Experimental Section

General Methods. All melting points were determined on a Koffler apparatus and are corrected; the IR spectra were recorded on a Beckmann Acculab 2 spectrometer and the UV spectra on a LERES-SPILA S28 photometer; ^{1}H NMR spectra were measured on a Perkin-Elmer R12B spectrometer (60 MHz) or on an IEF 400, a prototype built at the University of Orsay (401 MHz). Mass spectra were recorded on a JEOL D300 spectrometer. Elemental analyses were performed by Microanalysis Department of the Faculty of Sciences of Reims.

Preparation of Carboline 2. To a solution of N_b-ethyltryptamine (862 mg, 4.5 mmol) in 20 mL of boiling toluene was added aldehyde **4** (1.1 g, 1.15 equiv). After 30 min, 2 mL of glacial AcOH was added, and the mixture was refluxed for 6 h. After evaporation of toluene, the residue was partitioned between ether and 0.5 N aqueous NaOH. The organic layer was dried and evaporated, leaving 1.65 g (95%) of a solid, homogeneous by TLC. An analytical sample was prepared by crystallization of the camphosulfonate salt of **2** (mp 204 °C): MS, m/z (relative intensity) 386 ($M^{+\cdot}$, 12), 385 (10), 341 (40), 238 (30), 199 (100); IR 3410, 1750, 1730 cm^{-1}; ^{1}H NMR (base, 60 MHz, $CDCl_3$) δ 8.2 (s, 1 H), 4.2 (q, J = 7 Hz, 4 H), 1.25 (t, J = 7 Hz, 6 H), 1.1 (t, J = 7 Hz, 3 H). Anal. Calcd for $C_{31}H_{46}N_2O_8S$: C, 61.3; H, 7.6; N, 4.6. Found: C, 61.5; H, 7.4; N, 4.7.

Preparation of Carboline 3. To a solution of N_b-ethyltryptamine (4.5 g, 23.9 mmol) in 30 mL of refluxing benzene was added aldehyde **5** (5 g, then 1 h later 2 g, total 1.5 equiv). After being refluxed for 24 h, the solvent was evaporated and the residue chromatographed on 120 g of silica gel. Elution with a mixture of CH_2Cl_2 and MeOH (99:1) yielded 5.8 g (68%) of an oil, homogeneous by TLC: MS, m/z (relative intensity) 358 ($M^{+\cdot}$, 18), 238 (10), 212 (17), 199 (100); IR 3400, 1750, 1720 cm^{-1}; ^{1}H NMR (60 MHz, $CDCl_3$) δ 8.0 (s, 1 H), 3.75 (s, 3 H), 3.71 (s, 3 H), 3.5 (t, J = 7 Hz, 1 H), 1.1 (t, J = 7 Hz, 3 H).

Chlorination of 2 (6a,b). To a solution of **2** (1.5 g, 3.9 mmol) in 10 mL of CH_2Cl_2 was added Et_3N (810 μL, 588 mg, 5.8 mmol, 1.5 equiv) and then t-BuOCl (500 μL, 510 mg, 4.6 mmol, 1.2 equiv). After 10 min at room temperature, the solution was washed twice with water and evaporated in vacuo, leaving 1.7 g (96%) of a solid showing two spots on TLC: colors on TLC (Ce(IV) spray) **6a** colorless, **6b** orange; UV (mixture) λ_{max}^{MeOH} 227, 263, 292 (sh); MS m/z (relative intensity) 422 ($M^{+\cdot}$, 0.5), 420 ($M^{+\cdot}$, 1), 419 (1.5), 385 (30), 235 (10), (35), 212 (25), 199 (100), 197 (25); IR 1745, 1730, 1580 cm^{-1}.

Chlorination of 3 (7a,b). **3** (1.7 g) was treated with Et_3N and t-BuOCl as described for **2** to yield 1.67 g of solid, which was purified on a Merck Lobar column. In addition to fractions containing a mixture of **7a** and **7b**, pure **7a** (405 mg, 28%) and **7b** (455 mg, 31%) were obtained. Compound **7a**: TLC (Ce(IV)) colorless; UV λ_{max}^{MeOH} 230, 265, 303 nm; IR 1750, 1735, 1580 cm^{-1}; MS m/z (relative intensity) 394 ($M^{+\cdot}$, 0.5), 392 ($M^{+\cdot}$, 1.5), 357 (35), 235 (32), 233 (100), 199 (80), 197 (30), 178 (20); ^{1}H NMR (60 MHz, $CDCl_3$) δ 7.7–7.2 (m, 4 H), 3.8 (s, 6 H), 1.05 (t, 3 H, 7 Hz). Compound **7b**: TLC (Ce(IV)) orange; ^{1}H NMR (60 MHz, $CDCl_3$) δ 7.7–7.3 (m, 4 H), 3.75 (s, 3 H), 3.72 (s, 3 H), 1.05 (t, 3 H, 7 Hz); MS and UV same as **7a**; IR are superimposable except for fingerprint area.

Rearrangement of 6a,b (1). A mixture of compounds **6a,b** (800 mg, 1.9 mmol) was dissolved in 10 mL of dry THF (Na, benzophenone), and 50% NaH suspension in oil (100 mg, 1.1 equiv) was added. After 18 h at room temperature, the reaction mixture was partitioned between ether and water. The usual workup yielded 657 mg of a mixture, which was purified on 100 g of silica gel. Elution with $CHCl_3$ yielded **6a** (120 mg) followed by **1** (320 mg, 48%): UV 227, 298, 328 nm; MS, m/z (relative intensity) 312 ($M^{+\cdot}$, 20) [analyzed for $C_{19}H_{24}N_2O_2$ 312.1793, calcd 312.1836)], 241 (241.1091, $C_{15}H_{15}NO$; calcd 241.1101), 199, 166, 84 (100); IR 3370, 1670, 1610 cm^{-1}; ^{1}H NMR (401 MHz, $CDCl_3$) δ 9.09 (s, 1 H), 4.32(q, J = 7 Hz, 2 H), 3.23 (d, J = 5 Hz, 1 H), 3.04 and 2.83 (dq, J = 14 Hz, 7 Hz, 2 × 1 H), 1.43 (t, J = 7 Hz, 3 H), 1.33 (t, J = 7 Hz, 3 H).

Rearrangement of 7b (8). Pure chloroindolenine **7b** (400 mg, 1 mmol) was treated with NaH (50 mg) in 5 mL of dry THF. After 4 h at room temperature and 8 h at reflux, the usual workup gave a mixture which was purified by column chromatography to yield 230 mg (75%) of **8**: UV 226, 298, 328 nm; MS, m/z (relative intensity) 298 ($M^{+\cdot}$, 35) [$C_{18}H_{22}N_2O_2$, found 298.1628; calcd 298.1670], 267 (10), 239 (16), 227 (100), 214 (15), 168 (18), 167 (17), 84 (100); IR 3390, 1670, 1610 cm^{-1}; ^{1}H NMR (60 MHz, $CDCl_3$) 9.0 (s, 1 H), 3.75 (s, 3 H), 1.2 (t, J = 7 Hz, 3 H).

Rearrangement of 10. To compound **10**[2] (40 mg, 0.12 mmol, mixture of isomers) dissolved in 2 mL of CH_2Cl_2 were added Et_3N (26 μL, 1.5 equiv) and then t-BuOCl (17 μL, 1.2 equiv). After 20 min, the suspension was poured into 10 mL of saturated aqueous NH_4Cl. The usual workup followed by column chromatography of the residue gave 18 mg of pure **11**, in all regards identical with compound **1** of ref 3d.

Registry No. **1**, 91085-29-9; **2**, 75622-29-6; **3**, 91085-30-2; **4**, 19515-61-8; **5**, 72473-15-5; **6** (isomer 1), 91085-31-3; **6** (isomer 2), 91085-32-4; **7** (isomer 1), 91085-33-5; **7** (isomer 2), 91085-34-6; **8**, 91085-35-7; **10**, 91085-36-8; **11**, 91176-85-1; N-ethyltryptamine, 61-53-0.

(12) Lévy, J.; Sigaut, F. *Tetrahedron Lett.* **1983**, *24*, 4985.

Stereochemistry of Nucleophilic Substitution Reaction of 16-Bromo-17-oxo Steroids with Thiols

Mitsuteru Numazawa,* Misao Madarame, Mieko Ogata, and Katsuhiko Kimura

Tohoku College of Pharmacy, 4-1 Komatsushima-4-Chome, Sendai 983, Japan

Received March 13, 1984

Recent studies[1] on the reaction of 16-bromo-17-oxo steroids with nucleophiles, hydroxide ion, and morpholine, demonstrated that equilibration between the 16α- and 16β-bromo ketones precedes the displacement of bromine with nucleophiles, in which the true intermediate is the 16β-bromo isomer and not the 16α-isomer, and that 16α-substituted 17-oxo derivatives are formed by the direct S_N2 displacement of the 16β-bromine. 16α-Morpholino derivative initially produced is, then, almost completely epimerized to the thermodynamically stable 16β-epimer[2] in the presence of heated basic morpholine, while a 16α-hydroxy 17-one is quantitatively obtained under controlled conditions[1,3] (Scheme I).

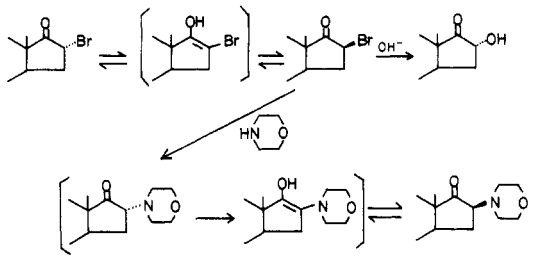
However, the reaction of the bromo ketones with a sulfur nucleophile is somewhat complicated and its reaction mechanism remains to be unclear. Takeda et al.[4] reported that both 16α- and 16β-bromo 17-ketones gave the same product, the 16β-thio ether derivative A (Scheme II), in the reaction with thioacetate. On the other hand, Pelc and Holmes[5] reported the conversion of 16α- and 16β-bromo ketones **1** and **2** with thioglycolic acid to the corresponding (carboxymethyl)thio derivatives **6** and **7** with retention of configuration at the C-16 position, respectively (Chart I).

In our continuing interest in the chemistry of 16-bromo 17-ketones, we found that direct S_N2 displacement of bromine by sulfur nucleophiles is possible in the α-bromo ketones without prior epimerization of the bromo ketones.

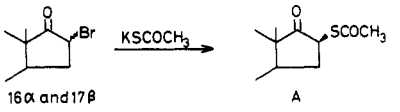
(1) Numazawa, M.; Osawa, Y. *J. Am. Chem. Soc.* **1980**, *102*, 5402. Numazawa, M.; Nagaoka, M.; Osawa, Y. *J. Org. Chem.* **1982**, *47*, 4024.
(2) Swenson, D. C.; Duax, W. L.; Numazawa, M.; Osawa, Y. *Acta Crystallogr., Sect. B* **1980**, *B36*, 1981.
(3) Numazawa, M.; Kimura, K.; Nagaoka, M. *Steroids* **1981**, *38*, 557. Numazawa, M.; Nagaoka, M. *Ibid.* **1982**, *39*, 345. Numazawa, M.; Nagaoka, M.; Tsuji, M.; Osawa, Y. *J. Chem. Soc., Perkin Trans. 1* **1983**, 121.
(4) Takeda, K.; Komeno, T.; Tokutake, N.; Kanematsu, Y. *Chem. Pharm. Bull.* **1964**, *12*, 905.
(5) Pelc, B.; Holmes, A. L. *J. Steroid Biochem.* **1981**, *14*, 1197.

0022-3263/84/1949-3231$01.50/0

Scheme I

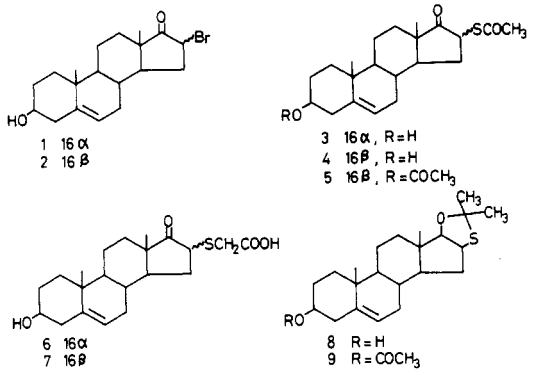


Scheme II



16α and 17β A

Chart I



1 16α
2 16β

3 16α, R=H
4 16β, R=H
5 16β, R=COCH$_3$

6 16α
7 16β

8 R=H
9 R=COCH$_3$

Results and Discussion

Reaction of 16α- and 16β-bromo-17-oxo steroids **1** and **2** with 1 equiv of potassium thioacetate (CH_3COSK) was initially explored under similar conditions (acetone, room temperature, 3.5 h) as previously reported.[4] Both **1** and **2** gave the same product, 16β-thio ester **4**, in high yields. The structure of **4** was identified by spectral data and by the fact that reduction of **4** with $LiAlH_4$, followed by treatment with acetone and *p*-toluenesulfonic acid gave the acetonide **8** in high yield. However, high performance liquid chromatography (HPLC) and ^1H NMR analysis of the crude **4** obtained above suggested that a small amount (ca. 10%) of the 16α-thioether **3** [HPLC t_R 4 min; ^1H NMR δ 1.00 (s, 18-CH_3)] along with **4** [HPLC t_R 5 min; ^1H NMR δ 0.88 (s, 18-CH_3)] might be also produced from **2**, while **1** gave only **4**. This led us to determine dynamic aspects of epimerization and displacement of **1** and **2** with potassium thioacetate (Table I). A brief (20 min) treatment of **2** with 1 equiv of CH_3COSK yielded **3** as a major product, in which **4** was also formed in 12% yield. The structure of **3** was determined by spectral data and elemental analysis, and **3** did not give an acetonide when reduced with $LiAlH_4$ and treated as indicated for **4**.[6]

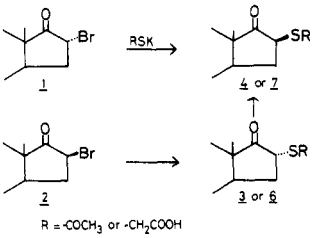
When the 16β-bromide **2** was treated with CH_3COSK for various times, an increased relative amount of 16β-thio ester **4** to the 16α-isomer **3** was obtained in proportion to the reaction time. In contrast, similar treatment of the 16α-bromo isomer **1** always gave **4** as the sole product. When **1** and **2** were separately treated with 0.5 equiv of the nucleophile for a long time (5 h), they were recovered (ca. 50%) without epimerization, along with the formation of the same product **4**, respectively. A solution of **4** in MeOD was allowed to stand at room temperature for 5 h in the presence or absence of CH_3COOK to give **4**-*16-d* (92 or 74 atom %). Moreover, when **1**-*16-d* and **2**-*16-d*, obtained by treatment of **1** with NaOD under the controlled conditions,[1] were separately subjected to the reaction with the nucleophile (1 equiv, 20 min), the products **4** and **3** isolated retained almost quantitatively a deuterium at their 16-position, respectively.

Table I. Reaction of 16-Bromo 17-Ketones 1 and 2 with Potassium Thioacetate[a]

substrate	conditions: $KSCOCH_3$, equiv	conditions: time, h	rel amt of products,[b] %: 1	2	3	4
1	0.5	5	55	0	0	45
1	1.0	0.33	5	0	0	95
1	1.0	3.5	0	0	0	100
1-*16-d*	1.0	0.33	0	0	0	100 (91)[c]
2	0.5	5	0	52	<3	>45
2	1.0	0.33	0	0	88	12
2	1.0	3.5	0	0	10	90
2	1.0	5	0	0	<5	>95
2-*16-d*	1.0	0.33	0	0	94 (94)[c]	6

[a] The 16-bromo ketones **1** and **2** were treated with potassium thioacetate at room temperature. [b] The relative amount of products was obtained from the HPLC analysis of the reaction mixtures without isolation. [c] Percent of deuterium retention at C-16 is shown is parentheses.

Scheme III



R = -COCH$_3$ or -CH$_2$COOH

These results indicated that the thermodynamic control of the substitution reaction strongly prefers the formation of the 16β-thio isomer **4** from the 16β-bromo ketone **2** through enolization similarly as reported in the formation of 16β-morpholino derivative[1] and that the displacement by CH_3COSK of the 16-bromo 17-ketone occurs initially to from 16α- and 16β-thioethers **3** and **4**, by S_N2 substitution on the 16β- and 16α-bromo ketones **2** and **1** and then **3** epimerizes to the thermodynamically stable **4** under the reaction conditions (Scheme III).

On repeating the reported reaction[5] of the bromo ketones **1** and **2** with potassium thioglycolic acid, we could also isolate the 16-substituted derivatives **7** and **6**, respectively. However, ^1H NMR spectra of the crude **6** and **7** obtained above showed that **2** yielded a 7:1 mixture of **6** and **7**, while **1** afforded only **7**. Furthermore, with a brief reaction time (10 min), **1** and **2** were recovered (ca. 30%) without epimerization, in which **7** and **6** were seemingly produced in about 50% yield, respectively. The products **6** and **7** obtained from **2**-*16-d* and **1**-*16-d* retained almost completely a deuterium at the 16α- and 16β-positions, respectively. Treatment of **7** with KOD in MeOD gave **7**-*16-d* (57 atom %).

The results showed that the bromo ketones **1** and **2** react with thioglycolic acid similarly as with CH_3COSK, to primarily give the 16β- and 16α-(carboxymethyl)thio derivatives **7** and **6** through an S_N2 mechanism involving inversion of configuration at C-16, respectively, thus refuting the previous assingment[5] of configuration at C-16 of **6** and **7**, and that since enolization of the 17-oxo function of **6** and **7** is less easy than that of the acetylthio compounds **3** and **4**, the thermodynamically unstable **6** can be isolated as the product of **2** even if a long reaction time (5 h) is employed.

Recently, 16-iodo-17-hydroxy steroids, which may be converted to the 17-ketones in man, have been developed as radioligands[7] for a steroid receptor, and their interesting biological activities are also reported.[8] The present results together with the previous ones[1] on chemistry of a 16-bromo 17-ketone would be helpful to

(6) When compound **3** was subjected to reaction sequences forming an acetonide, unexpectedlly, the acetonide **8**, which was identical with that obtained from **4**, was obtained in 10% yield. This should attribute to a partial epimerization of **3** to **4** in alkaline medium in the hydride reduction step.

(7) Arunachalam, T.; Longcole, C.; Caspi, E. *J. Biol. Chem.* **1979**, *254*, 5900. Hampl, R.; Horakova, J.; Bicikova, M.; Dvorak, P.; Starka, L. *J. Steroid Biochem.* **1980**, *13*, 1035.

(8) Longcope, C.; Arunachalam, T.; Rafkind, I.; Caspi, E. *J. Steroid Biochem.* **1981**, *14*, 261. Bronzert, D. A.; Hochberg, R. B.; Lippman, M. E. *Endocrinology (Baltimore)* **1982**, *110*, 2177.

understand biological aspects of the iodides, especially their interactions with a thiol group of a protein.

Experimental Section

General Methods. Melting points were measured on a Yanagimoto melting point apparatus and were uncorrected. IR spectra were recorded on a Shimazu 400 spectrophotometer in KBr pellets. ^{1}H NMR spectra were obtained with JEOL PMX 60 (60 MHz) and FX 100 (100 MHz) spectrometers using tetramethylsilane as an internal standard. Mass spectra were measured on a Hitachi RMU-7 spectrometer. High-performance liquid chromatography (HPLC) was carried out on a Waters ALC/PGC 244 liquid chromatography equipped with a U6K injector and a differential refractometer detector, in which a reversed-phase μ-Bondapak C_{18} column (30 × 0.39 i.d. cm) and MeOH/H_2O were employed as the stationary and mobile phases, respectively.

[16-^{2}H]-16α- and 16β-Bromo-3β-hydroxy-5-androsten-17-ones (1-*16-d* and 2-*16-d*). Treatment of 1[1] with 0.12 equiv of NaOD for 30 min under the controlled conditions[1] gave a mixture of 1-*16-d* and 2-*16-d*, which were purified by HPLC (MeOH/H_2O, 7/3, v/v; flow rate 2.0 mL/min). 1-*16-d*: mp 176–178 °C (lit.[1] mp 177–178 °C); MS, 19% d_0, 81% d_1; t_R 4.5 min. 2-*16-d*: mp 171–174 °C (lit.[1] mp 171–173 °C); MS, 4% d_0, 96% d_1; t_R 5.5 min.

Reaction of 1, 1-*16-d*, 2, and 2-*16-d* with CH_3COSK. CH_3COSK was suspended in 5 mL of dry acetone, and 1, 1-*16-d*, 2, or 2-*16-d* (100 mg, 0.27 mmol) was added to the suspension, and then the mixture was stirred at room temperature for an appropriate time. After the same workup as previously reported, the residue (95–105 mg) was obtained.

16α-(Acetylthio)-3β-hydroxy-5-androsten-17-one (3). The residue obtained above from 2, using 1 equiv of CH_3COSK and a 20-min reaction time, was repeatedly recrystallized from ether to give 3 (78 mg, 79%) as colorless needles: mp 134–135 °C; HPLC t_R 4 min (MeOH/H_2O, 7/3, v/v); IR (KBr) 3350 (OH), 1740 and 1683 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.00 (3 H, s, 18-CH_3), 1.03 (3 H, s, 19-CH_3), 2.38 (3 H, s, 16α-$SCOCH_3$), 3.49 (1 H, br m, 3α-H), 4.34 (1 H, dd, J = 2 and 8 Hz, 16β-H), 5.37 (1 H, m, 6-H). Anal. Calcd for $C_{21}H_{30}O_3S$: C, 69.58; H, 8.34; S, 8.84. Found; C, 69.25; H, 8.50; S, 8.71.

3 could not be obtained in pure form by preparative HPLC using the MeOH/H_2O system as the mobile phase, because of its partial epimerization to the 16β-isomer 4 during evaporation of the solvent.

2-*16-d* was converted similarly to 3-*16-d* in 75% yield: mp 134–135 °C; MS, 10% d_0, 90% d_1.

16β-(Acetylthio)-3β-hydroxy-5-androsten-17-one (4). Crystallization of the residue obtained above from 1, using 1 equiv of CH_3COSK and a 5-h reaction time, from acetone afforded 4 (85 mg, 87%) as colorless needles: mp 167–169 °C; HPLC t_R 5 min (MeOH/H_2O, 7/3, v/v); IR (KBr) 3480 (OH), 1740 and 1688 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.88 (3 H, s, 18-CH_3), 1.03 (3 H, s, 19-CH_3), 2.38 (3 H, s, 16β-$SCOCH_3$), 3.44 (1 H, br m, 3α-H), 3.98 (1 H, dd, J = 2 and 8 Hz, 16α-H), 5.40 (1 H, m, 6-H). Anal. Calcd for $C_{21}H_{30}O_3S$: C, 69.58; H, 8.34; S, 8.84. Found; C, 69.43; H, 8.73; S, 8.50.

Similar treatment of 1-*16-d* as above gave 4-*16-d* in 83% yield: mp 167–170 °C; MS, 26% d_0, 74% d_1.

16β-(Acetylthio)-3β-acetoxy-5-androsten-17-one (5). 4 (50 mg, 0.14 mmol) was acetylated by Ac_2O and pyridine. Crystallization of the crude product from ether gave 5 (45 mg, 84%) as colorless needles: mp 148–152 °C; IR (KBr) 1743, 1725, and 1690 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.83 (3 H, s, 18-CH_3), 1.02 (3 H, s, 19-CH_3), 2.03 (3 H, s, 3β-$OCOCH_3$), 2.37 (3 H, s, 16β-$SCOCH_3$), 4.98 (1 H, dd, J = 2 and 8 Hz, 16α-H), 4.93 (1 H, br m, 3α-H), 5.09 (1 H, m, 6-H).

Treatment of 4 with CH_3COOK in MeOD. A solution of 4 (50 mg, 0.14 mmol) and CH_3COOK (13.5 mg, 0.14 mmol) in MeOD (4 mL) was allowed to stand at room temperature for 1 h. After this time, the reaction mixture was poured into H_2O and extracted with AcOEt. After usual workup 4-*16-d* (mp 165–168 °C; 8% d_0, 92% d_1) was recovered (94%).

When 4 was subjected to the above treatment without CH_3COOK, 4-*16-d* (mp 166–169 °C; 26% d_0, 74% d_1) was isolated (100%).

16-*S*,17-*O*-Isopropylidene-16β-mercapto-5-androstene-3β,17β-diol (8). A solution of 4 (360 mg, 0.99 mmol) in 15 mL of anhydrous THF was added dropwise with stirring to a suspension of 180 mg of $LiAlH_4$ in 14 mL of anhydrous ether. The reaction mixture was heated under reflux for 7 h and then treated as usual. The reduction product, 16β-mercapto-5-androstene-3β,17β-diol (160 mg), was dissolved in a mixture of 14 mg of *p*-TsOH, 0.7 mL of anhydrous ether, and 7 mL of dried acetone, and the mixture was heated under reflux for 4 h. After an insoluble byproduct was filtered off, the filtrate was diluted with H_2O. The precipitate was collected by filtration, dried, and recrystallized from $CHCl_3$–MeOH to give 8 (178 mg, 57% from 4) as colorless leaflets: mp 211–214 °C; ^{1}H NMR ($CDCl_3$–CD_3OD) δ 0.93 (3 H, s, 18-CH_3), 1.03 (3 H, s, 19-CH_3), 1.60 and 1.72 (3 H, s, $OC(CH_3)_2S$), 3.48 (1 H, br m, 3α-H), 4.02 (1 H, br s, 17α-H), 5.37 (1 H, m, 6-H). Anal. Calcd for $C_{22}H_{34}O_2S$: C, 72.88; H, 9.45; S, 8.84. Found: C, 72.53; H, 9.46; S, 9.00.

3α-Acetoxy-16-*S*,17-*O*-isopropylidene-16β-mercapto-5-androsten-17β-ol (9). 8 (50 mg, 0.14 mmol) was acetylated by Ac_2O–pyridine. After usual workup, the crude product was recrystallized from $CHCl_3$–MeOH to give 9 (52 mg, 92%) as colorless leaflets: mp 151–154 °C; IR (KBr) 1740 (C=O) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 0.90 (3 H, s, 18-CH_3), 1.02 (3 H, s, 19-CH_3), 1.58 and 1.71 (3 H, s, $OC(CH_3)_2S$), 2.02 (3 H, s, 3β-$OCOCH_3$), 4.17 (1 H, br s, 17α-H), 4.60 (1 H, br m, 3α-H), 5.39 (1 H, m, 6-H). Anal. Calcd for $C_{24}H_{36}O_3S$: C, 71.25; H, 8.97; S, 7.92. Found: C, 71.13; H, 8.95; S, 8.10.

16α- and 16β-(Carboxymethylthio)-3β-hydroxy-5-androsten-17-one (6 and 7). Compounds 6 and 7 were separately synthesized from 2 and 1 according to Pelc and Holmes,[5] in 30% yield, respectively. 6: mp 195–198 °C (lit.[5] mp 196–200 °C, previously reported as mp of the 16β-thioether 7). ^{1}H NMR ($CDCl_3$) δ 1.02 (3 H, s, 18-CH_3), 1.05 (3 H, s, 19-CH_3), 3.36 and 3.74 (1 H, d, J = 15 Hz, -SCH_2-), 5.36 (1 H, m, 6-H). 7: mp 195–198 °C (lit.[5] mp 195–198 °C, previously reported as mp of the 16α-isomer 6); ^{1}H NMR (CD_3OD) δ 1.00 (3 H, s, 18-CH_3), 1.06 (3 H, s, 19-CH_3), 3.33 and 3.70 (1 H, d, J = 15 Hz, -SCH_2-), 5.34 (1 H, m, 6-H).

When 1-*16-d* and 2-*16-d* were subjected to the above reaction, 7-*16-d* (mp 196–198 °C; 22% d_0, 78% d_1) and 6-*16-d* (mp 195–198 °C; 8% d_0, 92% d_1) were obtained, respectively.

Treatment of 7 with KOH in MeOD. A solution of 7 (50 mg, 0.13 mmol) and KOH (11 mg, 0.20 mmol) in 5.7 mL of MeOD was allowed to stand at room temperature for 10 min. The reaction mixture was acidified by AcOH and then poured into H_2O. After extraction with AcOEt, the organic phase was washed with H_2O, dried (Na_2SO_4), and evaporated to give a solid. Crystallization of the solid from acetone–ether gave 7-*16-d*: mp 195–198 °C; MS 43% d_0, 57% d_1.

Acknowledgment. We thank Prof. Toshio Nambara and Dr. Kadzutake Shimada of Tohoku University for mass spectra and elemental analysis.

Registry No. 1, 1093-91-0; 1-*16-d*, 91191-05-8; 2, 74644-60-3; 2-*16-d*, 91191-06-9; 3, 91191-07-0; 3-*16-d*, 91191-08-1; 4, 91191-09-2; 4-*16-d*, 91191-10-5; 5, 91191-11-6; 6, 81354-95-2; 6-*16-d*, 91191-12-7; 7, 81354-96-3; 7-*16-d*, 91191-13-8; 8, 91191-14-9; 9, 91191-15-0; CH_3COSK, 10387-40-3; $KSCH_2CO_2H$, 34452-51-2; 16β-mercapto-5-androstene-3β,17β-diol, 91191-16-1.

Polystyryltri-*n*-butylphosphine[1]

Bong Kim, Mitsuo Kodomari,† and Steven L. Regen*

Department of Chemistry, Marquette University, Milwaukee, Wisconsin 53233

Received January 27, 1984

Diarylphosphine-functionalized polystyrene resins have been extensively utilized as polymeric ligands and reagents.[2] Surprisingly, analogous polymer-bound *trialkylphosphines* have not yet been reported. Because of their

† On leave from Shibaura Institute of Technology, Tokyo, Japan.

0022-3263/84/1949-3233$01.50/0