, 35.4, 31.5, 30.7, 28.3, 25.8, 25.1, 24.2, 23.2, 22.5, 21.7, 18.2. EI-MS: 362 ($[M]^+$). HR-MS ($[M]^+$) calcd. for $C_{21}H_{30}OS_2$: 362.1738; found: 362.1743. Minor product **2b**: $[\alpha]_D$ = –96.25° (*c* 0.40, $CHCl_3$). IR (film, cm^{-1}) ν: 2925, 1692, 1448, 1409, 1305, 1101, 894, 730. ^1H NMR (300 MHz, $CDCl_3$, ppm) δ: 5.91 (1H, s, C=C*H*), 4.85 and 4.62 (2H, 2s, $(CH_3)C=CH_2$), 3.30 (1H, m), 3.26 (1H, m), 2.90 (3H, m), 2.76 (1H, dd, *J* = 16.7 and 4.9 Hz), 2.63 (3H, m), 2.46–2.18 (3H, m), 2.12 (3H, m), 1.88 (3H, m), 1.77 (3H, s, $(CH_3)C=CH_2$), 1.66 (3H, m), 1.35 (3H, s, (C=O)-C-CH_3), 1.27 (1H, m). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ: 210.2, 147.5, 133.1, 128.3, 126.7, 111.0, 56.7, 44.2, 40.4, 35.9, 31.6, 30.6, 28.2, 25.8, 25.7, 24.0, 23.1, 22.4, 21.6, 17.4, 14.1. EI-MS: 362 ($[M]^+$). HR-MS ($[M]^+$) calcd. for $C_{21}H_{30}OS_2$: 362.1738; found: 362.1743. Compound **19**: $[\alpha]_D$ = –41.06° (*c* 2.63, $CHCl_3$). IR (film, cm^{-1}) ν: 2929, 1708, 1438, 1414, 892, 754. ^1H NMR (300 MHz, $CDCl_3$, ppm) δ: 5.45 (1H, m, C*H*=C), 4.74 (2H, d, J = 12.3 Hz, $C(CH_3) = CH_2$), 3.55 (1H, m), 3.17 (2H, m), 2.92 (1H, m), 2.85 (1H, m), 2.77 (1H, m), 2.60 (1H, dd, J = 15.0 and 4.4 Hz), 2.36 (1H, qu, J = 6.5 Hz), 2.18 (3H, m), 2.05 (4H, m), 1.90 (2H, m), 1.72 (3H, s, $(CH_3)C=CH_2$), 1.71–1.54 (4H, m), 1.06 (3H, d, J = 6.8 Hz, CH_3-CH). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ: 211.8, 147.9, 138.6, 128.3, 125.4, 112.4, 109.8, 47.2, 47.0, 45.3, 41.1, 36.6, 33.3, 32.5, 31.3, 28.4, 25.1, 22.7, 21.8, 20.6, 12.7. EI-MS: 362 ($[M]^+$). HR-MS ($[M]^+$) calcd. for $C_{21}H_{30}OS_2$: 362.1738; found: 362.1729.

Nitrobenzoate (20)

To a solution of cyclopropane **2a** (0.024 g, 0.066 mmol) in THF (1.3 mL) was added lithium aluminum hydride (3.7 mg, 0.099 mmol). The solution was stirred for 15 min at room temperature, neutralized with a dropwise addition of a saturated aqueous solution of NH_4Cl (5 mL), and extracted with ether (3 × 5 mL). The organic phase was dried with $MgSO_4$, filtered, and concentrated under reduced pressure. The crude product was purified by flash chromatography (hexane–ether 100:0 to 98:2) to give the alcohol as the major diastereoisomer (0.015 g, 63%) and the minor diastereoisomer (2.0 mg, 8%). Major diastereoisomer: $[\alpha]_D$ = –173.82° (*c* 1.10, $CHCl_3$). IR (film, cm^{-1}) ν: 3788, 3492, 2921, 1641, 1446, 1403, 1013, 885. ^1H NMR (300 MHz, $CDCl_3$, ppm) δ: 6.46 (1H, s, C*H*=C), 4.79 (2H, d, *J* = 24.2 Hz, $(CH_3)C=CH_2$), 3.75 (1H, t, *J* = 9.2 Hz, C*H*-OH), 3.25 (1H, m), 3.10 (1H, m), 2.87 (1H, m), 2.63 (2H, m), 2.40 (2H, m), 2.36–2.11 (3H, m), 2.07 (2H, m), 1.92 (2H, m), 1.78 (1H, m), 1.74 (3H, s, $(CH_3)C=CH_2$), 1.61 (5H, m), 1.14 (3H, s, (C=O)-C-CH_3), 1.11 (1H, m). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ: 147.4, 133.5, 127.3, 110.2, 73.9, 61.5, 46.0, 39.7, 36.9, 34.8, 34.7, 31.7, 30.6, 28.5, 25.8, 25.3, 23.8, 23.3, 23.0, 22.6, 22.3. EI-MS: 364 ($[M]^+$). HR-MS ($[M]^+$) calcd. for $C_{21}H_{32}OS_2$: 364.1894; found: 364.1888.

The major diastereoisomer of the preceding alcohol (4.5 mg, 0.012 mmol) was dissolved in dichloromethane (0.35 mL) and pyridine (0.35 mL). 4-Nitrobenzoyl chloride (0.023 g, 0.12 mmol) and DMAP (0.7 mg, 6.0 μmol) were added, and the solution was stirred for 16 h at room temperature and concentrated under reduced pressure, and the crude product was purified by flash chromatography (hexane–ether 95:5) to give nitrobenzoate **20** (2.5 mg, 40%) as a yellow solid. IR (film, cm^{-1}) ν: 2928, 1720, 1608, 1529, 1148, 1409, 1348, 1321, 1272, 1117, 1104, 755, 719. ^1H NMR (300 MHz, $CDCl_3$, ppm) δ: 8.32 (4H, m, *H* arom.), 6.46 (1H, s, C=C*H*), 5.35 (1H, dd, *J* = 7.7 and 10.9 Hz, C*H*-OAc), 4.91 (2H, d, *J* = 24.3 Hz, $(CH_3)C=CH_2$), 3.26 (1H, m), 3.13 (1H, m), 2.91 (1H, dt, *J* = 13.9 and 3.1 Hz), 2.67 (2H, m), 2.45 (1H, m), 2.37 (3H, m), 2.25 (1H, m), 1.98 (2H, m), 1.87 (1H, m), 1.83 (3H, s, $(CH_3)C=CH_2$), 1.65–1.46 (7H, m), 1.26 (1H, m), 1.14 (3H, s, -CO_2-C-C-CH_3). ^{13}C NMR (75 MHz, $CDCl_3$, ppm) δ: 164.5, 146.7, 134.1, 130.8, 126.6, 123.5, 110.8, 85.0, 78.0, 61.0, 46.9, 46.6, 39.8, 37.1, 32.0, 31.2, 30.5, 30.5, 28.3, 25.3, 25.2, 23.3, 23.2, 22.9, 22.4, 22.4. EI-MS: 513 ($[M]^+$). HR-MS ($[M]^+$) calcd. for $C_{28}H_{35}NO_4S_2$: 513.2007; found: 513.1997.

Conclusion

We have studied the plausibility of an S_N2' cyclization using a silyl enol ether onto an allylic acetate by varying the functional groups adjacent to the acetate leaving group. Clearly, the inductive effect of the neighboring group plays a significant role in the departure of the leaving group, as the results with the dithiane neighboring group revealed. Several other alternatives were pursued but without success. Unfortunately, the model studies discussed herein proved that this strategy cannot be employed to access the C_7–C_8 unsaturated tricyclic structures. However, in the case of the substrates containing a dithiane next to the allylic acetate, the synthesis of novel highly functionalized cyclopropanes was observed instead of the desired S_N2' cyclization. This cyclopropanation is due to the cyclization of the silyl enol ether with concomitant 1,2-migration of a thioether and displacement of the acetate.

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