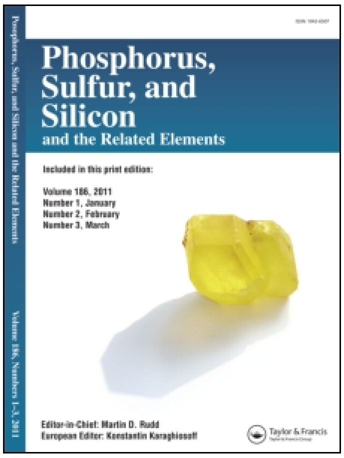


Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

Studies on the Carbonyl Transposition of (5αβ-H)-4,5,5a,6,7,8-Hexahydro-3*H*-Naphtho-[1,8-*bc*]Thiophen-3-One

Peter D. Clark[a]; Nicholas M. Irvine[a]
[a] Department of Chemistry, The University of Calgary, Calgary, Alberta, Canada

To cite this Article Clark, Peter D. and Irvine, Nicholas M.(1994) 'Studies on the Carbonyl Transposition of (5αβ-H)-4,5,5a,6,7,8-Hexahydro-3*H*-Naphtho-[1,8-*bc*]Thiophen-3-One', Phosphorus, Sulfur, and Silicon and the Related Elements, 89: 1, 5 — 15

To link to this Article: DOI: 10.1080/10426509408020426

URL: http://dx.doi.org/10.1080/10426509408020426

Phosphorus, Sulfur, and Silicon, 1994, Vol. 89, pp. 5-15
Reprints available directly from the publisher
Photocopying permitted by license only

STUDIES ON THE CARBONYL TRANSPOSITION OF (5$\alpha\beta$-H)-4,5,5a,6,7,8-HEXAHYDRO-3*H*-NAPHTHO-[1,8-*bc*]THIOPHEN-3-ONE†

PETER D. CLARK‡ and NICHOLAS M. IRVINE

Department of Chemistry, The University of Calgary, 2500 University Drive N.W., Calgary, Alberta, Canada, T2N 1N4

(Received March 16, 1994; in final form April 26, 1994)

This paper describes attempts to prepare the unconjugated naphtho[1,8-*bc*]thiophenone derivative **6** by transposition of the carbonyl in the conjugated compound **1** (Scheme 1). Methods involving epoxidation of the alkene **4** were unsuccessful because the double bond could not be oxidized selectively. Other routes to the epoxide via the bromo-alcohol **9** were also unsuccessful as a result of the necessary diastereomer **9b** being obtained in only very low yield. The major bromo-alcohol diastereomer **9a** was found to undergo elimination to the enol of **1** rather than ring closure to the desired epoxide **5**. Transposition of **1** to **6** was, however, achieved by a thiophenylation route (Scheme 3) involving hydrolysis of the thio-enol ether **15**. However, preference for the major diastereomer **11a** of the thiophenyl alcohol **11** to undergo reactions other than loss of water to form **15** resulted in a low overall yield of the desired unconjugated ketone **6**.

Key words: Naphtho[1,8-*bc*]thiophene; organosulfur synthesis; carbonyl transposition.

INTRODUCTION

In a previous paper, we reported the preparation of 4,5,5a,6,7,8-hexahydro-3*H*-naphtho[1,8-*bc*]thiophen-3- and 4-ones (**1**,**6**) from 6,7-dihydro-5*H*-benzo[*b*]thiophen-4-one.[1] Our interest in these ketones stems from their possible use in the synthesis of sulfur isosteres of important ergoline alkaloids and derivatives. Both of the synthetic schemes were reasonably short, but since the synthesis of the 3-keto derivative (**1**) was simpler and was more amenable to large-scale work, methods to carry out carbonyl transposition of **1** to **6** were investigated. Two separate schemes were examined and, although one was successful, isolated yields were not sufficient to allow the use of **6** in subsequent synthesis. Nevertheless, considerable new chemistry of the, as yet, poorly studied naphtho[1,8-*bc*]thiophene system was uncovered and is reported in the following paragraphs.

EXPERIMENTAL

General

Melting points were determined using a Thiele tube apparatus containing silicone oil and were uncorrected. The IR spectra were recorded on a Nicolet 5DX spectrometer as neat liquids, thin films or KBr discs. The ^{1}H and ^{13}C NMR spectra were obtained on a Bruker ACE 200 or a Bruker AM 400 spectrometer, at 200 and 400 MHz respectively, in $CDCl_3$ solution with either TMS or $CDCl_3$ as the internal standard. Assignments for ^{13}C spectra were made (where possible) on the basis of DEPT, 2D

---

†Taken in part from the Ph.D. Thesis of N. M. Irvine, The University of Calgary, 1993.

‡Author to whom correspondence may be addressed.

correlation experiments and chemical shift data. For compounds which were obtained as mixtures of diastereomers, NMR data for the minor isomer is given in parentheses [ ]. MS and GCMS were recorded on a Hewlett Packard 5970/5890 spectrometer. Elemental analyses were obtained either from the Canadian Microanalytical Service Ltd., B.C. or were conducted by Dorothy Fox in the Department of Chemistry at the University of Calgary. Column chromatography was performed on Merck silica gel, grade 60, 230–400 mesh. Reagents were obtained from the Aldrich Chemical Company and, unless stated otherwise, were used without further purification. Solvents were purified according to procedures outlined in reference 2.

Synthetic Procedures

(3α and β,5aβ-H)-4,5,5a,6,7,8-Hexahydro-3H-naphtho[1,8-bc]thiophen-3-ol (**3a** *and* **3b**). A solution of ketone **1**[1] (0.48 g, 2.5 mmol) in absolute ethanol (10 mL) was added over 10 minutes to a solution of sodium borohydride (0.105 g, 2.75 mmol) in absolute ethanol (15 mL). The reaction mixture was stirred at room temperature under Ar for 27 hours. The mixture was concentrated down to near dryness *in vacuo*, and the residue was suspended in water (10 mL). 3N HCl was added slowly to bring the pH < 7 and the aqueous layer was extracted with $CHCl_3$ (4 × 3 mL). The combined organic extracts were washed with water (1 × 10 mL), brine (1 × 10 mL) and were dried ($MgSO_4$). After filtration of the mixture, the solvent was evaporated *in vacuo* to give 0.47 g (98%) of the crude alcohol **3** as a mixture of diastereoisomers **3a** and **3b** (92:8). Recrystallization from hexanes gave a white solid, mp. 112°–115°C, but did not separate the isomers.

IR (neat) cm^{-1} 3370 (OH); 3015 (CH=); 2931 and 2852 (CH); 1450 (C=C). ^1H NMR (400 MHz) 7.11 (d, 1H, J = 0.9 Hz, H-2); 4.91 (m, 1H, H-3β); 4.75 (dd, 1H, $J_{3\alpha,4\beta}$ = 10.6 Hz, $J_{3\alpha,4\alpha}$ = 6.5, H-3α); 2.87 (br.dd, 1H, $J_{8\beta,8\alpha}$ = 16.9 Hz, $J_{8\beta,7\beta}$ = 6.3, H-8β); 2.75 (br.dddd, 1H, $J_{8\alpha,8\beta}$ = 16.9 Hz, $J_{8\alpha,7\beta}$ = 10.4, $J_{8\alpha,7\alpha}$ = 5.9, $J_{8\alpha,5a\beta}$ = 2.8 Hz, H-8α); 2.53 (m, 1H, H-5aβ), 2.34 (dddd, 1H, $J_{4\alpha,4\beta}$ = 12.8 Hz, $J_{4\alpha,3\alpha}$ = 6.5 Hz, $J_{4\alpha,5\beta}$ = 4.3 Hz, $J_{4\alpha,5\alpha}$ = 2.3, H-4α); 2.11 (m, 1H, H-7α); 1.97–1.87 (m, 2H, H-6β, H-5β); 1.83 (m, 1H, H-7β); 1.60 (ddt, 1H, $J_{4\beta,4\alpha}$ = 12.8 Hz, $J_{4\beta,3\alpha}$ = $J_{4\beta,5\alpha}$ = 10.6, $J_{4\beta,5\beta}$ = 2.7 Hz, H-4β); 1.25 (ddt, 1H, $J_{5\alpha,5\beta}$ 12.7 Hz, $J_{5\alpha,4\beta}$ = $J_{5\alpha,5a\beta}$ = 10.6 Hz, $J_{5\alpha,4\alpha}$ = 2.3 Hz, H-5α); 1.20 (ddt, $J_{6\alpha,6\beta}$ = 13.1 Hz, $J_{6\alpha,7\beta}$ = $J_{6\alpha,5a\beta}$ = 11.2 Hz, $J_{6\alpha,7\alpha}$ = 2.7 Hz, H-6α). ^{13}C NMR (100 MHz) 140.3, 137.9 and 134.6 (Cq); [120.2] 119.0 (C-2); 68.4 [64.7] (C-3); 37.2 (C-5a); 34.9 (C-4; 29.6 (C-5); 29.3 (C-6); 24.4 (C-8); 23.7 (C-7). MS *m/e* 194 (76, $M^{\cdot+}$), 176 (74, M-[H_2O]), 148 (83, 176-[$CH_2{=}CH_2$]), 147 (100, 148-[H]). Analysis calcd. for $C_{11}H_{14}OS$: C 68.00, H 7.26, S 16.50; found C 68.06, H 7.23, S 16.79.

(5aβ-H)-5a,6,7,8-Tetrahydro-5H-naphtho[1,8-bc]thiophen-3-ene (**4**). *p*-Toluenesulfonic acid (0.04 g, 0.2 mmol) was added to a refluxing solution of the alcohols **3** (0.62 g, 3.19 mmol) in toluene (70 mL) and the mixture was stirred at reflux for 15 minutes. The solution was cooled and was washed with 5% aqueous NaOH (2 × 10 mL), water (1 × 20 mL), brine (1 × 30 mL) and was dried ($MgSO_4$). The solvent was evaporated *in vacuo*, and the residue was purified by flash chromatography (hexanes) to afford the olefin **4**, 0.54 g (96%) as a clear oil unstable to prolonged exposure to the atmosphere.

IR (neat) cm^{-1} 3090 and 3029 (CH=); 2977 and 2923 (CH); 1445 (CH_2). ^1H NMR (400 MHz) 6.74 (s, 1H, H-2); 6.50 (dd, 1H, $J_{3,4}$ = 9.7 Hz, $J_{3,5\alpha}$ = 3.1, H-3); 5.94 (ddd, 1H, $J_{4,3}$ = 9.7 Hz, $J_{4,5\beta}$ = 6.3, H-4); 2.83–2.69 (m, 3H, H-5a, H-8α, H-8β); 2.36 (dt, 1H, $J_{5\beta,5\alpha}$ = 16.4 Hz, $J_{5\beta,4}$ = $J_{5\beta,5a\beta}$ = 6.2, H-5β); 2.11 (m, 1H, H-7α); 2.05 (ddt, 1H, $J_{6\beta,6\alpha}$ = 12.6 Hz, $J_{6\beta,5a\beta}$ = $J_{6\beta,7\beta}$ = 6.0, $J_{6\beta,7\alpha}$ = 3.3, H-6β); 1.90 (m, 1H, H-5α); 1.85–1.77 (m, 1H, H-7β); 1.36 (ddt, $J_{6\alpha,6\beta}$ = 12.6 Hz, $J_{6\alpha,5a\beta}$ = $J_{6\alpha,7\beta}$ = 11.2 Hz, $J_{6\alpha,7\alpha}$ = 2.7 Hz, H-6α). ^{13}C NMR (100 MHz) 135.8, 135.3 and 133.9 (Cq); 128.2 (C-4); 123.5 (C-3); 115.1 (C-2); 33.5 (C-5a); 31.0 (C-5); 29.3 (C-6); 24.6 (C-8); 24.0 (C-7). MS *m/e* 176 (42, $M^{\cdot+}$), 148 (52, M-[$CH_2{=}CH_2$]), 147 (100, 148-[H]); exact mass calcd. for $C_{11}H_{12}S$: 176.0660; found: 176.0646.

Alternatively, MeLi (1.4 M in ether, 1.44 mmol) was added by syringe to a suspension of the tosyl hydrazone **2** (see below for preparation) (0.216 g, 0.60 mmol) in anhydrous ether (5 mL) at room temperature under Ar. After 1.5 hours, the mixture was quenched with water (10 mL), the organic layer was separated and the aqueous phase was extracted with ether (3 × 5 mL). The combined organic layers were washed with brine (1 × 10 mL), were dried ($MgSO_4$) and the solvent was evaporated *in vacuo*. Purification of the residue by preparative TLC (hexanes) gave 0.049 g (46%) of a compound with spectroscopic properties identical to olefin **4**.

(5aβ-H)-3-p-Toluenesulphenylhydrazone-4,5,5a,6,7,8-hexahydro-3H-naphtho-[1,8-bc]-thiophene (**2**). A solution of *p*-toluenesulfonylhydrazide (0.31 g, 1.66 mmol) in hot acetic acid (1 mL) was added to ketone **1** (0.32 g, 1.66 mmol) dissolved in a minimal amount of acetic acid. The mixture was brought to reflux for 5 minutes and then was cooled and kept at 5°C for 2 hours. The precipitate was collected and was washed with cold aqueous acetic acid, was air dried and was recrystallized from methanol to afford 0.46 g (78%) of the tosyl hydrazone **2** as a pale yellow/green powder, mp. 217°–218°C.

IR (KBr) cm^{-1} 3198 (CH═); 2927 (CH); 1333 and 1160 (SO_2). ^{1}H NMR (400 MHz) 7.90 (d, 2H, $J_{11,12}$ = 8.3 Hz, H-11); 7.53 (s, 1H, H-2); 7.35 (br.s, 1H, H-9); 7.32 (d, 2H, $J_{12,11}$ = 8.3 Hz, H-12); 2.82 (br.dd, $J_{8\beta,8\alpha}$ = 16.7 Hz, $J_{8\beta,7\beta}$ = 6.1, H-8β); 2.75–2.69 (m, 1H, H-8α); 2.69 (ddd, 1H, $J_{4\alpha,4\beta}$ = 17.1 Hz, $J_{4\alpha,5\alpha}$ = 4.6 Hz, $J_{4\alpha,5\beta}$ = 2.0 Hz, H-4α); 2.51 (m, 1H, H-5aβ); 2.42 (s, 3H, H-14); 2.16 (ddd, 1H, $J_{4\beta,4\alpha}$ = 17.1 Hz, $J_{4\beta,5\alpha}$ = 13.4 Hz, $J_{4\beta,5\beta}$ = 5.3 Hz, H-4β); 2.11 (m, 1H, H-7α); 2.06–1.95 (m, 2H, H-5β, H-6β), 1.80 (m, 1H, H-7β), 1.30 (dq, $J_{5\alpha,5\beta}$ = $J_{5\alpha,5a\beta}$ = $J_{5\alpha,4\beta}$ = 12.8 Hz, $J_{5\alpha,4\alpha}$ = 4.5 Hz, H-5α); 1.21 (ddt, $J_{6\alpha,6\beta}$ = 12.8 Hz, $J_{6\alpha,5a\beta}$ = $J_{6\alpha,7\beta}$ = 11.6 Hz, $J_{6\alpha,7\alpha}$ = 2.5 Hz, H-6α). ^{13}C NMR (100 MHz) 151.1 (C-3): 144.0, 138.2, 135.4, 134.8 and 132.9 (Cq); 129.5 (C-11); 128.1 (C-12); 119.7 (C-2); 34.8 (C-5a); 29.3 (C-4); 29.1 (C-5); 25.7 (C-6); 24.4 (C-8); 23.4 (C-7); 21.6 (C-14); MS *m/e* 360 (4, $M^{+\cdot}$), 176 (78, M-[NNHTs]), 148 (85, 176-[CH_2═CH_2]), 147 (98, 148-[H]). Analysis calcd. for $C_{18}H_{20}N_2O_2S_2$: C 59.97, H 5.59, N 7.77, S 17.79; found: 59.67, H 5.60, N 7.77, S 16.62.

(4α and β,5aβ-H)-4-Bromo-4,5,5a,6,7,8-hexahydro-3H-naphtho[1,8-bc]Thiophen-3-one (**7a** *and* **7b**). Bromides **7a** and **7b** were prepared according to literature procedures.[3–7] The optimum yield was obtained using the procedure described in reference 5. This involved heating the ketone **1** (0.135 g, 0.7 mmol) under reflux with a suspension of $CuBr_2$ (0.70 g, 3.15 mmol) in 50/50 ethyl acetate/chloroform (7 mL) for 1 hour. The bromides **7a** and **7b** were isolated by flash chromatography [0.128 g (65%)], as a mixture of diastereomers (79:21), respectively, and were recrystallized (without separation) from hexanes (charcoal) to yield a pale yellow solid, mp. 89°–96°C.

IR (neat) cm^{-1} 3092 (CH;), 2927 (C;), 1679 (C═;), 502 (C—Br). ^{1}H NMR (400 MHz) [8.05] 8.09 (s, 1H, H-2); [4.82 (dd, $J_{4\beta,5\alpha}$ = 13.3 Hz, $J_{4\beta,5\beta}$ = 4.7, H-4β)]; 4.63 (t, 1H, $J_{4\alpha,5\alpha}$ = $J_{4\alpha,5\beta}$ = 3.0 Hz, H-4α); 3.17 (m, 1H, H-5aβ), 2.93 (br.dd, $J_{8\beta,8\alpha}$ = 16.9 Hz, $J_{8\beta,7\beta}$ = 6.4 Hz, H-8β); 2.76 (br.dddd, 1H, $J_{8\alpha,8\beta}$ = 16.9 Hz, $J_{8\alpha,7\beta}$ = 11.6 Hz, $J_{8\alpha,7\alpha}$ = 6.4 Hz, $J_{8\alpha,5a\beta}$ = 2.9 Hz, H-8α); 2.40 (ddd, 1H, $J_{5\beta,5\alpha}$ = 14.5 Hz, $J_{5\beta,5a\beta}$ = 3.9, $J_{5\beta,4\alpha}$ = 3.0 Hz, H-5β); 2.22 (m, 1H, H-7α); 2.06 (ddt, 1H, $J_{6\beta,6\alpha}$ = 12.4 Hz, $J_{6\beta,5a\beta}$ = $J_{6\beta,7\beta}$ = 6.3 Hz, $J_{6\beta,7\alpha}$ = 3.0 Hz, H-6β); 1.98 (ddd, 1H, $J_{5\alpha,5\beta}$ = 14.5 Hz, $J_{5\alpha,5a\beta}$ = 11.7, $J_{5\alpha,4\alpha}$ = 3.0 Hz, H-5α); 1.96–1.88 (m, 1H, H-7β); 1.34 (ddt, 1H, $J_{6\alpha,6\beta}$ = 12.4 Hz, $J_{6\alpha,5a\beta}$ = $J_{6\alpha,7\beta}$ = 11.2 Hz, $J_{6\alpha,7\alpha}$ = 2.8 Hz, H-6α).

Major isomer: ^{13}C NMR (100 MHz) **102a** 186.0 (C-3); 139.1, 136.5 and 133.0 (Cq); 131.1 (C-2); 50.7 (C-4); 38.9 (C-5); 30.9 (C-5a); 27.9 (C-6); 24.0 (C-8); 23.2 (C-7). Minor isomer: ^{13}C NMR (50 MHz) **102b** 186.0 (C-3); 139.6, 136.2 and 132.8 (Cq); 129.9 (C-2); 53.9 (C-4); 43.1 (C-5); 36.0 (C-5a); 28.3 (C-6); 23.8 (C-8); 23.0 (C-7). MS *m/e* 270, 272 (99, 100, $M^{\cdot+}$), 190 (95, M-[HBr]). Exact mass calcd. for $C_{11}H_{11}Br^{79}OS$: 269.9714; found: 269.9721; $C_{11}H_{11}Br^{81}OS$: 271.9694;:271.9717.

The dibromide **8**, 0.053 g (22%), was also isolated (spectral characteristics shown below) from this reaction mixture.

(5aβ-H)-4,4-Dibromo-4,5,5a,6,7,8-hexahydro-3H-naphtho[1,8-bc]thiophen-3-one (**8**). Dibromide **8** was prepared according to the procedure described in reference 5. Thus, ketone **1** (0.135 g, 0.7 mmol) was treated with $CuBr_2$ (0.70 g, 3.15 mmol) in a refluxing ethyl acetate/chloroform mixture (7 mL) for 12 hours. The dibromide **8** was isolated by flash chromatography [0.191 g (78%)], and was obtained as a white solid, mp. 117°–118°C, on recrystallization from hexanes (charcoal).

IR (neat) cm^{-1} 3098 (CH═); 2935 and 2855 (CH); 1695 (C═O); 1452 (CH_2). ^{1}H NMR (400 MHz) 8.19 (s, 1H, H-2); 3.17 (m, 1H, H-5aβ); 3.11 (dd, 1H, $J_{5\beta,5\alpha}$ = 15.0 Hz, $J_{5\beta,5a\beta}$ = 3.9 Hz, H-5β); 2.92 (br.dd, $J_{8\beta,8\alpha}$ = 16.9 Hz, $J_{8\beta,7\beta}$ = 6.3, H-8β); 2.76 (br.dddd, 1H, $J_{8\alpha,8\beta}$ = 16.9 Hz, $J_{8\alpha,7\beta}$ = 11.4, $J_{8\alpha,7\alpha}$ = 6.2 Hz, $J_{8\alpha,5a\beta}$ = 2.7 Hz, H-8α); 2.61 (dd, 1H, $J_{5\alpha,5\beta}$ = 15.0 Hz, $J_{5\alpha,5a\beta}$ = 12.3 Hz, H-5α); 2.22 (m, 1H, H-7α); 2.09 (ddt, 1H, $J_{6\beta,6\alpha}$ = 12.7 Hz, $J_{6\beta,5a\beta}$ = $J_{6\beta,7\beta}$ = 6.2 Hz, $J_{6\beta,7\alpha}$ = 3.2 Hz, H-6β); 1.94 (m, 1H, H-7β); 1.39 (ddt, 1H, $J_{6\alpha,6\beta}$ = 12.7 Hz, $J_{6\alpha,5a\beta}$ = $J_{6\alpha,7\beta}$ = 12.2 Hz, $J_{6\alpha,7\alpha}$ = 2.8 Hz, H-6α). ^{13}C NMR (100 MHz) 179.6 (C-3); 138.2 and 136.7 (Cq); 133.1 (C-2); 129.7 (Cq); 68.3 (C-4); 53.6 (C-5); 34.6 (C-5a); 27.3 (C-6); 23.9 (C-8); 23.1 (C-7). MS *m/e* 348, 350, 352 (8, 14, 12, $M^{\cdot+}$), 270, 272 (74, 69, M-[Br]), 164 (90, M-[CH_2═CBr_2]), 136 (100, 164-[CO]); exact mass calcd. for $C_{11}H_{10}Br^{79}Br^{81}OS$: 349.8799; found: 349.8797.

(3α,4α and β,5aβ-H)-4-Bromo-4,5,5a,6,7,8-hexahydro-3H-naphtho[1,8-bc]thiophen-3-ol (**9a** *and* **9b**). A mixture of the bromo-ketones **7a** and **7b** (80:20) (0.136 g, 0.5 mmol, 87:13) in absolute ethanol (3 mL) was added over 10 minutes to a solution of sodium borohydride (0.021 g, 0.55 mmol) in absolute ethanol (6 mL). The reaction mixture was stirred at room temperature under Ar for 1 hour. The mixture was concentrated to near dryness *in vacuo* and the residue was suspended in water (10 mL). 3 M HCl was added slowly to bring the pH < 7 and the aqueous layer was extracted with $CHCl_3$ (4 × 3 mL). The combined organic extracts were washed with water (1 × 10 mL), brine (1 × 10 mL) and were dried ($MgSO_4$). After filtration of the mixture, the solvent was evaporated *in vacuo* to give bromo-alcohols **9a** and **9b**, 0.122 g (89%), as an inseparable mixture of diastereoisomers (94:6), mp. 97°C dec., recrystallized from hexanes (charcoal).

IR (neat) cm^{-1} 3311 (OH); 3019 (CH=); 2926 (CH); 520 (C—Br). ^{1}H NMR (400 MHz) $CDCl_3$ + Na_2CO_3, [7.14] 7.19 (s, 1H, H-2); [4.92 (m, H-4β)]; 4.87 (ddd, 1H, $J_{4\alpha,5\beta}$ = 4.6 Hz, $J_{4\alpha,3\alpha}$ = 4.0 Hz, $J_{4\alpha,5\alpha}$ = 1.9 Hz, H-4α); [4.10 (m, H-3α)]; 4.69 (dd, 1H, $J_{3\alpha,OH}$ = 11.6 Hz, $J_{3\alpha,4\alpha}$ = 4.0 Hz, H-3α), 3.09 (m, 1H, H-5aβ); 2.91 (br.dd, 1H, $J_{8\beta,8\alpha}$ = 17.4 Hz, $J_{8\beta,7\beta}$ = 6.7, H-8β); 2.76 (br.dddd, 1H, $J_{8\alpha,8\beta}$ = 17.4 Hz, $J_{8\alpha,7\beta}$ = 11.3, $J_{8\alpha,7\alpha}$ = 6.5 Hz, $J_{8\alpha,5a\beta}$ = 2.7 Hz, H-8α); 2.43 (d, 1H, $J_{OH,3\alpha}$ = 11.6 Hz, OH); 2.39 (dt, 1H, $J_{5\beta,5\alpha}$ = 14.1 Hz, $J_{5\beta,5a\beta}$ = $J_{5\beta,4\alpha}$ = 4.6, H-5β); 2.10 (m, 1H, H-7α); 1.98–1.87 (m, 2H, H-6β, H-7β); 1.79 (ddd, 1H, $J_{5\alpha,5\beta}$ = 14.1 Hz, $J_{5\alpha,5a\beta}$ = 11.8 Hz, $J_{5\alpha,4\alpha}$ = 1.9 Hz, H-5α); 1.33 (ddt, 1H, $J_{6\alpha,6\beta}$ = 12.3 Hz, $J_{6\alpha,5a\beta}$ = $J_{6\alpha,7\beta}$ = 11.1, $J_{6\alpha,7\alpha}$ = 2.12 Hz, H-6α). ^{13}C NMR (100 MHz) $CDCl_3$ + Na_2CO_3, 137.1, 135.4 and 135.0 (Cq); 120.4 (C-2); 69.8 (C-3); 61.5 (C-4); 36.8 (C-5); 32.1 (C-5a); 28.3 (C-6); 24.3 (C-8); 23.7 (C-7). MS *m/e* 272, 274 (38, 39, M$^{\cdot +}$), 193 (82, M-[Br]), 175 (100, 193-[H_2O]). Analysis calcd. for $C_{11}H_{13}BrOS$: C 48.05, H 4.77; found: C 48.36, H 4.80; exact mass calcd. for $C_{11}H_{13}Br^{81}OS$: 273.9848; found: 273.9850.

(4α and β,5aβ-H)-4-Phenylthio-4,5,5a,6,7,8-hexahydro-3H-naphtho[1,8-bc]thiophen-3-one (**10a** *and* **10b**). Lithium isopropylcyclohexylamide (5.2 mmol) was prepared by stirring a mixture of *n*-BuLi (2.45 M in hexanes, 5.2 mmol) and isopropylcyclohexylamine (0.86 mL, 5.2 mmol) in THF (10 mL) at −78°C for 15 minutes under Ar. A solution of the ketone **1** (0.5 g, 2.6 mmol) in HMPA (10 mL) was added *via* syringe and the temperature was allowed to warm to −25°C. The mixture was stirred for 1 hour and was added to a solution of diphenyl disulfide (1.13 g, 5.2 mmol) in THF (15 mL). The reaction mixture was then stirred at −25°C for 1 hour and then at room temperature for a further 30 minutes. After dilution with ether (50 mL), the organic phase was separated and washed successively with 5% aqueous HCl (3 × 10 mL), saturated $NaHCO_3$ (1 × 10 mL), brine (1 × 50 mL) and was dried ($MgSO_4$). After filtration of the mixture, the solvent was evaporated *in vacuo* and the residue was purified by flash chromatography to afford 0.64 g (81%) of the sulfenylated ketone as an mixture of diastereoisomers **10a** and **10b** (72:28), mp. 95°–102°C, from methanol.

IR (neat) cm^{-1} 1675 (C=;), 1561 (C=C); 1465 (CH_2). ^{1}HNMR (400 MHz) [8.00], 8.00 (s, 1H, H-2); 7.52 (m, 2H, H-10); 7.31 (m, 3H, H-11, H-12); [4.10 (dd, $J_{4\beta,5\alpha}$ = 13.2 Hz, $J_{4\beta,5\beta}$ = 4.4 Hz, H-4β)], 3.99 (dd, 1H, $J_{4\alpha,5\alpha}$ = 3.3 Hz, $J_{4\alpha,5\beta}$ = 2.9 Hz, H-4α); 3.12 (m, 1H, H-5aβ); 2.80 (br.dd, $J_{8\beta,8\alpha}$ = 16.9 Hz, $J_{8\beta,7\beta}$ = 6.3, H-8β); 2.77 (br.dddd, 1H, $J_{8\alpha,8\beta}$ = 16.9 Hz, $J_{8\alpha,7\beta}$ = 11.4 Hz, $J_{8\alpha,7\alpha}$ = 6.4 Hz, $J_{8\alpha,5a\beta}$ = 2.8 Hz, H-8α); 2.39 (ddd, 1H, $J_{5\beta,5\alpha}$ = 13.6 Hz, $J_{5\beta,5a\beta}$ = 4.1, $J_{5\beta,4\alpha}$ = 2.9 Hz, H-5β); 2.17 (m, 1H, H-7α); 2.14 (m, 1H, H-6β); [1.67 (q, $J_{5\alpha,5\beta}$ = $J_{5\alpha,5a\beta}$ = $J_{5\alpha,4\beta}$ = 12.6 Hz, H-5α)], 2.05 (ddd, 1H, $J_{5\alpha,5\beta}$ = 13.6 Hz, $J_{5\alpha,5a\beta}$ = 12.6 Hz, $J_{5\alpha,4\alpha}$ = 3.3 Hz, H-5α); 1.94 (m, 1H, H-7β); 1.29 (ddt, 1H, $J_{6\alpha,6\beta}$ = 12.6 Hz, $J_{6\alpha,5a\beta}$ = $J_{6\alpha,7\beta}$ = 11.6 Hz, $J_{6\alpha,7\alpha}$ = 2.8 Hz, H-6α).

Major isomer: ^{13}C NMR (100 MHz) **10a** 188.0 (C-3); 139.2, 136.0, 134.0 and 133.2 (Cq); 132.7 (C-11); 130.0 (C-2); 128.9 (C-10); 127.8 (C-12); 53.7 (C-4); 36.6 (C-5); 31.1 (C-5a); 28.6 (C-6); 24.0 (C-8); 23.2 (C-7). Minor isomer: ^{13}C NMR (100 MHz) **10b** 189.8 (C-3); 140.2, 135.8, 135.2 and 133.4 (Cq); 132.6 (C-11); 129.2 (C-2); 128.9 (C-10); 127.2 (C-12); 56.7 (C-4); 38.9 (C-5); 35.6 (C-5a); 28.5 (C-6); 23.9 (C-8); 23.1 (C-7). MS *m/e* 300 (24, M$^{\cdot +}$), 191 (100, M-[SPh]). Analysis calcd. for $C_{17}H_{16}OS_2$: C 67.96, H 5.37, S 21.34%; found: C 67.78, H 5.13, S 21.56.

Alternatively, a solution of PhS^-Na^+ (0.198 g, 1.50 mmol) in absolute ethanol (2 mL) was added *via* syringe to a stirred mixture of the bromides **7a** and **7b** (80:20) (0.203 g, 0.75 mmol, 87:13) at room temperature. After 1 hour, the solution was concentrated and the residue was taken up into dichloromethane (20 mL). The organic mixture was extracted with 5% aqueous HCl (1 × 5 mL), saturated $NaHCO_3$ (1 × 5 mL), brine (1 × 20 mL) and dried ($MgSO_4$). The solvent was evaporated *in vacuo* and the residue was purified by flash chromatography to yield 0.214 g (95%) of a mixture of the sulphenylated ketones **10a** and **10b** (55:45).

(3α,4αβ,5aβ-H)-4-Phenylthio-4,5,5a,6,7,8-hexahydro-3H-naphtho[1,8-bc]thiophen-3-ol (**11a** *and* **11b**). A mixture of ketones **10a** and **10b** (0.80 g, 2.66 mmol, ratio 72:28) in absolute ethanol (30 mL) was added over 10 minutes to a solution of sodium borohydride (0.12 g, 3.2 mmol) in absolute ethanol (20 mL). The reaction mixture was stirred at room temperature under Ar for 8 hours. The mixture was concentrated to near dryness *in vacuo* and the residue was suspended in water (50 mL). 3 M HCl was added slowly to bring the pH < 7 and the aqueous layer was extracted with $CHCl_3$ (4 × 10 mL). The combined organic extracts were washed with water (1 × 20 mL), brine (1 × 30 mL) and were dried ($MgSO_4$). After filtration of the mixture, the solvent was evaporated *in vacuo* to give 0.75 g (93%) of the crude alcohols **11a** and **11b** (87:13). The major isomer **11a** was separated by crystallization from methanol, and the mother liquor was concentrated *in vacuo* to afford the minor isomer **11b**, which was recrystallized from hexanes.

Alcohol **11a** was obtained as a white solid, mp. 172°C dec., from methanol.

IR (KBr) cm^{-1} 3408 (OH); 2925 (CH). ^{1}H NMR (400 MHz) 7.53 (d, 2H, $J_{10,11}$ = 8.2 Hz, H-10); 7.29 (m, 3H, H-11, H-12); 7.16 (s, 1H, H-2); 4.88 (dd, $J_{3\alpha,OH}$ = 10.1 Hz, $J_{3\alpha,4\alpha}$ = 4.3 Hz, H-3α); 3.87

(ddd, $J_{4\alpha,5\beta}$ = 4.7 Hz, $J_{4\alpha,3\alpha}$ = 4.3, $J_{4\alpha,5\alpha}$ = 3.3 Hz, H-4α); 3.02 (m, 1H, H-5aβ); 2.90 (br.dd, $J_{8\beta,8\alpha}$ = 16.6 Hz, $J_{8\beta,7\beta}$ = 6.6 Hz, H-8β); 2.79–2.72 (m, 1H, H-8α); 2.30 (ddd, 1H, $J_{5\beta,5\alpha}$ = 13.2 Hz, $J_{5\beta,5a\beta}$ = 5.1, $J_{5\beta,4\alpha}$ = 4.7, H-5β); 1.96–1.88 (m, 2H, H-6β, H-7β); 1.94 (m, 1H, H-7α); 1.75 (ddd, 1H, $J_{5\alpha,5\beta}$ = 13.2 Hz, $J_{5\alpha,5a\beta}$ = 11.7, $J_{5\alpha,4\alpha}$ = 3.3, H-5α); 1.28 (m, 1H, H-6α). ^{13}C NMR (100 MHz) 138.3, 136.1, 135.9 and 135.0 (Cq); 131.2 (C-11); 129.1 (C-10); 126.9 (C-12); 120.1 (C-2); 69.1 (C-3); 55.0 (C-4); 35.2 (C-5); 31.7 (C-5a); 29.2 (C-6); 24.3 (C-8); 23.8 (C-7). MS *m/e* 302 (5, $M^{\cdot +}$), 175 (100, M-[PhSH][OH]). Analysis calcd. for $C_{17}H_{18}OS_2$: C 67.51, H 6.00%; found: C 66.28, H 5.33%; exact mass calcd. for $C_{17}H_{18}OS_2$: 302.0799; found: 302.0779.

Alcohol **11b** was recovered as a white solid, mp. 125°–126°C, from hexanes.

IR (KBr) cm^{-1} 3386 (O;), 2920 (CH); ^{1}H NMR (400 MHz) 7.55 (dd, 2H, $J_{10,11}$ = 7.9 Hz, $J_{10,12}$ = 1.8, H-10); 7.33 (m, 3H, H-11, H-12); 7.14 (s, 1H, H-2); 4.58 (dd, 1H, $J_{3\alpha,4\beta}$ = 9.8 Hz, $J_{3\alpha,OH}$ = 2.7 Hz, H-3α); 3.26 (ddd, 1H, $J_{4\beta,3\alpha}$ = 9.8 Hz, $J_{4\beta,5\alpha}$ = 12.5 Hz, $J_{4\beta,5\beta}$ = 2.8 Hz, H-4β); 3.03 (d, 1H, $J_{OH,3\alpha}$ = 2.7 Hz, OH); 2.85 (br.dd, $J_{8\beta,8\alpha}$ = 16.9 Hz, $J_{8\beta,7\beta}$ = 6.6 Hz, H-8β); 2.72 (m, 1H, H-8α); 2.64 (m, 1H, H-5aβ); 2.22 (ddd, 1H, $J_{5\beta,5\alpha}$ = 12.5 Hz, $J_{5\beta,5a\beta}$ = 4.0, $J_{5\beta,4\beta}$ = 2.8 Hz, H-5β); 2.10 (m, 1H, H-7α); 1.92 (m, 1H, H-6β); 1.80 (m, 1H, H-7β); 1.44 (q, 1H, $J_{5\alpha,5\beta}$ = $J_{5\alpha,4\beta}$ = $J_{5\alpha,5a\beta}$ = 12.5 Hz, H-5α); 1.20 (ddt, 1H, $J_{6\alpha,6\beta}$ = 12.6 Hz, $J_{6\alpha,5a\beta}$ = $J_{6\alpha,7\beta}$ = 11.4, $J_{6\alpha,7\alpha}$ = 2.6, H-6α). ^{13}C NMR (100 MHz) 137.5, 136.8, 134.4 and 133.7 (Cq); 133.7 (C-11); 129.0 (C-10); 127.9 (C-12); 119.7 (C-2); 71.2 (C-3); 55.0 (C-4); 37.7 (C-5a); 36.8 (C-5); 29.0 (C-6); 24.3 (C-8); 23.6 (C-7). MS *m/e* 302 (57, $M^{\cdot +}$), 175 (100, M-[PhSH][OH]). Analysis calcd. for $C_{17}H_{18}OS_2$: C 67.51, H 6.00%; found: C 67.10, H 5.45%; exact mass calcd. for $C_{17}H_{18}OS_2$: 302.0799; found: 302.0804.

(5aβ-H)-4-Phenylthio-5a,6,7,8-tetrahydro-5H-naphtho[1,8-bc]thiophen-3-ene (**15**). A solution of the alcohols **11a** and **11b** (0.5 g, 1.65 mmol) in benzene (30 mL) was brought to reflux, *p*-toluenesulfonic acid (26 mg, 0.14 mmol) was added and the mixture was stirred at reflux for 15 minutes. The reaction mixture was cooled and was washed with 5% aqueous NaOH (1 × 5 mL), water (1 × 20 mL), brine (1 × 30 mL) and was dried ($MgSO_4$). The solvent was evaporated *in vacuo* and the residue purified by flash chromatography (hexanes) to afford the olefin **15** 0.101 g (21%), mp. 94°–95°C, from hexanes.

IR (neat) cm^{-1} 2944 (CH); 1474 and 1439 (C=C). ^{1}H NMR (400 MHz) 7.38 (m, 5H, H-10, H-11, H-12); 6.69 (s, 1H, H-2); 6.55 (d, 1H, $J_{3,5\alpha}$ = 2.7 Hz, H-3); 2.88–2.82 (m, 1H, H-5aβ); 2.81 (br.dd, $J_{8\beta,8\alpha}$ = 16.3 Hz, $J_{8\beta,7\beta}$ = 6.3, H-8β); 2.77–2.69 (m, 1H, H-8α); 2.40 (dd, 1H, $J_{5\beta,5\alpha}$ = 16.1 Hz, $J_{5\beta,5a\beta}$ = 6.1 Hz, H-5β); 2.18 (ddd, 1H, $J_{5\alpha,5\beta}$ = 16.1 Hz, $J_{5\alpha,5a\beta}$ = 13.7 Hz, $J_{5\alpha,3}$ = 2.7 Hz, H-5α); 2.13–2.09 (m, 1H, H-7α); 2.00 (ddt, $J_{6\beta,6\alpha}$ = 12.9 Hz, $J_{6\beta,5a\beta}$ = $J_{6\beta,7\beta}$ = 6.7 Hz, $J_{6\beta,7\alpha}$ = 2.9 Hz, H-6β); 1.89–1.77 (m, 1H, H-7β); 1.34 (ddt, 1H, $J_{6\alpha,6\beta}$ = 12.9 Hz, $J_{6\alpha,5a\beta}$ = $J_{6\alpha,7\beta}$ = 11.6, $J_{6\alpha,7\alpha}$ = 2.8 Hz, H-6α). ^{13}C NMR (100 MHz) 135.4, 135.2, 134.7, 134.2 and 133.8 (Cq); 131.7 (C-11); 129.1 (C-10); 127.4 (C-12); 123.6 (C-3); 115.0 (C-2); 36.7 (C-5); 34.2 (C-5a); 28.9 (C-6); 24.5 (C-8); 23.9 (C-7). MS *m/e* 284 (100, $M^{\cdot +}$), 175 (47, M-[SPh]); exact mass calcd. for $C_{17}H_{16}S$: 284.0693; found: 284.0690.

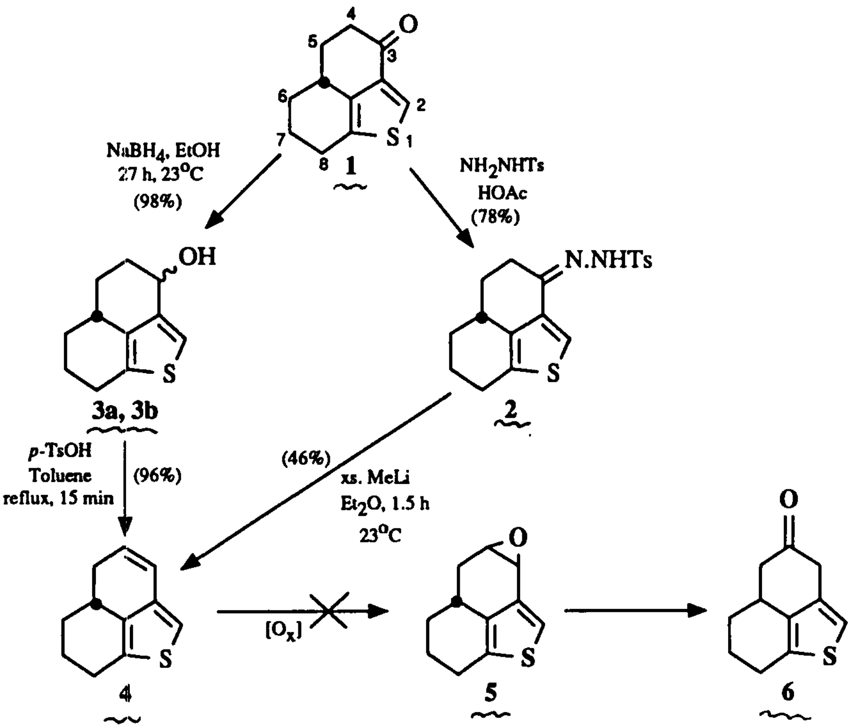
Further elution with hexane yielded a viscous oil which was assigned the structure of the dimer **14** on the following basis. MS *m/e* 568 consistent with the required molecular formula $C_{34}H_{32}S_4$; ^{1}H NMR (200 MHz), 7.60–7.20 (phenyl, 10 H by intergration); 6.76 (s, thiophenic proton); 6.22 (d, olefinic proton with small allylic coupling), 4.63 and 3.69 (both multiplets, intergrating to 1 proton each, assigned either/or to methine hydrogens situated between the two thiophene rings and α to thiophenyl ring). Other signals 3.00 to 1.20 were unresolved.

(5aβ-H)-4,5,5a,6,7,8-Hexahydro-3H-naphtho[1,8-bc]thiophen-4-one (**6**). A mixture of the phenylthio olefin **15** (24.0 mg, 0.084 mmol), $TiCl_4$ (19 μL, 0.0169 mmol) and water (7.6 μL, 0.42 mmol) in acetonitrile (1 mL) was stirred at reflux for 3 days under Ar. The reaction mixture was then quenched with water (5 mL) and was extracted thoroughly with dichloromethane. The organic extracts were combined, washed with brine and were dried ($MgSO_4$). After the solvent was removed *in vacuo*, the residue was purified by preparative TLC (25% EtOAc in hexanes) to afford 9.90 mg (62%) of compound **6**. The spectra of this product were identical to those described in reference 1.

RESULTS AND DISCUSSION

Carbonyl Transposition of 1 *to* 6 *Via the Alkene* 4

Lewis-acid-catalyzed ring opening of epoxides of the type shown by structure **5** (Scheme 1) has been shown by Woodward[8] and by Floss[9] and their co-workers to be an efficient route for transforming conjugated ketones to unconjugated ketones



SCHEME 1 Attempted carbonyl transposition via the alkene 4.

in benzo[*c*,*d*]indoles. This route is attractive in that it involves few steps but may not be practical for thiophene derivatives unless the double bond in **4** could be oxidized selectively (Scheme 1). Since a variety of reagents are available for selective oxidation of double bonds to epoxides, we proceeded to synthesize the alkene **4** *via* alkyllithium mediated decomposition of the tosylhydrazone **2**. Although good yields of the tosylhydrazone **2** were obtained (78%), conversion to the alkene **4** occurred in only moderate yields (46%). Much better yields of the alkene **4** were obtained by reduction of the ketone **1** with sodium borohydride (98%) and acid-catalyzed elimination of water from the alcohol **3** (96%). The alcohol **3** was obtained as a mixture of diastereomers (92:8), the major isomer being tentatively assigned as the β-isomer§ on the basis of expected attack of hydride at the less hindered α-face of the molecule, and on H-3 - H-4 coupling constant values obtained by irradiation of the 4-H resonances in the ^{1}H NMR spectrum of the major isomer of **3**. Further discussion of the stereochemistry of these systems is given later.

Unfortunately, attempts to convert the alkene **4** to the epoxide **5** using peroxides and other standard procedures[10] all led to very complex and unstable reaction mixtures in which none of the desired product could be detected (GCMS and

---

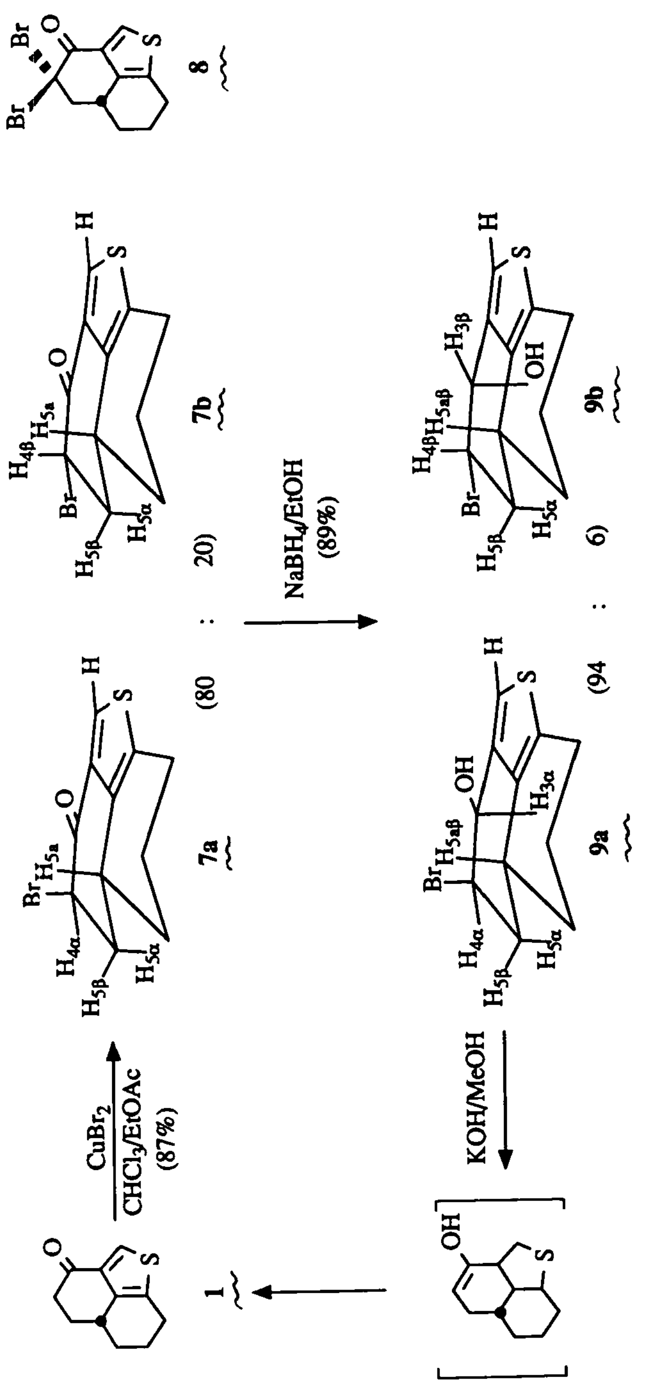
§The β-face of the molecule is designated as the top face of the molecule when it is numbered anticlockwise from sulfur using IUPAC rules. NMR spectra were assigned on the basis that H-5a was positioned on the β-face.

NMR). The polar nature of the products in these mixtures implies that oxidation has proceeded largely at the sulfur atom producing sulfoxides and sulfones. Secondary reactions of these products, likely of Diels-Alder type,[11] probably account for the complexity and instability of the reaction mixtures.

An alternate route to the epoxide **4** would be through ring closure of the bromo-alcohol **9** (Scheme 2). This method has an advantage in that it does not require an oxidation step but does depend on the bromo-alcohol **9** having the correct stereochemistry, since if H-3 and the bromo-substituent on C-4 of **9** are anti-periplanar to one another (as in **9a**), elimination of HBr could be a competing reaction pathway to ring closure to the epoxide **5**. High recovered yields (77–87%) of brominated products were obtained by reaction of **1** with either phenyltrimethylammonium perbromide or Cu(II)bromide. However, GCMS analysis of reaction mixtures obtained with either reagent indicated that a mixture of mono- and dibrominated products were obtained with both reagents and ^{1}H NMR analysis of mono-substituted products isolated by column chromatography revealed that diastereomers had been formed (80:20). No bromination in the thiophene ring was observed. Reduction of the monobromo diastereomeric mixture (**7a** and **7b**) with sodium borohydride led to a diastereomeric mixture (94:6) of the bromo-alcohols (**9a** and **9b**) in 89% isolated yield. These isomers could not be separated either by column chromatography or by crystallization. The change in isomer ratio from 80:20 to 94:6 during the reduction may be due to loss of the more soluble minor isomer during isolation or, perhaps, due to equilibration prior to reduction.

The bromo-alcohols (**9a** and **9b**) underwent conversion to the ketone **1** when samples were dissolved in $CDCl_3$ for NMR analysis unless the $CDCl_3$ was first treated with Na_2CO_3 to remove acidic impurities. Moreover, all attempts to convert the bromo-alcohols to the epoxide **5** under base catalysis resulted in the ketone **1** as the only product. This result suggests that the major diastereomer was **9a** in which H-3α was *anti* to the bromo-substituent thus facilitating elimination over ring closure to the epoxide **5**. ^{1}H NMR analysis supports this contention as the resonance for H-3α consisted of a doublet of doublets (J = 11.6 and 4.0 Hz) which collapsed to doublet (J = 11.6 Hz) on irradiation of the resonance at δ 4.87 (H-4) or to a doublet (J = 4.0 Hz) on shaking the sample with D_2O. The low value of 4.0 Hz is consistent[12,13] with a dihedral angle of ca. 45° for H-3α - C-3 - C-4 - C-4α (see Scheme 2) and places H-3α *anti* to the bromo-substituent. The conformation shown for the bromo-alcohol **9a** (Scheme 2) suggests that dihedral angle for H-4α - C4 - C5 - H-5β should also be around 45°. This assertion was supported by irradiation of the resonance for H-5α (δ 1.79, assigned by virtue of its coupling to H-5aβ) which caused the signal at δ 4.67 for H-4α to collapse to a broad triplet (J = ca. 4.2 Hz) as a result of the overlapping doublet of doublets arising from the coupling of H-4α with H-3α and H-5β (J = 4.0 and 4.2 Hz, respectively).

These observations suggest the major isomer formed in the bromination of the conjugated ketone was **7a** since attack of hydride at the less hindered α-face of **7a** would lead to **9a** as the major bromo-alcohol. ^{1}H NMR chemical shift data and selective irradiation experiments on **7a** supported this conclusion.[14] Although it is clear that the bromo-alcohol **9** does not represent a viable route to the unconjugated ketone **6**, the stereochemistries of the reactions leading to **9a** are interesting since



SCHEME 2 Attempted formation of the epoxide **5** from the bromo-alcohols **9**.

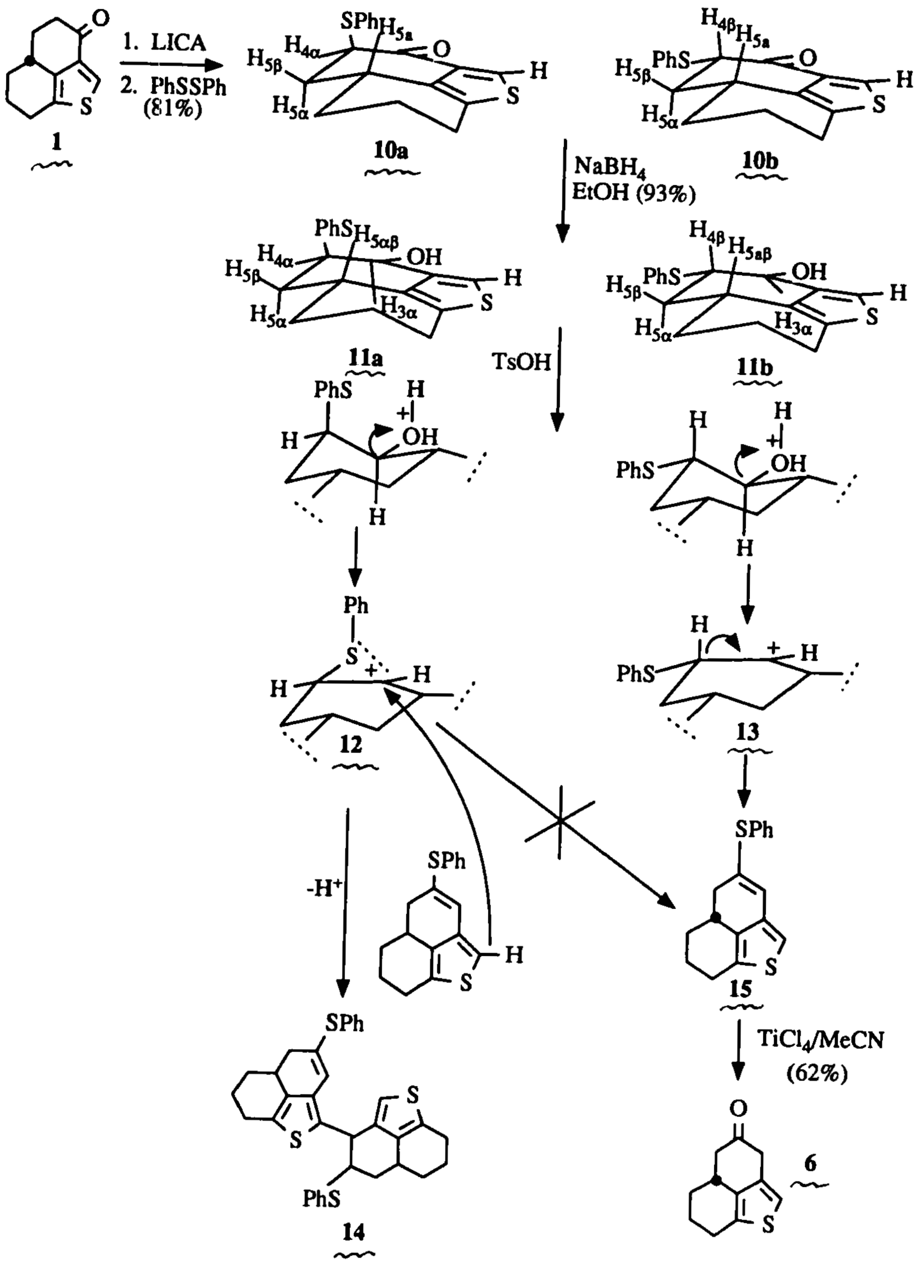
the results imply that either the first step of the bromination of **1** (hydrogen abstraction from C-4) occurs, in the main (80%), at the α-face of the molecule with immediate reaction of "Br" at the β-face or that the radical formed by H-abstraction is hindered to attack by "Br" at the α-face. Neither possibility can be confirmed, but it is interesting to note that Kochi,[7] in his original kinetic investigations on the halogenation of ketones with copper halides, concluded that the active halogenating agent was a complex copper species. We suggest that in our work, such a species approaches the less hindered (molecular modelling) α-face of **1** and transfers "Br" to the β-face in a single step process.

Carbonyl Transposition of **1** *to* **6** *Via Thiophenylation*

1,2-Carbonyl transposition has been achieved in a number of systems by thiophenylation, reduction of the carbonyl group, dehydration and hydrolysis of thioenol ethers so formed.[15,16] In this case thiophenylation proceeded smoothly by reaction of **1** with lithium *N*-isopropylcyclohexylamide and treatment of the subsequent enolate with diphenyl disulfide (Scheme 3). The resulting thiophenyl derivative **10** was obtained as a mixture of diastereomers (72:28 for the crude product) which, according to *J* values obtained from ^{1}H NMR data (see Experimental section) contained the β-isomer **10a** as the major product. The thiophenyl derivatives were also obtained by reaction of a diastereomeric mixture (87:13) of the bromoketones (**7a** and **7b**) with sodium benzenethiolate in ethanol. The crude reaction mixture had a **10a:10b** diastereomeric ratio of 54:46 indicating that the substitution occurred by an S_N1 mechanism, at least to some extent.

Reduction of a 72:28 diastereomeric mixture of compounds **10a** and **10b** with sodium borohydride in ethanol gave an 87:13 mixture of the diastereomeric thiophenyl alcohols **11a** and **11b**. This ratio was determined on the crude product, implying that some equilibration of **10a** and **10b** occurred prior to reduction. The thiophenyl alcohol diastereomers were separated by crystallization and their structures were obtained by analysis of the various couplings in the ^{1}H NMR spectra (see Experimental Section for *J* values). For each compound it was deduced that hydride had attacked the α-face of the molecule placing the —OH substituent on the β-face.

Acid-catalyzed elimination of water from a diastereomeric mixture of the thiophenyl alcohols gave poor yields of the thio-enol ether **15** and a mixture of products from which the dimer **14** could be isolated. Conversion of the hydroxyl group to a better leaving group or use of base catalysis failed to improve the yield of the desired product. Individual reaction of the separated diastereomers under acidic catalysis was interesting since it showed that the minor isomer **11b** reacted cleanly to give the desired thio-enol ether **15** as the only product whereas the major isomer resulted in a complex mixture containing the dimer **14** as the major product. It is surmised that the major diastereomer **11a** undergoes protonation and loss of water to form a carbocation **12** stabilized by the adjacent thiophenyl group. The increased carbocation lifetime resulting from this stabilization would then allow the system to undergo intermolecular reaction leading to the dimer **14** and other unidentified products. In the case of the minor diastereomer **11b**, stabilization of the carbocation



SCHEME 3 Carbonyl transposition via thiophenylation of 1.

13 by the thiophenyl group is not possible and elimination occurs to give the desired product.

Treatment of the thio-enol ether **15** with $TiCl_4$ resulted in a reasonable yield (62%) of the desired unconjugated ketone **6**. However, since it was clear that the thiophenylation route would not be a practical synthesis of **6**, no attempt was made to optimize this reaction. Analysis of other carbonyl transposition methods showed that similar stereochemical barriers could thwart these attempts. Consequently, we abandoned the use of these naphthothiophene derivatives in the synthesis of thia-ergoline compounds. Other, more successful approaches to thia-ergoline compounds will be described in future publications.

ACKNOWLEDGEMENTS

We wish to thank The Natural Sciences and Engineering Research Council of Canada and Alberta Sulphur Research Ltd., Calgary, Alberta, Canada for financial support.

REFERENCES

1. P. D. Clark, N. M. Irvine and P. Sarkar, *Can. J. Chem.*, **69**, 1011 (1991).
2. Edited by B. S. Pulniss, A. J. Hannaford, P. W. G. Smith and A. R. Tatchell, "Vogel's Textbook of Practical Organic Chemistry," 5th ed., Longman Scientific (1989).
3. A. Marquet and J. Jaques, *Bull. Soc. Chim.* France, 90 (1962).
4. J. I. Degraw, J. G. Kennedy and W. A. Skinner, *J. Heterocyclic Chem.*, **3**, 9 (1966).
5. B. L. Chenard, J. R. McConnell and J. S. Swenton, *J. Org. Chem.*, **48**, 4312 (1983).
6. L. C. King and G. K. Ostrum, *J. Org. Chem.*, **29**, 3459 (1964).
7. J. F. Kochi, *J. Am. Chem. Soc.*, **77**, 5274 (1955).
8. E. C. Kornfeld, E. J. Kornfeld, G. B. Kline, M. J. Mann, D. E. Morrison, R. G. Jones and R. B. Woodward, *J. Am. Chem. Soc.*, **78**, 3087 (1956).
9. D. E. Nicols, J. M. Robinson, G. S. Li, J. M. Cassady and H. G. Floss, *Org. Preps. and Procedures*, **9**, 277 (1977).
10. R. C. Larock, "Comprehensive Organic Transformations" (VCH Publishers, Inc., New York, 1989).
11. R. M. Scrowston and B. Iddon, *Recent Advances in the Chemistry of Benzothiophenes*, **11**, 177, p. 360 (1970).
12. R. M. Silverstein, G. C. Bassler and T. C. Morril, "Spectrometric Identification of Organic Compounds," 4th ed., John Wiley and Sons, 1981.
13. M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959).
14. N. M. Irvine, Ph.D. Thesis, The University of Calgary, 1993.
15. B. M. Trost, *Chem. Rev.*, **78**, 363 (1978); B. M. Trost, *Acc. Chem. Res.*, **11**, 453 (1978).
16. V. V. Kane, V. Singh, A. Martin and D. L. Doyle, *Tetrahedron*, **39**, 345 (1983).