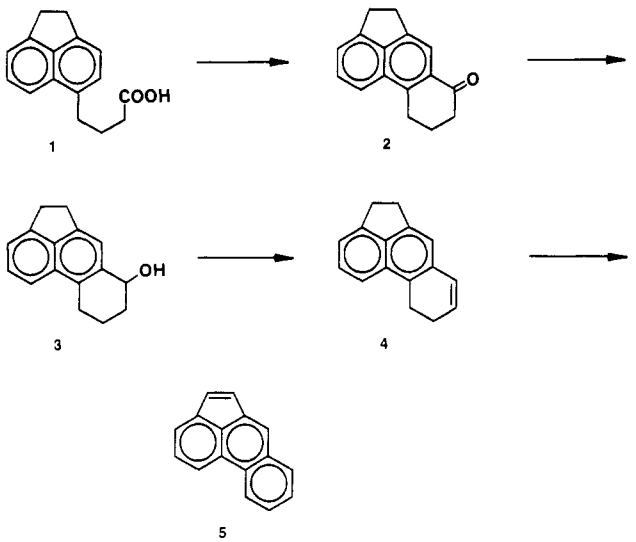
Scheme I



poured over 500 g of ice. This mixture was extracted with CH_2Cl_2 (3 × 200 mL), and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure to yield 8.2 g (88%) of **2** as pale yellow crystals: mp 146–147 °C (lit.[6] 147 °C); ^1H NMR ($CDCl_3$) δ 7.7–7.0 (m, 4 H), 3.14 (s, 4 H), 3.10 (m, 2 H), 2.62 (m, 2 H), 2.12 (m, 2 H); IR (KBr) 2940, 2910, 2860, 2810, 1655, 1390, 1340, 1175, 765, 758 cm^{-1}.

4,5,7,8,9,10-Hexahydro-7-hydroxyacephenanthrylene (3). To a solution of 500 mL of tetrahydrofuran and 250 mL of methanol was added ketone **2** (9.0 g, 40 mmol). This solution was cooled to 0 °C in an ice bath, and $NaBH_4$ (5 g, 140 mmol) was added in several portions over a 2-h period. Upon completion of the addition, the solution was stirred for 5 h and allowed to warm to room temperature. The solution was then poured on 1 kg of ice, and the mixture was extracted with CH_2Cl_2 (3 × 300 mL). The combined organic layers were washed with water (2 × 200 mL), dried over Na_2SO_4, and concentrated under reduced pressure to yield 9.0 g (99%) of **3** as a white crystalline solid: mp 112–113 °C; ^1H NMR ($CDCl_3$) δ 7.5–6.9 (m, 4 H), 4.65 (m, 1 H), 3.18 (m, 4 H), 2.82 (m, 2 H), 2.12 (s, 1 H), 1.83 (m, 4 H); IR (KBr) 3340, 2930, 2915, 2850, 1605, 1163, 1065, 1055, 770 cm^{-1}. Anal. Calcd for $C_{16}H_{16}O$: C, 85.67; H, 7.19. Found: C, 85.55; H, 7.19.

4,5,9,10-Tetrahydroacephenanthrylene (4). To a slurry of Al_2O_3 (2 g, washed with concentrated hydrochloric acid, dried 16 h at 180 °C (0.1 mm)) in 30 mL of dry toluene was added alcohol **3** (290 mg, 1.3 mmol). The mixture was refluxed for 1 h and filtered, and the Al_2O_3 was washed with toluene (2 × 20 mL). The combined organic layers were concentrated under reduced pressure, and the product was recrystallized from hexane to yield 257 mg (96%) of **4** as a white crystalline solid: mp 99–100 °C; ^1H NMR ($CDCl_3$) δ 7.7–7.2 (m, 3 H), 7.0 (s, 1 H), 6.56 (dt, J = 9 Hz, J = 1 Hz, 1 H), 6.08 (dt, J = 9 Hz, J = 4 Hz, 1 H), 3.34 (s, 4 H), 3.12 (t, J = 8 Hz, 2 H), 2.45 (m, 2 H). Anal. Calcd for $C_{16}H_{14}$: C, 93.16; H, 6.84. Found: C, 93.15; H, 6.85.

Acephenanthrylene (5). To a solution of dichlorodicyanoquinone (4.9 g, 21.6 mmol) dissolved in 150 mL of dioxane was added hydrocarbon **4** (1.5 g, 7.20 mmol). This solution was heated to reflux for 2 h, cooled to room temperature, and filtered. The organic layer was concentrated and chromatographed on a 2 × 30 cm silica gel column with benzene. The product was recrystallized from methanol with rapid cooling to yield 1.112 g (75%) of **5** as a yellow[7] crystalline solid: mp 141–142 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 8.64 (d, J = 8 Hz, 1 H), 8.38 (d, J = 7.5 Hz, 1 H), 8.00 (d, J = 5.5 Hz, 1 H), 7.99 (s, 1 H), 7.75 (m, 3 H), 7.60 (dd, J = 7.5 Hz, J = 7.0 Hz, 1 H), 7.20 (d, J = 5 Hz, 1 H), 7.10 (d, J = 5 Hz, 1 H); ^{13}C NMR ($CDCl_3$) 139.58, 138.27, 134.17, 132.17, 131.20, 130.52, 128.60, 128.37, 127.84, 127.30, 126.47, 126.13, 125.89, 123.16, 122.33, 121.35; IR (KBr) 3070, 2920, 1605, 905, 830, 755, 720 cm^{-1}; UV λ_{max} (MeOH) 362 nm (ε 12 000), 359 (8800), 344 (11 000), 328 (11 000), 317 (10 000), 298 (13 000), 287 (10 000), 258 (30 000), 228 (33 000); MS (70 eV), m/z (rel abund) 203 (18), 202 (M^+, 100), 201 (15), 200 (20), 101 (33), 100 (22), 88 (15). Anal. Calcd for $C_{16}H_{10}$: C, 95.02; H, 4.98. Found: C, 94.89; H, 5.04.

Acknowledgment. We thank the National Science Foundation and the National Institutes of Health for financial support.

Note added in proof: An alternative synthesis of the title compound has recently been reported.[8]

Registry No. 1, 38036-08-7; 2, 7467-80-3; 3, 76170-18-8; 4, 76170-19-9; 5, 201-06-9.

(7) Slow crystallization and slow sublimation give crystals that are more red, but the solution spectra of the two crystalline forms are the same.

(8) Neumann, G.; Müllen, K. *Chimia* **1985**, *39*, 275–276.

A Convenient Synthesis of Vinyl Spiro Epoxides from α,β-Unsaturated Ketones

Steven P. Tanis,*[1] Mark C. McMills, and Paul M. Herrinton

Department of Chemistry, Michigan State University, East Lansing, Michigan 48824

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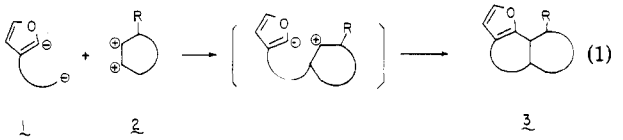
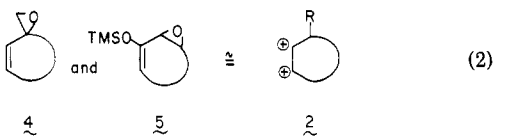
During the course of another study,[2] we became interested in developing bis electrophile equivalents for the annulation shown in eq 1. Our major concern in this



(1)

sequence is the selectivity of the initial carbon–carbon bond formation. To ensure selectivity, we envisioned employing bis electrophile equivalents in which the second reactive site is produced as a result of the first C–C bond formation.

As a result of this analysis, we selected cyclic vinyl spiro epoxides **4**[2,3] and epoxy enol silyl ethers **5**[2,4] as the operational equivalents of **2** (eq 2). Vinyl epoxides have been



(2)

widely employed as electrophiles in S_n2' type of addition reactions providing allylic alcohols as products.[3] Enol silyl ethers of α,β-epoxy ketones have been used by Marino[4a] and Wender[4b] as electrophiles, yielding α′-alkyl α-β-unsaturated cycloalkenones as products. Both sequences allow the construction of a C–C bond and provide a potential electrophilic center at the adjacent carbon.

Numerous variants of **5** have been prepared; however, few cycloalkenone spiro epoxides have been reported.[5]

(1) Recipient of a Camille and Henry Dreyfus Foundation Grant for Young Faculty in Chemistry, 1980–1984.

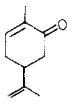
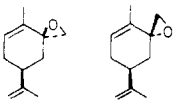
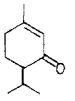
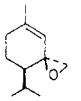
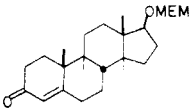
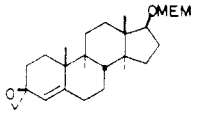
(2) Tanis, S. P.; Herrinton, P. M. *J. Org. Chem.* **1985**, *50*, 3988.

(3) For recent examples of the reaction of cuprates with vinyl epoxides, see: (a) Marino, J. P.; Abe, H. *J. Am. Chem. Soc.* **1981**, *103*, 2907. (b) Ziegler, F. E.; Cady, M. A. *J. Org. Chem.* **1981**, *46*, 122. (c) Marino, J. P.; Abe, H. *Synthesis* **1980**, *11*, 892. (d) Marino, J. P.; Hatanaka, N. *J. Org. Chem.* **1979**, *44*, 4467. (e) Marino, J. P.; Floyd, D. M. *Tetrahedron Lett.* **1979**, 675.

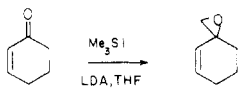
(4) For reactions of cuprates with enol ethers of α,β-epoxy kjetones, see: (a) Marino, J. P.; Jaen, J. C. *J. Am. Chem. Soc.* **1982**, *104*, 3165. (b) Wender, P. A.; Erhardt, J. M.; Letendre, L. J. *J. Am. Chem. Soc.* **1981**, *103*, 2114.

0022-3263/85/1950-5887$01.50/0

Table I

Enone	Thio-alcohol	Sulfonium Salt	Spiro-Epoxide(s)
 9	80%	86%	 10 (84%)
 11	94%	89%	 12 (92%, 4.5:1) 13
 14	82%	62%	 15 (90%, 15:1)
 16	61%	72%	 17 (91%)
 18	87%	84%	 19 (78%)

However, to the best of our knowledge, one of the simplest analogues of **4**, 1-oxaspiro[2.5]oct-4-ene, derived from cyclohexenone, has never been prepared. The most direct approach to the cyclohexenone-derived spiro epoxides **6** (eq 3) employed Corey's dimethylsulfonium methylide.[5f]

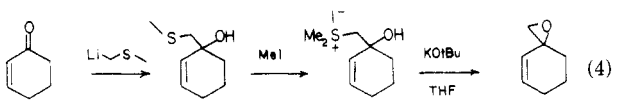


(3)

6 (0–35%)

The "standard" reaction conditions ($NaCH_2SOCH_3$, Me_3SI, THF)[5b,f] in our hands failed to provide **6**. However, replacing dimsylsodium with LDA as the base (THF) provided **6**[6] in variable yield (0–35%, eq 3).

The low and variable yields of **6**, obtained via the sulfur ylide route, caused us to consider performing the same basic spiro epoxidation, but in three discrete steps. As is illustrated in eq 4, [(methylthio)methyl]lithium[7a] adds



(4)

7 (88%) 8 (100%) 6 (91%)

smoothly to 2-cyclohexen-1-one to afford alcohol **7**[6] in 88% distilled yield. Treatment of **7** with CH_3I provided sulfonium salt **8**[6] (100%), which was used without further purification. The closure of the hydroxy sulfonium salt **8** was attempted under three sets of reaction conditions. In the first, treatment of **7** with dimsylsodium in THF[5e] provided a 66% yield of **6**. Reaction of **7** with NaH in THF[5e,8] afforded 52% of **6**. Finally, exposure of **7** to freshly sublimed KO-*t*-Bu in THF gave 91% of **6** after purification by distillation (80% from cyclohexenone).

A variety of α,β-unsaturated ketones were converted to the corresponding vinyl spiro epoxides as is illustrated in Table I. Reaction of 2-methylcyclopentenone with $LiCH_2SCH_3$ gave the corresponding hydroxy sulfide (80%) as a very acid-sensitive, viscous, colorless liquid. Smooth formation of the sulfonium salt (86%) followed by treatment with KO-*t*-Bu in THF gave a (80%, 1:1) mixture of the desired epoxide **10** and the related β,γ-unsaturated aldehyde. Repetition of the epoxide formation in carefully base-washed glassware afforded 85% of **10**. Compound **10** was extremely acid labile, forming the unconjugated aldehyde even in $CDCl_3$; therefore, the spiro epoxides of the remaining entries in Table I were formed in base-washed glassware, and ^1H NMR were measured in C_6D_6.

Carvone **11** provided a mixture (4.5:1) of **12**[6,10] and **13**[6,10] in 92% yield. Piperitone **14**,[6,11] isophorone **16**, and the androstenone **18**[11] yielded single spiro epoxides in excellent yields from starting enones. Our results are summarized in Table I.[13]

Experimental Section

General Procedures. Tetrahydrofuran (THF) was dried by distillation under argon from sodium benzophenone ketyl; tetramethylethylenediamine (TMEDA) was dried by distillation, under argon, from calcium hydride; dimethyl sulfide was dried by filtration through a column of activity 1 basic alumina; acetone was dried over calcium chloride. *n*-Butyllithium in hexane was purchased from Aldrich Chemical Co., Milwaukee, WI, and titrated by the method of Watson and Eastham.[12] Potassium *tert*-butoxide was purified by sublimation. All other reagents were used as received unless otherwise stated; all reactions were carried out under a blanket of argon with the rigid exclusion of moisture from all reagents and glassware unless otherwise mentioned. The conversion of sulfonium salts to the corresponding vinyl spiro epoxides was performed in carefully base-washed glassware [(i) KOH–EtOH, (ii) distilled water, (iii) saturated aqueous NH_4OH, (iv) distilled water, (v) EtOH)] that had been heated to 150 °C for 4 h and cooled in a desiccator.

Melting points were determined on a Thomas Hoover capillary melting point apparatus and are uncorrected. Infrared spectra were recorded on a Pye-Unicam SP-1000 infrared spectraphotometer with polystyrene as standard. Proton magnetic resonance spectra were recorded on a Bruker WM-250 spectrometer at 250 MHz as solutions in the solvents indicated. Chemical shifts are reported on the δ scale relative to a tetramethylsilane internal standard. Data are reported as follows: chemical shift (multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad), coupling constant (Hz), integration). Electron-impact mass spectra (EI/MS) were recorded in a Finnigan 4000 with an Inces 4021 data system. High-resolution mass spectra were performed by the MSU Department of Biochemistry, Mass Spectroscopy Facility, East Lansing, MI.

(5) (a) Burfurd, C.; Cooke, F.; Roy, G.; Magnus, P. *Tetrahedron* **1983**, *39*, 867. (b) Maurer, B.; Hauser, A.; Thommen, A.; Schulte-Elte, K. H.; Ohloff, G. *Helv. Chim. Acta* **1980**, *63*, 293. Rosenberger, M.; Jackson, W.; Saucy, G. *Helv. Chim. Acta* **1980**, *63*, 1665. (c) Trost, B. M.; Keeley, D. E.; Arndt, H. C.; Rigby, J. H.; Bogdanowicz, M. J. *J. Am. Chem. Soc.* **1977**, *99*, 3080. (d) van Ende, D.; Krief, A. *Tetrahedron Lett.* **1976**, 457. (e) Johnson, C. R.; Schroeck, C. W.; Shanklin, J. R. *J. Am. Chem. Soc.* **1973**, *95*, 7424. (f) Corey, E. J.; Chaykovsky, M. *J. Am. Chem. Soc.* **1964**, *86*, 1899. (h) Shanklin, J. R.; Johnson, C. R.; Ollinger, J.; Coates, R. M. *J. Am. Chem. Soc.* **1973**, *95*, 3429.

(6) All yields refer to isolated, purified products. Infrared, ^1H NMR, and mass spectra are fully consistent with the assigned structures.

(7) (a) Peterson, D. J. *J. Org. Chem.* **1967**, *32*, 1717. For the addition of other sulfur-stabilized carbanions to carbonyl compounds, see for example: (b) Corey, E. J.; Seebach, D. *J. Org. Chem.* **1966**, *31*, 4097. (c) Durst, T.; Viau, R.; Van DeuElzen, R.; Nguyen, C. H. *J. Chem. Soc., Chem. Commun.* **1971**, 1334.

(8) Townsend, J. M.; Sharpless, K. B. *Tetrahedron Lett.* **1972**, 3313.

(9) Prepared by a modification of the procedure of: Stowell, J. C.; Hauck, H. F., Jr. *J. Org. Chem.* **1981**, *46*, 2629.

(10) Assigned by analogy to the precedent established by Trost. See ref 5c.

(11) **15** is expected to be the major isomer; however, this has not been unequivocally established.

(12) Watson, S. L.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.

(13) For very sensitive vinyl spiro epoxides, we have found that in situ generation of the sulfonium salt (30 equiv of CH_3I, THF–HMPA, 24 h) and cyclization (NaH, THF) after CH_3I removal in vacuo provides reproducibly high yields.

General Procedure for the Preparation of Vinyl Spiro Epoxides. 1-[(Methylthio)methyl]cyclohex-2-en-1-ol (7). To *n*-butyllithium (28.6 mL, 1.75 M in hexane, 50 mmol) chilled in an ice water bath was added TMEDA (5.8 g, 50 mmol). The mixture was warmed to room temperature and allowed to stir for 30 min. The mixture was cooled to 0 °C, and dimethyl sulfide[7] (3.13 g, 50.0 mmol) was added. The resulting pale yellow solution was stirred for 3.5 h at room temperature and cooled to −78 °C (dry ice–2-propanol), and a solution of 2-cyclohexen-1-one (4.85 g, 50 mmol) in THF (30 mL) was added over 5 min. The mixture was warmed to room temperature and cast into ether (150 mL) and saturated aqueous NH_4Cl (150 mL). The organic phase was separated, washed with water (150 mL), dried (Na_2SO_4), and concentrated in vacuo to provide a viscous yellow liquid. The crude product was purified by distillation, bp 65–68 °C (0.007 mm), to provide 6.7 g, 88%, of 1-[(methylthio)methyl]cyclohex-2-en-1-ol (7) as a colorless, viscous liquid. ^1H NMR (250 MHz): δ 5.85 (ddd, J = 10, 4, 3.15 Hz, 1 H), 5.66 (dddd, J = 9.5, 2.4, 2.0, 0.77 Hz, 1 H), 2.75 (d, J = 13.4 Hz, 1 H), 2.67 (d, J = 13.4 Hz, 1 H), 2.50 (br s, 1 H), 2.20 (s, 3 H), 2.09–1.95 (2 H), 1.85–1.57 (4 H). EI/MS (70 eV): 158 (M^+, 6.65), 141 (32.3), 95 (base). IR (neat): 3470 (br), 3050, 2950, 2855, 1645, 1435, 1220, 1185, 1055, 1000, 965 (br), 740 cm^{-1}.

1-[(Dimethylsulfonio)methyl]cyclohex-2-en-1-ol (8). To a solution of allylic alcohol 7 (3.16 g, 20 mmol) in dry acetone (10 mL) was added methyl iodide (5.67 g, 40 mmol). The mixture was allowed to stir at room temperature overnight and then concentrated in vacuo to provide 6.0 g, 100%, of the sulfonium salt 8 as a white solid, mp 155 °C dec, that was used without further purification.

8-Oxaspiro[5.2]oct-2-ene (6). To a suspension of the sulfonium salt 8 (6.0 g, 20 mmol) in 250 mL of THF was added 2.9 g (25.9 mmol) of freshly sublimed KO-*t*-Bu. The mixture was allowed to stir at room temperature for 4 h, quenched with saturated aqueous $NaHCO_3$ (50 mL), and was cast into ether (250 mL). The aqueous phase was separated and extracted with ether (4 × 100 mL), and the combined organic extracts were washed with saturated aqueous $NaHCO_3$ (0.5 L) and brine (0.5 L) and dried ($MgSO_4$, K_2CO_3). The solvent was removed by distillation at atmospheric pressure, and the residue was purified by distillation, bp 70–72 °C (0.37 mm), to provide 2.0 g, 91%, of 6 as a colorless liquid. ^1H NMR (250 MHz, $CDCl_3$): δ 6.12 (ddd, J = 10.07, 3.97, 3.66 Hz, 1 H), 5.25 (br d, J = 10.07 Hz, 1 H), 2.84 (d, J = 4.88 Hz, 1 H), 2.79 (d, J = 4.88 Hz, 1 H), 2.3–1.5 (6 H). EI/MS (70 eV): 110 (M^+, 83), 93 (51), 79 (base). IR (neat): 3080, 3020, 1460, 950, 810, 760 cm^{-1}. MS: M^+ calcd for $C_7H_{10}O$ 110.073160, M^+ found 110.07320.

Vinyl Spiro Epoxides 10. ^1H NMR (250 MHz, C_6D_6): δ 5.34 (m, 1 H), 3.61 (dd, J = 10.15, 0.45 Hz, 1 H), 3.42 (d, J = 10.15 Hz, 1 H), 2.15–1.62 (4 H), 1.73 (m, 3 H). EI/MS (70 eV): 110 (M^+, 22), 95 (6), 81 (base), 79 (61), 77 (24), 67 (11), 53 (35), 40 (37). IR (neat): 3040, 2995, 1460, 910, 860, 740 cm^{-1}.

Vinyl Spiro Epoxides 12 and 13. ^1H NMR (250 MHz, C_6D_6): δ 5.64 (m, 0.18 H), 5.53 (m, 0.82 H), 4.69 (m, 2 H), 2.78 (d, J = 4.74 Hz, 0.18 H), 2.59 (dd, J = 5.22, 1.73 Hz, 0.82 H), 2.33 (d, J = 4.74 Hz, 0.18 H), 2.27 (d, J = 5.22 Hz, 0.82 H), 2.1–1.3 (5 H), 1.54 (br s, 3 H), 1.47 (m, 3 H). EI/MS (70 eV): 164 (M^+, 13), 149 (44), 133 (16), 123 (58), 119 (79), 107 (91), 91 (base), 79 (49), 67 (21). IR (neat): 2945, 1685 (w), 1650, 1383, 1340, 1068, 945, 900, 842, 810 cm^{-1}.

Vinyl Spiro Epoxide 15. ^1H NMR (250 MHz, C_6D_6): δ 4.93 (m, 1 H), 2.50 (d, J = 5.24 Hz, 1 H), 2.32 (d, J = 5.24 Hz, 1 H), 1.51 (d, J = 0.84 Hz, 3 H), 1.85–1.2 (6 H), 1.08 (d, J = 7.55 Hz, 3 H), 0.94 (d, J = 7.55 Hz, 3 H). EI/MS (70 eV): 166 (M^+, 11), 149 (9.3), 137 (27), 121 (20), 105 (34), 93 (73), 81 (base), 69 (34), 55 (25), 43 (62). IR (neat): 2990, 2900, 2870, 1470, 1375, 1205, 1170, 1068, 720 cm^{-1}.

Vinyl Spiro Epoxide 17. ^1H NMR (250 MHz, C_6D_6): δ 5.54 (br s, 1 H), 3.45 (ab q, J = 13.26, 10.78 Hz, 2 H), 1.59 (br s, 3 H), 0.90 (br s, 6 H), 1.8–1.2 (4 H). EI/MS (70 eV): 152 (M^+, 11), 151 (11), 123 (39), 109 (18), 107 (23), 95 (30), 91 (21), 81 (35), 69 (base), 55 (22). IR (neat): 2990 (br), 2890, 2850, 1680 (w), 1460, 1375, 1285, 1195, 1140, 1070, 1040, 915, 830 cm^{-1}.

Vinyl Spiro Epoxide 19. ^1H NMR (250 mHz, C_6D_6): δ 4.97 (br s, 1 H), 4.69 (br s, 2 H), 3.65 (d q, J = 3.65, 1.67 Hz, 2 H), 3.50 (t, J = 8.48 Hz, 1 H), 3.39 (t, J = 5.02 Hz, 1 H), 3.14 (s, 3 H), 2.53 (br s, 2 H), 2.16–1.86 (4 H), 1.70–0.55 (16 H), 0.89 (s, 3 H), 0.87 (s, 3 H). EI/MS (70 eV): 390 (M^+, 0.32), 377 (0.41), 312 (0.28), 300 (0.96), 147 (4), 133 (4), 119 (5), 105 (9), 89 (base), 79 (7), 59 (56). IR (neat): 2955, 2870, 1460, 1360, 1170, 1140, 1060, 990, 940, 870, 750 cm^{-1}.

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Preparation of an Aromatic Synthon for Maytansinoid Synthesis†

Thomas E. Goodwin,* Shari G. Orlicek, N. Renee Adams, Lynn A. Covey-Morrison, J. Steve Jenkins, and Gary L. Templeton

Department of Chemistry, Hendrix College, Conway, Arkansas 72032

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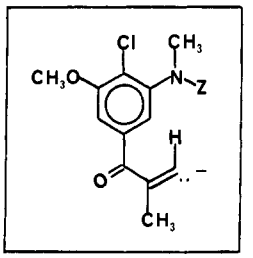
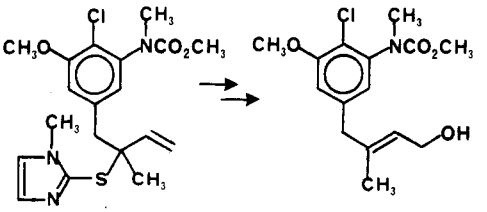
Maytansine is a complex, antileukemic natural product[1] whose total synthesis has been achieved in three laboratories[2] thus far. Several maytansine congeners have been discovered which are oxygenated on carbon number 15 (maytansine numbering system[1]).[3] A synthon for the vinyl anion 1 should be a useful reagent for the construction of 15-oxygenated maytansinoids, and this paper details the preparation and alkylation of such a reagent.



1

A number of reports deal specifically with the preparation of aromatic maytansinoid moieties,[2b,4] and one of these involves a [2,3]-sigmatropic rearrangement. Ho has described[4d] the preparation of allylic sulfide 2 from 2-amino-5-methylphenol, as well as its oxidation and rearrangement to the sulfenate ester, followed by desulfurization to provide alcohol 3.



2 3

The present paper details a similar allylic sulfoxide–sulfenate ester rearrangement and is an extension of earlier model studies.[5] Herein is described the preparation of

† Dedicated to Professor Ernest Wenkert on the occasion of his 60th birthday.

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