7.3–7.8 (m, 15 H). Physical data of pure compounds **1** and **2** are described below.

4-(Benzyloxy)-2-(triphenylstannyl)-1-butene and 4-(Benzyloxy)-1-(triphenylstannyl)-1-butene. The reaction of 4-(benzyloxy)-1-butyne with $(Ph_3Sn)_2Zn$·TMEDA in the presence of CuCN catalyst according to the general procedure gave a mixture of the title compounds. Isomeric ratio (4-(benzyloxy)-2-(triphenylstannyl)-1-butene/the 1-triphenylstannyl isomer = 79/21) was determined by ^1H NMR and ^{119}Sn NMR spectra. Each isomer was purified by preparative TLC on silica gel (10:1 hexane/ethyl acetate). 4-(Benzyloxy)-2-(triphenylstannyl)-1-butene: bp 220–225 °C (0.08 torr, bath temperature); IR (neat) 3062, 2900, 2854, 1481, 1429, 1099, 1075, 997, 929, 728, 698 cm^{-1}; NMR (200 MHz, $CDCl_3$) δ 2.73 (t, J = 6.4 Hz, 2 H), 3.48 (t, J = 6.4 Hz, 2 H), 4.13 (s, 2 H), 5.46 (br s, 1 H), 6.06 (br s, 1 H), 7.10–7.75 (m, 20 H). Anal. Calcd for $C_{29}H_{28}OSn$: C, 68.13; H, 5.52. Found: C, 68.41; H, 5.57. 4-(Benzyloxy)-1-(triphenylstannyl)-1-butene (semisolid): IR (neat) 3060, 2922, 2852, 1428, 1100, 1074, 1024, 998, 726, 696 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.50–2.70 (m, 2 H), 3.59 (t, J = 6.7 Hz, 2 H), 4.52 (s, 2 H), 6.29 (m, 2 H), 7.10–7.78 (m, 20 H).

1-Phenyl-1-(triphenylstannyl)ethene and (*E*)-1-Phenyl-2-(triphenylstannyl)ethene. A solution of phenylacetylene in THF was treated with $(Ph_3Sn)_2Zn$·TMEDA to give a mixture of title compounds. Each isomer was prepared in a pure form from 1-[((trifluoromethyl)sulfonyl)oxy]-1-phenylethene or (*E*)-β-bromostyrene (see below).

General Procedure for the Reaction of Acetylenic Compound with $(Ph_3Sn)_2Zn$ Generated in Situ. Phenyllithium (1.81 M, cyclohexane/ether (70/30) solution, 6.6 mL, 12 mmol) was added to a suspension of $SnCl_2$ (0.76 g, 4.0 mmol) in THF (10 mL) at 0 °C under an argon atmosphere. After being stirred for 30 min at 0 °C, the resulting solution of Ph_3SnLi[8] was treated with $ZnBr_2$ (0.45 g, 2.0 mmol). The mixture was stirred for another 15 min, and a solution of 1-dodecyne (0.17 g, 1.0 mmol) in THF (2.0 mL) was added. A catalytic amount of CuCN (9 mg, 0.1 mmol) was added, and the whole was stirred at 0 °C for 15 min and then at 25 °C for 2 h. Workup followed by purification as described above gave a mixture of **1** and **2** (76:24) in 68% combined yield. (Triphenylstannyl)lithium prepared from Ph_3SnH and lithium diisopropylamide could also be used for the reaction.

2-[((Trifluoromethyl)sulfonyl)oxy]-1-heptene. This compound was produced from 1-heptyne and trifluoromethanesulfonic acid according to the reported procedure.[17] 2-[((Trifluoromethyl)sulfonyl)oxy]-1-dodecene and 1-phenyl-1-[((trifluoromethyl)sulfonyl)oxy]ethene were produced in the same manner.

General Procedure for the Transformation of Alkenyl Iodides and Enol Triflate into Vinylstannanes. Conversion of 2-[((trifluoromethyl)sulfonyl)oxy]-1-dodecene into 2-(triphenylstannyl)-1-dodecene is representative. A solution of 2-[((trifluoromethyl)sulfonyl)oxy]-1-dodecene (0.32 g, 1.0 mmol) in THF (2.0 mL) was added to a suspension of $(Ph_3Sn)_2Zn$·TMEDA (1.76 g, 2.0 mmol) in THF (10 mL). A catalytic amount of $Pd(PPh_3)_4$ (58 mg, 0.05 mmol) was added, and the resulting mixture was stirred at 25 °C for 3 h. Ice-cooled 1 N HCl was added, and the mixture was extracted with ethyl acetate. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated. The resulting residue was purified by preparative TLC on silica gel (hexane) to give 2-(triphenylstannyl)-1-dodecene (0.40 g) in 78% yield: bp 175 °C (0.08 torr, bath temperature); IR (neat) 3062, 2922, 1429, 1074, 922, 726, 698 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.88 (t, J = 6.5 Hz, 3 H), 1.0–1.55 (m, 16 H), 2.42 (t, J = 7.5 Hz, 2 H), 5.38 (s, 1 H), 5.95 (s, 1 H), 7.3–7.8 (m, 15 H). Anal. Calcd for $C_{30}H_{38}Sn$: C, 69.65; H, 7.40. Found: C, 69.65; H, 7.67.

(*E*)-1-(Triphenylstannyl)-1-octene: bp 160 °C (0.1 torr, bath temperature); IR (neat) 3062, 2924, 2852, 1598, 1429, 1075, 997, 726, 697 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.80–0.95 (m, 3 H), 1.05–1.55 (m, 8 H), 2.15–2.35 (m, 2 H), 6.21 (m, 2 H), 7.30–7.70 (m, 15 H). Anal. Calcd for $C_{26}H_{30}Sn$: C, 67.71; H, 6.56. Found: C, 67.52; H, 6.60.

A mixture of (*E*)- and (*Z*)-1-(triphenylstannyl)-1-dodecene: bp 170 °C (0.08 torr, bath temperature); IR (neat) 3060, 2922, 1598, 1429, 1075, 726, 697 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 0.80–0.95 (m, 3 H), 0.95–1.50 (m, 16 H), 2.00–2.10 (m, 1.5 H), 2.13–2.30 (m, 0.5 H), 6.10 (d, J = 12 Hz, 0.75 H), 6.20 (m, 0.5 H), 6.80 (dt, J = 12 and 7.0 Hz, 0.75 H), 7.25–7.78 (m, 15 H). Anal. Calcd for $C_{30}H_{38}Sn$: C, 69.65; H, 7.40. Found: C, 69.76; H, 7.62.

2-(Triphenylstannyl)-1-heptene: bp 150 °C (0.08 torr, bath temperature); IR (neat) 3062, 2926, 1429, 1075, 726, 698 cm^{-1}; NMR (200 MHz, $CDCl_3$) δ 0.73 (br t, J = 6.0 Hz, 3 H), 0.95–1.70 (m, 9 H), 2.4 (t, J = 7.0 Hz, 2 H), 5.37 (br s, 1 H), 5.93 (br s, 1 H), 7.1–7.9 (m, 15 H). Anal. Calcd for $C_{25}H_{28}Sn$: C, 67.15; H, 6.31. Found: C, 67.13; H, 6.39.

2-(Triphenylstannyl)-2-propene: mp 77–79 °C (from hexane/CH_2Cl_2); IR (KBr) 3058, 2926, 1427, 1078, 728, 697 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 2.15 (t, J = 1.6 Hz, 3 H), 5.37 (br s, 1 H), 5.98 (br s, 1 H), 7.25–7.75 (m, 15 H). Anal. Calcd for $C_{21}H_{20}Sn$: C, 64.50; H, 5.16. Found: C, 64.46; H, 5.02.

1-Phenyl-1-(triphenylstannyl)ethene: bp 180–185 °C (0.1 torr, bath temperature); IR (neat) 3060, 2925, 1480, 1428, 1075, 1023, 998, 727, 697 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.64 (d, J = 1.8 Hz, 1 H), 6.36 (d, J = 1.8 Hz, 1 H), 7.10–7.75 (m, 20 H). Anal. Calcd for $C_{26}H_{22}Sn$: C, 68.91; H, 4.89. Found: C, 68.66; H, 4.86.

(*E*)-1-Phenyl-2-(triphenylstannyl)ethene. According to the literature,[18] the Grignard reagent derived from (*E*)-β-bromostyrene was treated with Ph_3SnCl to give the title compound: mp 120–121 °C (hexane); IR (KBr) 3060, 1428, 1075, 1000, 990, 728, 698 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 7.10 (s, 2 H), 7.23–7.80 (m, 20 H).

(*Z*)-1-Phenyl-2-(triphenylstannyl)ethene. The compound was prepared from (*Z*)-β-bromostyrene in similar fashion as the *E* isomer: bp 190 °C (0.08 torr, bath temperature); IR (neat) 3060, 2986, 1567, 1481, 1429, 1074, 1022, 997, 727, 697 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 6.48 (d, J = 13 Hz, 1 H), 7.06–7.75 (m, 20 H), 7.86 (d, J = 13 Hz, 1 H). Anal. Calcd for $C_{26}H_{22}Sn$: C, 68.91; H, 4.89. Found: C, 68.96; H, 4.96.

Registry No. **1**, 104849-57-2; **2**, 104849-58-3; **5**, 104849-59-4; **6**, 104849-60-7; **7**, 104849-61-8; **8**, 104849-62-9; I (R = $PhCH_2OCH_2CH_2$), 104849-63-0; I (R = Ph), 104849-65-2; II (R = $PhCH_2OCH_2CH_2$), 104849-64-1; II (R = Ph), 57682-80-1; $(Ph_3Sn)_2Zn$·TMEDA, 39587-92-3; $PdCl_2(PPh_3)_2$, 13965-03-2; $Pd(PPh_3)_4$, 14221-01-3; $RhCl(PPh_3)_3$, 40237-23-8; $(Ph_3Sn)_2Zn$, 104849-66-3; Et_2Zn, 557-20-0; CuCN, 544-92-3; *n*-$C_{10}H_{21}C{\equiv}CH$, 765-03-7; $PhCH_2OCH_2CH_2C{\equiv}CH$, 22273-77-4; $PhC{\equiv}CH$, 536-74-3; *n*-$C_{10}H_{21}{\equiv}CD$, 86014-19-9; Ph_3SnH, 892-20-6; $SnCl_2$, 7772-99-8; $ZnBr_2$, 7699-45-8; (*E*)-1-iodo-1-octene, 42599-17-7; (*Z*)-1-iodo-1-dodecene, 66553-45-5; 2-iodo-1-dodecene, 104849-67-4; 2-[((trifluoromethyl)sulfonyl)oxy]-1-dodecene, 103885-03-6; 2-[((trifluoromethyl)sulfonyl)oxy]-1-heptene, 104849-68-5; 2-bromo-1-propene, 557-93-7; 1-phenyl-1-[((trifluoromethyl)sulfonyl)oxy]ethene, 28143-79-5; (*E*)-1-bromo-2-phenylethene, 588-72-7; (*Z*)-1-bromo-2-phenylethene, 588-73-8; (*E*)-1-(triphenylstannyl)-1-octene, 104849-72-1; 2-(triphenylstannyl)-1-heptene, 104849-69-6; 2-(triphenylstannyl)-2-propene, 104849-70-9; (*Z*)-1-(triphenylstannyl)-1-dodecene, 104849-71-0; (*Z*)-1-phenyl-2-(triphenylstannyl)ethene, 17421-59-9.

(17) Stang, P. J.; Hanack, M.; Subramanian, L. R. *Synthesis*, **1982**, 85. Summerville, R. H.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1974**, *96*, 1110.

(18) Wardell, J. L. *J. Chem. Soc., Dalton Trans.* **1975**, 1786.

Regioselective Alkylation of 3-Substituted 3-Sulfolenes

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The deprotonation/alkylation of 2,5-dihydrothiophene 1,1-dioxide (3-sulfolene), in conjunction with the cheletropic extrusion of SO_2, has recently been shown to be a

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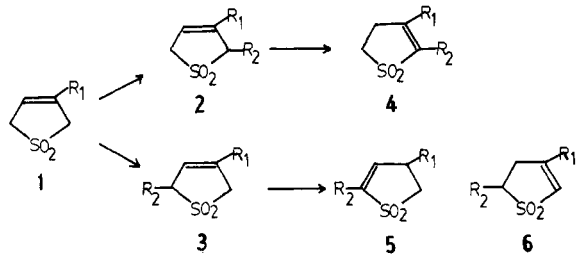
Scheme I



1a, R_1 = Me; **b**, R_1 = Et; **c**, R_1 = *i*-Pr; **d**, R_1 = *t*-Bu; **e**, R_1 = Cl; **1f**, R_1 = Br; **g**, R_1 = C_6H_5; **h**, R_1 = C_6H_5S; **i**, R_1 = $SiMe_3$; **j**, R_1 = COOMe

convenient entry to certain substituted butadienes.[1-3] Furthermore, a methyl group at 3-position was reported[4] to exert a directing effect on the regiochemistry of the alkylation reaction, so that only 2-alkylated 3-methyl-3-sulfolene was obtained.

From analysis of the two possible intermediates in the deprotonation of 3-substituted 3-sulfolene, **A** and **B**, one

A B

would predict that an anion-stablizing group should favor the formation of **B**, and thus 5-alkylated product, while an anion-destablizing group should favor the formation of **A**, and thus 2-alkylated product. Here we report our study of the regiochemistry of deprotonation/alkylation of various 3-substituted 3-sulfolenes.

3-Sulfolenes carrying various substituents were subjected to deprotonation and alkylation under two sets of reaction conditions. Under condition A, the sulfolenes dissolved in THF–HMPA were deprotonated by *n*-butyllithium at −105 °C, a condition under which the carbanion intermediate was found to be stable.[5] The electrophile, methyl iodide, was then added. Under condition B, the deprotonation was carried out with lithium hexamethyldisilazide (LiHMDS) at −78 °C, in the presence of methyl iodide, a procedure that was reported[1,2,4] earlier for successful alkylation. The products were separated by HPLC and identified through isomerization experiment or thermolysis[6] (Scheme I).

The results are compiled in Table I. The regiochemical outcome is well within expectation. Thus under condition A, **1a–1d** gave 2-alkylated products only, exemplifying the insignificance of steric effect under this reaction condition. With **1e** and **1f**, considerable polymerization of starting material occurred. Yet given the low yield of the reaction, again only 2-alkylated product or its isomer was found. For **1g**, **1h**, and **1i**, the alkylation occurred only at the 5-position. With a carbomethoxy group as substituent (**1j**), deprotonation occurred at the 5-position as expected; however, the alkylation occurred at the γ-position instead of the α-position, probably due to a higher charge density at the 3-position. Under condition B, similar regioselectivity was found except with isopropyl- and *tert*-butyl-substituted 3-sulfolens, where the ratio of **2** to **3** was found to be 4:1 and 3:1 respectively, together with a small amount of dialkylated product in each case. If the temperature was further lowered to −105 °C, the ratio of **2d** to **3d** could reach 2:1, with no dialkylated product detected. Apparently the steric effect sets in in these cases but never overrides the electronic effect.

Table I. Deprotonation/Alkylation of 3-Sulfolenes

entry	substrate	condition[a]	products (yield, %)[b]
1	**1a**	A	**2a** (91), **3a** (0)
		B	**2a** (78), **3a** (0)
2	**1b**	A	**2b** (45),[d] **3b** (0)
		B	**2b** (80), **3b** (4)
3	**1c**	A	**2c** (92), **3c** (0)
		B	**2c** (76), **3c** (8)
4	**1d**	A	**2d** (93), **3d** (0)
		B	**2d** (63), **3d** (21)
5	**1e**	A	**2e** (10), **3e** (0)
		B	**2e** (32), **3e** (0)
6	**1f**	A	**2f** (9), **3f** (0)
		B	**2f** (39), **3f** (0)
7	**1g**	A	**2g** (0), **3g** (95)
		B	**2g** (0), **3g** (21)
8	**1h**	A	**2h** (0), **3h** (67)
		B	**2h** (0), **3h** (31)
9	**1i**	A	**2i** (0), **3i** (90)
		B	**2i** (0), **3i** (64)
10	**1j**	A	**2j** (0), **3j** (0)[c]

[a] Condition A: To a solution of 3-sulfolene (2 equiv) and HMPA (4 equiv) in THF at −105 °C was added *n*-BuLi (1 equiv); the methyl iodide (2 equiv) was added 10 min later. Condition B: To a solution of 3-sulfolene (2 equiv), HMPA (4 equiv), and methyl iodide (2 equiv) in THF at −78 °C was added LiHMDS. [b] The yield was corrected for the recovered starting material. [c] γ-Alkylation yielding 3-methylated derivative occurred in 60% yield. [d] Also obtained was the isomer of **2b**, 3-ethylidene-2-methylthiophene 1,1-dioxide, in 30% yield.

Worth comment here is the directing effect of the halo groups (Cl^-, Br^-) and trimethylsilyl group. These are known to be ortho–para directors in electrophilic substitution of phenyl ring.[7,8] That means they all can stabilize an adjacent carbonium intermediate, through either resonance effect (halo groups) or bond polarization (Me_3Si group). While in the deprotonation of 3-sulfolene, Me_3Si still stablizes an adjacent carbanion, but through resonce effect instead. Halo groups destablize an adjacent carbanion, presumably through electrostatic repulsion.[9]

With the high regioselectivity and the moderate to high yield (except for halo-substituted cases[10]), these reactions should be useful in preparing various regiospecific butadiene derivatives in masked (and also stable) form.

Experimental Section

General Procedures. Melting points are uncorrected. ^1H NMR spectra were taken on a Varian EM360 NMR spectrometer or a Bruker MSL-200 NMR spectrometer with $CDCl_3$ as solvent.

(1) Yamada, S.; Ohsawa, H.; Takayama, H. *Chem. Lett.* **1983**, 1003.
(2) Chou, T. S.; Tso, H. H.; Chang, L. J. *J. Chem. Soc., Perkin Trans. 1* **1985**, 515.
(3) (a) Mock, W. L. *J. Am. Chem. Soc.* **1966**, *88*, 2857. (b) McGregor S. D.; Lemal, D. M. *J. Am. Chem. Soc.* **1966**, *88*, 2858. (c) Kellog, R. M.; Prins, W. L. *J. Org. Chem.* **1974**, *39*, 2366.
(4) Chou, T. S.; Tso, H. H.; Chang, L. J. *J. Chem. Soc. Chem. Commun.* **1984**, 1323; *Ibid.* **1985**, 236.
(5) Chou, T. S.; Tso, H. H.; Lin, L. C. *J. Org. Chem.*, in press.
(6) For **3i**, the standard isomerization condition leads to desilylation product.
(7) March, J. *Advanced Organic Chemistry* 3rd ed.; McGraw-Hill: New York, 1985.
(8) For the directing effect of trimethylsilyl group, see: (a) Vcelak, J.; Chvalovsky, V. *Collect. Czech. Chem. Commun.* **1973**, *38*, 1055. (b) Limouzin, Y.; Marie, J. C.; Llinas, J. R. *J. Organomet. Chem.* **1973**, *63*, 51.
(9) Stock, L. M. *Aromatic Substitution Reactions*; Prentice-Hall: Englewood Cliffs, NJ, 1968.
(10) The situation is a little better with LiHMDS as base, since the electrophile was present already in the mixture.

IR spectra were taken on a Perkin-Elmer 297 IR spectrometer. Mass spectra were obtained on a Finnigan MAT 112S spectrometer. Elemental analyses were performed with a Perkin-Elmer 240B elemental analyzer at the Food and Drug Bureau, Department of Health, Taipei.

Materials. The starting sulfolenes **1a**, **1b**, **1c**, **1d**, **1e**, **1g**, and **1i** were prepared from corresponding butadienes[11] and SO_2 following literature procedures. **1f** was converted from **1i** through a bromination–debromosilylation reaction[12]. **1h** was prepared from 3-sulfolene following known procedure.[10] All were recrystallized from ethanol to constant melting point. **1j** was obtained from Fluka.

3-Methyl-3-sulfolene (**1a**): mp 35 °C (lit.[14] mp 35.5 °C). 3-Ethyl-3-sulfolene (**1b**): mp 59–60 °C (lit.[14] mp 57–58 °C). 3-Isopropyl-3-sulfolene (**1c**): mp 40.5–41.5 °C (lit.[14] mp 42–43 °C). 3-*tert*-Butyl-3-sulfolene (**1d**): mp 79–80 °C; ^{1}H NMR δ 1.14 (9 H, s), 3.7–4.0 (4 H, m), 5.68 (1 H, br s); IR 1630, 1310, 1130 cm^{-1}; MS m/z 174 (M^+), 159, 110 (M^+–SO_2), 95. Anal. Calcd for $C_8H_{14}O_2S$: C, 55.14; H, 8.10. Found: C, 55.10; H, 8.07. 3-Chloro-3-sulfolene (**1e**): mp 99.5–100.5 °C (lit.[15] mp 100–100.5 °C). 3-Bromo-3-sulfolene (**1f**): mp 128–129 °C; ^{1}H NMR δ 3.6–4.0 (4 H, m), 6.27 (1 H, br s); IR 1630, 1310, 1130 cm^{-1}; MS m/z 198, 196 (M^+), 134, 132 ($M^+ - SO_2$), 79. Anal. Calcd for $C_4H_5BrO_2S$: C, 24.38; H, 2.56. Found: C, 24.61; H, 2.54. 3-Phenyl-3-sulfolene (**1g**): mp 130–131 °C (lit.[14] mp 133 °C). 3-(Phenylthio)-3-sulfolene (**1h**): mp 55–56 °C (lit.[12] mp 55.5–56.5 °C). 3-(Trimethylsilyl)-3-sulfolene (**1i**): mp 47.5–48.5 °C; ^{1}H NMR δ 0.14 (9 H, s), 3.75 (4 H, br s), 6.18 (1 H, br s); MS m/z 190 (M^+), 126 ($M^+ - SO_2$), 111. Anal. Calcd for $C_7H_{14}O_2SSi$: C, 44.20; H, 7.40. Found: C, 44.12; H, 7.42.

Alkylation Reactions with *n*-Butyllithium as Base (Condition A). To a mixture of 3-substituted 3-sulfolene (0.5 mmol) and hexamethylphosphoramide (HMPA, 2 mmol) in anhydrous THF (10 mL) cooled to −105 °C was added dropwise a solution of *n*-butyllithium (1.4 M, 0.25 mmol). The reaction mixture was stirred at −105 °C for 10 min, after which a brownish red solution was obtained. Methyl iodide (0.5 mmol) was added and the reaction mixture was allowed to come to room temperature grudually. The reaction mixture was concentrated and eluted through a silica column (hexane/EtOAc, 1:1) to remove HMPA and inorganic salt. The products were separated and collected on a HPLC (LiChrosorb column, hexane/EtOAc, 2:1).

Alkylation Reactions with Lithium Hexamethyldisilazide as Base (Condition B). The mixture of 3-substituted 3-sulfolene (0.5 mmol), HMPA (2.0 mmol), and methyl iodide (0.5 mmol) was cooled to −78 °C and stirred efficiently. Freshly prepared LiHMDS (0.25 mmol, from *n*-BuLi and hexamethyldisilazane) was added slowly. The reaction mixture was allowed to come to room temperature gradually and worked up by the same procedure in the condition A above.

Isomerization of Substituted 3-Sulfolenes. The starting sulfolene (1.0 mmol) was dissolved in 10 mL of 0.5 N NaOH solution (enough MeOH was added to make up a homogeneous solution) and stirred at 50 °C overnight. The mixture was then neutralized with ammonium chloride and extracted with ether. The product was isolated and purified by HPLC (Lichrosorb column).

2,3-Dimethyl-3-sulfolene (**2a**): colorless liquid; ^{1}H NMR δ 1.40 (3 H, d, J = 7.0 Hz), 1.81 (3 H, br s), 3.54 (1 H, q, J = 7.0 Hz), 3.67 (2 H, s), 5.60 (1 H, br s); IR 3050, 1642, 1320, 1120 cm^{-1}; MS m/z 146 (M^+), 82 ($M^+ - SO_2$), 67. The NMR data are same as those reported.[2] Isomerization of this gave 2,3-dimethyl-4,5-dihydrothiophene-1,1-dioxide (**4a**): ^{1}H NMR δ 1.86 (3 H, s), 1.92 (3 H, s), 2.70 (2 H, t, J = 7.0 Hz), 3.23 (2 H, t, J = 7.0 Hz).

3-Ethyl-2-methyl-3-sulfolene (**2b**): colorless liquid; ^{1}H NMR δ 1.10 (3 H, t, J = 7.0 Hz), 1.40 (3 H, d, J = 7.0 Hz), 2.14 (2 H, q, J = 7.0 Hz), 3.54 (1 H, q, J = 7.0 Hz), 3.68 (2 H, s), 5.64 (1 H, br s); MS m/z 96 ($M^+ - SO_2$). Anal. Calcd for $C_7H_{12}SO_2$: C, 52.47; H, 7.55. Found: C, 52.45; H, 7.60. Isomerization of this compound gave 3-ethyl-2-methyl-4,5-dihydrothiophene 1,1-dioxide (**4b**): ^{1}H NMR δ 1.06 (3 H, t, J = 7.0 Hz), 1.93 (3 H, br s), 2.23 (2 H, q, J = 7.0 Hz), 2.6–3.0 (2 H, m), 3.1–3.5 (2 H, m).

3-Isopropyl-2-methyl-3-sulfolene (**2c**): colorless liquid; ^{1}H NMR δ 1.04 (3 H, d, J = 7.0 Hz), 1.13 (3 H, d, J = 7.0 Hz), 1.40 (3 H, d, J = 7.0 Hz), 1.9–2.6 (1 H, m), 3.4–4.0 (3 H, m), 5.55 (1 H, m); IR 1630, 1450, 1300, 1225 cm^{-1}; MS m/z 174 (M^+), 110 ($M^+ - SO_2$), 95. Anal. Calcd for $C_8H_{14}SO_2$: C, 55.14; H, 8.90. Found: C, 54.90; H, 8.85. Isomerization of this compound gave 3-isopropyl-2-methyl-4,5-dihydrothiophene 1,1-dioxide (**4c**): ^{1}H NMR δ 1.10 (6 H, d, J = 7.0 Hz), 1.97 (3 H, br s), 1.9–2.4 (1 H, m), 2.5–3.0 (2 H, m), 3.0–3.5 (2 H, m); MS m/z 174 (M^+).

3-Isopropyl-5-methyl-3-sulfolene (**3c**): ^{1}H NMR δ 1.09 (3 H, d, J = 7.0 Hz), 1.24 (3 H, d, J = 7.0 Hz), 1.42 (3 H, d, J = 7.0 Hz), 3.5–4.0 (3 H, m), 5.56 (1 H, m); MS m/z 174 (M^+).

3-*tert*-Butyl-2-methyl-3-sulfolene (**2d**): ^{1}H NMR δ 1.07 (9 H, s), 1.40 (3 H, d, J = 7.0 Hz), 3.50 (1 H, q, J = 7.0 Hz), 3.57 (2 H, d, J = 3.0 Hz), 5.68 (1 H, t, J = 3.0 Hz); IR 1630, 1300, 1225 cm^{-1}; MS m/z 188 (M^+), 124 ($M^+ - SO_2$), 109. Anal. Calcd for $C_9H_{16}O_2S$: C, 57.41; H, 8.56. Found: C, 56.98; H, 8.51. Isomerization of this compound gave 3-*tert*-butyl-2-methyl-4,5-dihydrothiophene 1,1-dioxide (**4d**): ^{1}H NMR δ 1.20 (9 H, s), 2.08 (3 H, br s), 2.4–3.3 (4 H, m); IR 1640, 1290, 1210, 1110 cm^{-1}; MS m/z 188 (M^+), 173, 131, 95.

3-*tert*-Butyl-5-methyl-3-sulfolene (**3d**): mp 58.5–59.5 °C; ^{1}H NMR δ 1.09 (9 H, s), 1.41 (3 H, d, J = 7.0 Hz), 3.73 (2 H, s), 3.87 (1 H, q, J = 7.0 Hz), 5.59 (1 H, m); MS m/z 188 (M^+), 124 ($M^+ - SO_2$), 109. Anal. Calcd for $C_9H_{16}O_2S$: C, 57.41; H, 8.56. Found: C, 57.77; H, 8.36. Isomerization of this compound gave two isomers. 4-*tert*-Butyl-2-methyl-4,5-dihydrothiophene 1,1-dioxide (**5d**): ^{1}H NMR δ 0.95 (9 H, s), 2.05 (3 H, br s), 2.83 (1 H, m), 3.03 (1 H, dd, J = 14, 6 Hz), 3.28 (1 H, dd, J = 14, 8 Hz), 6.30 (1 H, br s); MS m/z 188 (M^+), 173, 124, 109. 3-*tert*-Butyl-5-methyl-4,5-dihydrothiophene 1,1-dioxide (**6d**): ^{1}H NMR δ 1.10 (9 H, s), 1.40 (3 H, d, J = 7.0 Hz), 2.0–3.5 (3 H, m), 6.25 (1 H, br s); MS m/z 188 (M^+), 173, 124, 109.

3-Chloro-2-methyl-3-sulfolene (**2e**): colorless liquid; ^{1}H NMR δ 1.50 (3 H, d, J = 8.0 Hz), 3.7–3.9 (3 H, m), 6.0 (1 H, br s); IR 1620, 1310, 1130, 1100 cm^{-1}; MS m/z 168, 166 (M^+), 104, 102, 67, 65. Anal. Calcd for $C_5H_7ClO_2S$: C, 36.04; H, 4.23. Found: C, 35.74; H, 4.20. Isomerization of this compound gave 3-chloro-2-methyl-4,5-dihydrothiophene 1,1-dioxide (**4e**): mp 89.5–90.5 °C; ^{1}H NMR δ 2.00 (3 H, s), 2.9–3.1 (2 H, m), 3.3–3.5 (2 H, m); IR 3050, 1660, 1320, 1130 cm^{-1}; MS m/z 168, 166 (M^+), 125, 123, 118. Anal. Calcd for $C_5H_7ClO_2S$: C, 36.04; H, 4.23. Found: C, 36.12; H, 4.20.

3-Bromo-2-methyl-3-sulfolene (**2f**): colorless liquid; ^{1}H NMR δ 1.49 (3 H, d, J = 7.0 Hz), 3.5–4.0 (3 H, m), 6.23 (1 H, br s); IR 3050, 1610, 1450, 1320, 1130 cm^{-1}; MS m/z 148, 146 ($M^+ - SO_2$), 67. Anal. Calcd for $C_5H_7BrO_2S$: C, 28.45; H, 3.34. Found: C, 28.72; H, 3.37. Isomerization of this compound gave 3-bromo-2-methyl-4,5-dihydrothiophene 1,1-dioxide (**4f**): solid; mp 128.5–129.5 °C; ^{1}H NMR δ 2.03 (3 H, br s), 2.9–3.6 (4 H, m); IR 1620, 1320, 1130 cm^{-1}; MS m/z 212, 210 (M^+).

3-Phenyl-5-methyl-3-sulfolene (**3g**): mp 90.5–91.5 °C; ^{1}H NMR δ 1.53 (3 H, d, J = 7.0 Hz), 4.07 (1 H, q, J = 7.0 Hz), 4.14 (2 H, s), 6.30 (1 H, br s), 7.38 (5 H, br s); MS m/z 208 (M^+), 144. Anal. Calcd for $C_{11}H_{12}O_2S$: C, 63.44; H, 5.81. Found: C, 63.23; H, 5.76. Isomerization of this compound gave 5-methyl-3-phenyl-4,5-dihydrothiophene 1,1-dioxide (**6g**): ^{1}H NMR δ 1.52 (3 H, d, J = 7.0 Hz), 2.7–2.9 (1 H, m), 3.3–3.7 (2 H, m), 6.98 (1 H, s), 7.45 (5 H, s).

5-Methyl-3-(phenylthio)-3-sulfolene (**3h**): ^{1}H NMR δ 1.35 (3 H, d, J = 7.0 Hz), 3.63 (2 H, br s), 3.83 (1 H, q, J = 7.0 Hz), 5.7 (1 H, br s), 7.4 (5 H, s); IR 3050, 1590, 1580, 1310, 1125 cm^{-1}; MS m/z 240 (M^+), 176. Anal. Calcd for $C_{11}H_{12}O_2S_2$: C, 54.97; H, 5.03. Found: C, 54.65; H, 5.03. Isomerization of this compound gave two isomers. 2-Methyl-4-(phenylthio)-4,5-dihydrothiophene 1,1-dioxide (**5h**): ^{1}H NMR δ 1.98 (3 H, br s), 3.16 (1 H, dd, J = 14, 5 Hz), 3.60 (1 H, dd, J = 14, 8 Hz), 4.30 (1 H, m), 6.20 (1 H, br s), 7.45 (5 H, s); IR 1590, 1580, 1300, 1130, 1105 cm^{-1}; MS m/z 240 (M^+), 110. 5-Methyl-3-(phenylthio)-4,5-dihydrothiophene 1,1-dioxide (**6h**): ^{1}H NMR δ 1.4 (3 H, d, J = 7.0 Hz), 2.2–3.6 (3

(11) (a) Craig, D.; Shipman, J. J.; Fowler, R. B. *J. Am. Chem. Soc.* **1961**, *83*, 2885. (b) Backer, H. J.; Strating, J. *Recl. Trav. Chim. Pays-Bas* **1934**, *53*, 525.

(12) The reaction will be published elsewhere. **1i** was made by an adoption of Ganem's procedure: Batt, B. D.; Ganem, B. *Tetrahedron Lett.* **1978**, 3323.

(13) Hopkins, P. B.; Fuchs, P. L. *J. Org. Chem.* **1978**, *43*, 1208.

(14) Issacs, N. S.; Laila, A. A. A. R. *J. Chem. Soc. Perkin Trans. 2* **1976**, 1470.

(15) Prochazka, M. *Collect. Czech. Chem. Commun.* **1960**, *25* 465.

H, m), 5.78 (1 H, br s), 7.5 (5 H, s); IR 1580, 1300, 1130 cm^{-1}; MS m/z 240 (M^+), 175, 174, 147.

5-Methyl-3-(trimethylsilyl)-3-sulfolene (**3i**): ^1H NMR δ 0.13 (9 H, s), 1.39 (3 H, d, J = 7.0 Hz), 3.71 (3 H, m), 6.08 (1 H, br s); IR 1590, 1300, 1240 1120 cm^{-1}; MS m/z 204 (M^+), 140, 125, 73. Anal. Calcd for $C_8H_{16}O_2SSi$: C, 47.05; H, 7.84. Found: C, 46.6; H, 7.92. A minor product found in the reaction mixture was the isomer of **3i**, 2-methyl-4-(trimethylsilyl)-4,5-dihydrothiophene 1,1-dioxide (**5i**): ^1H NMR δ 0.12 (9 H, s), 2.0 (3 H, br s), 2.31 (1 H, m), 2.95 (1 H, dd, J = 14, 5 Hz), 3.35 (1 H, dd, J = 14, 9 Hz), 6.20 (1 H, m). Also, the thermolysis of **3i** on a preparative GC (Carbowax column, injection port temperature 180 °C, oven temperature 70 °C) gave 2-(trimethylsilyl)-1,3-pentadiene: ^1H NMR δ 0.15 (9 H, s), 1.75 (3 H, d, J = 5 Hz), 5.28 (1 H, d, J = 3.8 Hz), 5.85 (1 H, dq, J = 5, 16 Hz), 6.21 (1 H, d, J = 16 Hz); MS m/z 140 (M^+), 125, 73.

3-Carbomethoxy-3-methyl-2,3-dihydrothiophene 1,1-dioxide: ^1H NMR δ 1.58 (3 H, s), 3.08 (1 H, d, J = 14 Hz), 3.75 (3 H, s), 3.82 (1 H, d, J = 14 Hz), 6.56 (1 H, d, J = 6.0 Hz), 6.75 (1 H, d, J = 6.0 Hz); IR 3080, 1745, 1315, 1270, 1110 cm^{-1}; MS 131 ($M^+ - COOCH_3$), 115, 103. Anal. Calcd for $C_7H_{10}O_4S$: C, 44.20; H, 5.30. Found: C, 43.9; H, 5.3.

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Registry No. **1a**, 1193-10-8; **1b**, 62157-91-9; **1c**, 62157-92-0; **1d**, 62157-93-1; **1e**, 7311-87-7; **1f**, 104664-70-2; **1g**, 57465-40-4; **1h**, 64741-13-5; **1i**, 104692-94-6; **1j**, 67488-50-0; **2a**, 10033-87-1; **2b**, 104664-71-3; **2c**, 104664-72-4; **2d**, 104664-73-5; **2e**, 104664-74-6; **2f**, 104664-75-7; **3c**, 104664-76-8; **3d**, 104664-77-9; **3g**, 104664-78-0; **3h**, 104664-79-1; **3i**, 104664-80-4; **4a**, 71483-55-1; **4b**, 104664-81-5; **4c**, 104664-82-6; **4d**, 104664-83-7; **4e**, 104664-84-8; **4f**, 104664-85-9; **5d**, 104664-86-0; **5h**, 104664-87-1; **5i**, 104664-88-2; **6d**, 104664-89-3; **6g**, 104664-90-6; **4h**, 104664-91-7; 2-(trimethylsilyl)-1,3-pentadiene, 29943-00-8; 3-carbomethoxy-3-methyl-2,3-dihydrothiophene 1,1-dioxide, 104664-92-8; methyl iodide, 74-88-4.

Methoxide-Catalyzed Rearrangement of Methyl (*S*)-Dihydroorotate to Methyl Hydantoin-5-acetate

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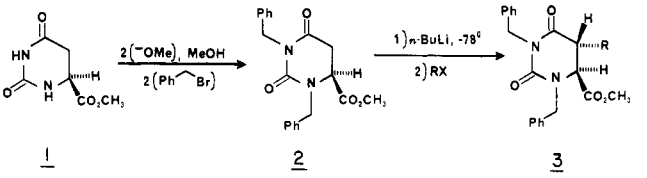
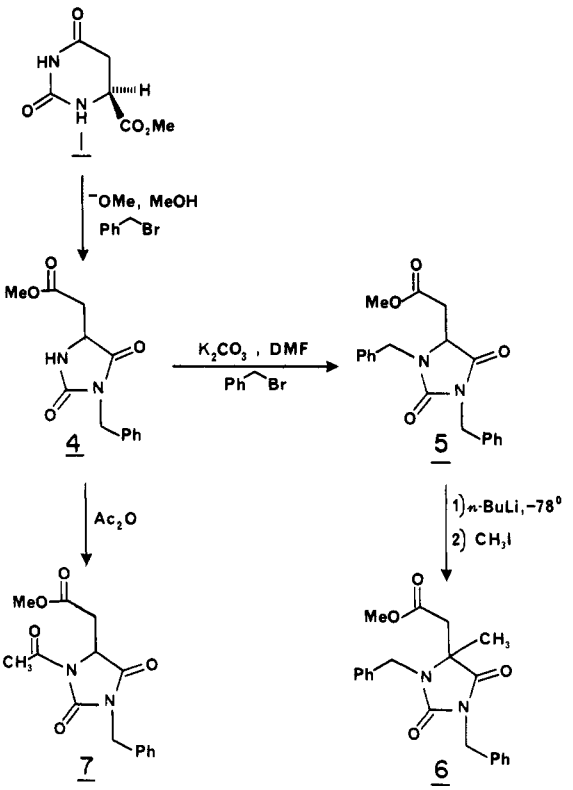
We required, in connection with our studies of the dihydroorotate dehydrogenases,[1] a method for preparation of *trans*-5-alkylated-6(*S*)-dihydroorotates, such as **3**. The only previous synthesis of this type of compound is that provided by Heidelberger and colleagues,[2] who showed that 1,3-dibenzyl and 1,3-dibenzyloxymethyl uracils and related pyrimidines can be reductively alkylated at C5 using lithium (tri-*sec*-butyl)borohydride (L-Selectride, Aldrich) and an alkylating agent. This method, applied to a 1,3-diprotected orotate, would at best afford the pair of 5*R*,6*S* and 5*S*,6*R* isomers of **3**. A plausible entry into the series providing only the 5*R*,6*S* compounds appeared to be by way of diastereospecific alkylation of a suitably 1,3-diprotected-(*S*)-dihydroorotate ester, such as **2**. During attempts to benzylate dihydroorotate **1** at N-3, we discovered that sodium methoxide in methanol readily converts **1** to methyl hydantoin-5-acetate (**10**) in an apparently irreversible reaction. Using this rearrangement, we prepared methyl 1,3-dibenzylhydantoin-5-acetate (**5**), which undergoes alkylation at position 5 of the hydantoin ring.

Scheme I



Scheme II



Results and Discussion

Methyl (*S*)-dihydroorotate (**1**) was prepared from (*S*)-dihydroorotic acid by reaction with diazomethane.[3] We chose to initiate our preparation of **3** by the stepwise protection of the amide nitrogens of the dihydroorotate ester. Thus, **1** was treated with 1 equiv of sodium methoxide and then reacted with benzyl bromide under refluxing conditions. This gave a monobenzylated product later confirmed to be the hydantoin **4**; a monobenzyl dihydroorotate was not obtained. Formation of the hydantoin proceeds with loss of optical activity.

Treatment of **4** with a second equivalent of methoxide and subsequent reaction with benzyl bromide did not give incorporation of a second benzyl group, most likely due to incomplete deprotonation of the second amide hydrogen. However, when **4** was reacted with benzyl bromide and potassium carbonate in DMF at 50 °C, a pale oil was obtained after purification on silica gel. The NMR spec-

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(1) (a) Keys, L. D., III; Johnston, M. *J. Am. Chem. Soc.* **1985**, *107*, 486. (b) Hines, V.; Keys, L. D., III; Johnston, M. *J. Biol. Chem.* **1986**, *261*, 11386.
(2) Hannon, S. J.; Kundu, N. G.; Hertzberg, R. P.; Bhatt, R. S.; Heidelberger, C. *Tetrahedron Lett.* **1980**, *21*, 1105.
(3) Batt, R. D.; Martin, J. K.; Ploeser, J. M.; Murray, J. *J. Am. Chem. Soc.* **1954**, *76*, 3663.

0022-3263/86/1951-4721$01.50/0