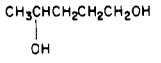
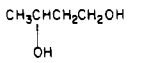
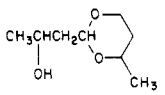
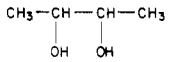
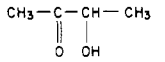
Table II. Oxidation of Diols with IIb[a]

diol	product	IIb (eq)	time, min	yield,[b] %	bp, °C/mmHg
		1	5	17	
		2	60	45 (33)[c]	93/18
		3	60	83	
		0.5	5	53	
		1	5	100 (61)[c]	100/7
		2	10	9	
		1	30	74	

[a] In CH_2Cl_2 at 25 °C. [b] GLC yield based on the starting alcohol. [c] Isolated yield.

II, the acetal VI was further oxidized by excess use of IIb to give a complicated mixture. These results might suggest that a primary hydroxyl group was initially oxidized faster than a secondary hydroxyl moiety to give hydroxy aldehyde V as a intermediate. Subsequently V reacts with **IV**, and dehydration will occur by hydrogen chloride derived from IIb to give VI as shown in eq 4.

2,3-butanediol was selectively oxidized by equimolar IIb to give acetoin in 74% yield, as shown in Table II.

As described above, we found the selective oxidation of alcohols by oxoaminium salt IIb and applied this method to the oxidative lactonization of diols. In view of the simple procedure that requires a mild condition, the present reaction offers the useful method for the oxidative laconization of limited diols.

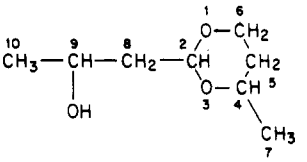
Experimental Section

Nuclear magnetic resonance spectra were measured on a JEOL JNM-GX400 FT NMR spectrometer in $CDCl_3$ with tetramethylsilane as internal standard. The infrared spectra were measured on a JASCO FT/IR-3. 4-Methoxy-2,2,6,6-tetramethylpiperidine-1-oxyl (Ib) and the oxidizing agent IIb were prepared by the method reported previously.[13]

4-Methoxy-1-oxo-2,2,6,6-tetramethylpiperidinium Chloride (IIb). Anhydrous chlorine was bubbled into the stirred solution of 2.0 g (10.7 mmol) of Ib in 100 mL of CCl_4. The orange precipitate appeared, and it was filtered and washed with CCl_4 to give 2.1 g (9.5 mmol, 89%) of IIb: mp 121–123 °C dec; IR (KBr) 2951, 2897, 2827, 1616, 1466, 1446,1388, 1377, 1219, 1161, and 1106 cm^{-1}. Anal. Calcd for $C_{10}H_{20}NO_2Cl$: C, 54.17; H, 9.09; N, 6.32; Cl, 15.99. Found: C, 53.60; H, 9.22; N, 6.29; Cl, 16.88.

Oxidation of 1,4-Butanediol by Use of IIb. To a solution containing 2.05 g (22.7 mmol) of 1,4-butanediol in 200 mL of anhydrous methylene chloride was added 10.6 g (47.8 mmol) of IIb under an atmosphere of argon at room temperature. After the reaction was over, the solution was washed with water (200 mL) and dried with anhydrous sodium sulfate. The solvent was evaporated in vacuo. The residue was distilled under reduced pressure to give 1.59 g (18.5 mmol, 81%) of γ-butyrolactone. The physical and spectral data of the obtained product agreed with those of authentic sample of γ-butyrolactone, completely.

Oxidation of 1,3-Butanediol by Use of IIb. To a solution containing 4.26 g (47.4 mmol) of 1,3-butanediol in 200 mL of anhydrous methylene chloride was added 10.5 g (47.4 mmol) of IIb under an atmosphere of argon at room temperature. After the reaction was over the solution was washed with water (200 mL) and dried with anhydrous sodium sulfate. The solvent was evaporated in vacuo. The residue was distilled under reduced pressure to give 2.32 g (14.5 mmol, 61%) of 2-(2-hydroxypropyl)-4-methyl-1,3-dioxane (**VI**): bp 100 °C (7 mmHg); mass spectrum, *m/e* 160; IR (neat) 802, 895, 1107, 1126, 1168, 1380, 2858, 2932, 2970, and 3458 cm^{-1}. ^1H NMR ($CDCl_3/Me_4Si$ int) δ 1.18 (dd, 3 H, *J* = 6.2 and 0.6 Hz, H-10), 1.23 and 1.24 (d, *J* = 6.3 Hz, H-7, diastereoisomer), 1.44–1.48 (m, 1 H, H-5_{ax}), 1.63–1.75 (m, 1 H, H-5_{eq}), 1.76 (t, 2 H, *J* = 4.8 Hz, H-8), 2.85–3.04 (s, 1 H, OH), 3.71–3.81 (m, 2 H, H-4 and H-6_{ax}), 4.08–4.13 (, 2 H, H-9 and H-6_{eq}), 4.78 (t, 1 H, *J* = 4.8 Hz, H-2); ^{13}C NMR ($CDCl_3/Me_4Si$ int) δ 21.7 (q, C-7), 23.3 (q, C-10), 32.9 (t, C-5), 43.1 (t, C-8), 64.2 (d, C-9), 66.6 (dd, C-6), 72.9 (d, C-4) 101.0 (d, C-2); determined by off-resonance method. Anal. Calcd for $C_8H_{16}O_3$: C, 59.97; H, 10.07. Found: C, 60.11; H, 10.07.



Oxidation of 1,4-Pentanediol by Use of IIb. To a solution containing 2.82 g (27.1 mmol) of 1,4-pentanediol in 150 mL of anhydrous methylene chloride was added 12 g (54.2 mmol) of IIb at room temperature. After the reaction was over, the solution was washed with water and dried with anhydrous sodium sulfate. The solvent was evaporated in vacuo. The residue was distilled under reduced pressure to give 900 mg (9.0 mmol) of γ-valerolactone. The physical and spectral data of the obtained product completely agreed with those of authentic sample of γ-valerolactone.

Registry No. IIb, 95407-70-8; $HO(CH_2)_3OH$, 504-63-2; $HO(CH_2)_4OH$, 110-63-4; $HO(CH_2)_5OH$, 111-29-5; $HO(CH_2)_6OH$, 629-11-8; $CH_3CH(OH)(CH_2)_3OH$, 626-95-9; $CH_3CH(OH)(CH_2)_2OH$, 107-88-0; $CH_3CH(OH)CH(OH)CH_3$, 513-85-9; $CH_3C(O)CH(OH)CH_3$, 513-86-0; 2-oxetanone, 57-57-8; dihydro-2(3*H*)-furanone, 96-48-0; tetrahydro-2*H*-pyran-2-one, 542-28-9; 2-oxepanone, 502-44-3; 5-methyldihydro-2(3*H*)-furanone, 108-29-2; β,4-dimethyldioxane-2-methanol, 96948-63-9.

(13) Miyazawa, T.; Endo, T.; Shiihashi, S.; Okawara, M.; *J. Org. Chem.* **1985**, *50*, 1332.

Preparation and Acid-Catalyzed Rearrangement of a C-17 Isopropylidene and a C-17 Isopropenyl Sterol

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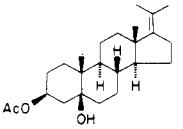
In connection with a study directed toward the biogenetic-type synthesis of 3,5-dioxygenated steroids via acid-catalyzed cyclization of a polyene epoxide,[2] we had interest in preparing steroids **1** and **2** and studying their acid-catalyzed rearrangement.



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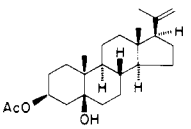


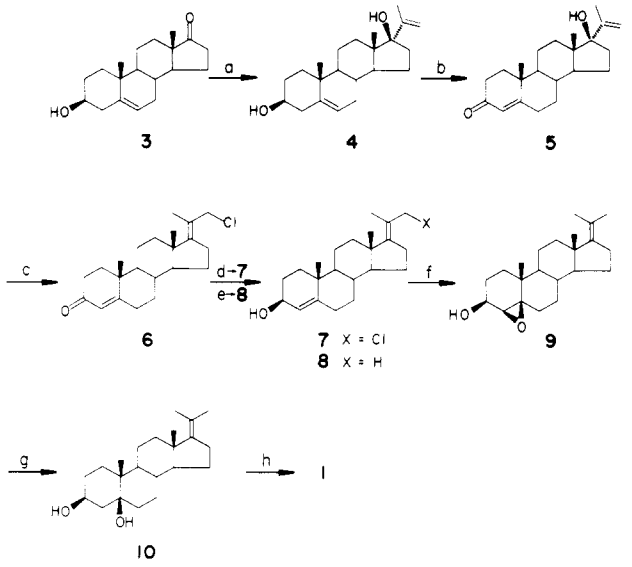
2

(1) Present address: Syntex Research, Palo Alto, CA 94304.

(2) van Tamelen, E. E.; Loughhead, D. G. *J. Am. Chem. Soc.* **1980**, *102*, 869.

0022-3263/85/1950-3931$01.50/0

Scheme I[a]



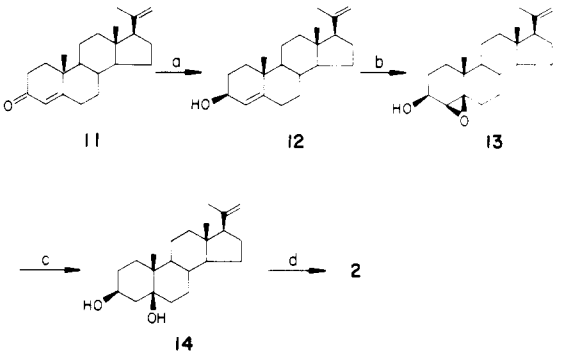
[a] (a) 2-Lithiopropene, THF/HMPA; (b) aluminum isopropoxide, cyclohexanone, $PhCH_3$; (c) $SOCl_2$, lutidine, CH_2Cl_2; (d) $Li(t\text{-}BuO)_3AlH$, THF; (e) $LiEt_3BH$, THF; (f) t-BuOOH, $Mo(CO)_6$, $PhCH_3$; (g) LAH, THF; (h) Ac_2O, pyridine.

With the goal of preparing $\Delta^{17(20)}$ isomer **1**, the three carbons of the isopropylidene group were introduced by allowing 17-one **3** to react with 2-lithiopropene[3] (see Scheme I). Oppenauer oxidation of diol **4** then provided the 4-en-3-one **5**. This material was treated with $SOCl_2$, which effected a substitution reaction with allylic rearrangement to give a single allylic chloride presumed to have the *E* stereochemistry as shown in **6**. This material was subjected to a two-step reduction sequence: treatment with $Li(t\text{-}BuO)_3AlH$ provided 3β-ol **7**, which was converted, by $LiEt_3BH$[4] reduction of the allylic chloride function, to dienol **8**. Regio- and stereospecific epoxidation of **8** to provide **9** was accomplished via the $Mo(CO)_6$-catalyzed action of t-BuOOH.[5] Reduction of epoxide **9** with LAH provided diol **10**, which was converted to acetate **1** using acetic anhydride/pyridine.

Preparation of Δ^{20} isomer **2** was more straightforward. The known 17-isopropenyl steroid **11**,[6] obtained in the present case by Oppenauer oxidation of the corresponding 5-en-3β-ol,[7] was reduced with $Li(t\text{-}BuO)_3AlH$ to provide 3β-ol **12** (see Scheme II). Regio- and stereospecific epoxidation of this dienol was achieved using $Mo(CO)_6/t$-BuOOH[5] to provide **13**. Reductive opening of the epoxide with LAH provided diol **14**, which was converted, by treatment with acetic anhydride/pyridine, to acetate **2**.

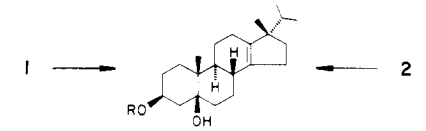
When steroid isomers **1** and **2** were separately subjected to various acidic conditions, both materials were substantially converted to the same product, as indicated by gas chromatographic analysis of the reaction mixtures. Several reagents (e.g., $BF_3{\cdot}Et_2O$, $SnCl_4$, and F_3CCO_2H) could be used to effect this conversion. When $BF_3{\cdot}Et_2O$ was used at reduced temperature, a particularly clean and preparatively useful reaction took place. The structure of

Scheme II[a]



[a] (a) $Li(t\text{-}BuO)_3AlH$, THF; (b) t-BuOOH, $Mo(CO)_6$, $PhCH_3$; (c) LAH, THF; (d) Ac_2O, pyridine.

the material obtained by $BF_3{\cdot}Et_2O$ treatment of steroid **1** or **2** was determined to be the rearranged, Δ^{13} isomer **15**.[8]



15 R = Ac
16 R = H

Samples of **15** derived from steroids **1** and **2** were separately hydrolyzed to the more easily crystallized diol **16**. The identity of the samples of **16** obtained from **1** and **2** was confirmed by mixed melting point.

Although Wagner–Meerwein rearrangements of steroids involving migration of the C-18 angular methyl group have been known for some time,[8] the present examples seem especially noteworthy. That these rearrangements could be effected by treatment of an unactivated olefin with a Lewis acid under conditions which leave the C-5 tertiary hydroxyl group unaffected clearly highlights the extreme facility of this rearrangement.

Experimental Section

Melting points are uncorrected. IR and NMR spectra of all compounds were consistent with the assigned structures. IR spectra were obtained in KBr on a Perkin-Elmer Model 137 prism spectrometer. ^1H NMR spectra were obtained in $CDCl_3$ using a Varian XL-100 pulsed Fourier transform 100-MHz spectrometer with a Nicolet 1180 computer and pulsing unit. Chemical shifts are reported in δ units using Me_4Si as an internal standard. Microanalyses were performed at Stanford by E. Meier and J. Consul. Low-resolution mass spectra were obtained with a Varian MAT-44 system. Computerized high-resolution mass spectra were obtained on a Varian MAT-711 mass spectrometer by A. Wegmann. Medium-pressure liquid chromatography (MPLC) was performed with Woelm silica gel (0.032–0.063 mm) from ICN Pharmaceuticals. Materials to be chromatographed were first passed through a 15 mm × 25 cm scrubber column. Separations were obtained on either a 15- or a 25-mm diameter column, both 100 cm in length.

20-Methyl-17α-pregna-5,20-diene-3β,17-diol (4). A solution of 2.11 g (7.30 mmol) of 3β-hydroxyandrost-5-en-17-one (**3**) in 40 mL of THF and 10 mL of HMPA was chilled to −40 °C under an atmosphere of dry argon. Then 20 mL of a 1 M solution of 2-lithiopropene in ether was added slowly as the mixture was allowed to warm to 0 °C. After being stirred an additional 2 h at room temperature, the mixture was partitioned between brine

(3) Attempted introduction of the isopropylidene group via Wittig olefination of androstan-17-one derivatives was unsuccessful, presumably owing to the hindered nature of this carbonyl.
(4) Brown, H. C.; Krishnamurthy, S. *J. Am. Chem. Soc.* **1973**, *95*, 1669.
(5) Sharpless, K. B.; Michaelson, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6136. Chong, A. O.; Sharpless, K. B. *J. Org. Chem.* **1977**, *42*, 1587.
(6) Meystre, C.; Miescher, K. *Helv. Chim. Acta* **1949**, *32*, 1758.
(7) Sondheimer, F.; Mechoulam, R. *J. Am. Chem. Soc.* **1957**, *79*, 5029.
(8) For related rearrangements, see: Cohen, A.; Cook, J. W.; Hewett, C. L. *J. Chem. Soc.* **1935**, *445*. Kagi, H.; Miescher, K. *Helv. Chim. Acta* **1939**, *22*, 683. Ouannes, C.; Dvolaitzky, M.; Jacques, J. *Bull. Soc. Chim. Fr.* **1964**, 776. Kohen, F.; Mallory, R. A.; Scheer, I. *J. Org. Chem.* **1971**, *36*, 716.

and CH_2Cl_2. The brine was washed with additional CH_2Cl_2. After drying over Na_2SO_4, the CH_2Cl_2 solution was concentrated under reduced pressure to give a residue, which was chromatographed on a 25-mm MPLC column eluting with 30% EtOAc/hexane. This procedure provided 1.3 g of starting material **3** and 0.917 g (38%, 99% based on recovered **3**) of the desired diol **4**. Recrystallization from EtOAc/hexane gave 0.735 g (31%) of **4**, mp 169–171 °C. Anal. Calcd for $C_{22}H_{34}O_2$: C, 79.94; H, 10.37. Found: C, 80.04; H, 9.94.

17-Hydroxy-20-methyl-17α-pregna-4,20-dien-3-one (5). Diol **4** (5.4 g, 16 mmol), cyclohexanone (40 mL, 0.39 mol), and aluminum isopropoxide (8.2 g, 40 mmol) were mixed in 250 mL of toluene and brought to reflux. After it had refluxed for 10 h, the mixture was cooled to room temperature and diluted with 400 mL of EtOAc. The mixture was washed three times with 150-mL portions of 20% aqueous potassium sodium tartrate, once with water, and once with brine. After drying over Na_2SO_4, the organic phase was concentrated under reduced pressure. Chromatography of the residue on a 250 g SiO_2 column eluting with 40% EtOAc/hexane gave a solid. Recrystallization of this material from EtOAc/hexane with one reworking of the mother liquor provided a total of 3.9 g (74%) of product. The analytical sample had a mp of 171–173 °C. Anal. Calcd for $C_{22}H_{32}O_2$: C, 80.44; H, 9.82. Found: C, 80.47; H, 9.59.

20-(Chloromethyl)pregna-4,17(20)-dien-3-one (6). A solution of 1.50 g (4.57 mmol) of allylic alcohol **5** and 4.2 mL (36 mmol) of 2,6-lutidine in 150 mL of CH_2Cl_2 was chilled to 0 °C under an atmosphere of dry N_2 and then treated with 3.0 mL (4.2 mmol) of $SOCl_2$ in one portion. After 1 h of stirring at 0 °C, the mixture was quenched by the addition of saturated aqueous $NaHCO_3$ and diluted with additional CH_2Cl_2. After the organic solution was washed twice with saturated $NaHCO_3$ and once with brine, it was dried ($MgSO_4$) and concentrated under reduced pressure to give 1.8 g of crude product **6** as a semisolid. An analytical sample of this material (prepared by MPLC (20% EtOAc/hexane) and recrystallization (hexane)) had a mp of 120–124 °C. Anal. Calcd for $C_{22}H_{31}ClO$: C, 76.16; H, 9.01; Cl, 10.22. Found: C, 76.36; H, 9.05; Cl, 9.97.

20-(Chloromethyl)pregna-4,17(20)-dien-3β-ol (7). A solution of 40 mmol of $Li(t\text{-}BuO)_3AlH$ (prepared from 1.51 g of LAH and 13.5 mL of *t*-BuOH) in 85 mL of THF was chilled to −20 °C and then treated dropwise with a solution of 1.8 g of crude **6** in 100 mL of THF. After being stirred at −20 °C for 1 h, the mixture was quenched by the addition of saturated aqueous Na_2SO_4 until a white precipitate was observed. The THF solution was then decanted. The salts were washed with additional THF, and the combined organic solution was dried over $MgSO_4$ and concentrated under reduced pressure to give 1.8 g of crude product. An analytical sample was obtained by recrystallization from hexane, mp 103–105 °C. Anal. Calcd for $C_{22}H_{33}ClO$: C, 75.72; H, 9.53; Cl, 10.16. Found: C, 77.26; H, 9.51; Cl, 10.28.

20-Methylpregna-4,17(20)-dien-3β-ol (8). A solution of 1.8 g of crude allylic chloride **7** in 100 mL of THF was chilled to below 5 °C under an atmosphere of dry N_2. Then portions of a 1 M THF solution of $LiEt_3BH$[4] were added as the disappearance of starting material was followed by TLC (20% EtOAc/hexane). A total of 27 mmol of hydride was added during 5 h. Then 15 mL of 3 N aqueous NaOH was added followed by 15 mL of 30% H_2O_2. After being stirred for 5 min, the phases were separated. The aqueous phase was washed with CH_2Cl_2. The THF solution was concentrated under reduced pressure, and the residue was dissolved in CH_2Cl_2. The combined CH_2Cl_2 solution was washed twice with water and once with brine, dried over $MgSO_4$, and concentrated under reduced pressure. The residue was chromatographed on a 25-mm MPLC column eluting with 20% EtOAc/hexane, providing 0.723 g (50% from **5**) of dienol **8**. An analytical sample was prepared by MPLC (20% EtOAc/hexane) and two recrystallizations (hexane), mp 139–142 °C. Anal. Calcd for $C_{22}H_{34}O$: C, 84.02; H, 10.90. Found: C, 84.06; H, 10.98.

4β,5β-Epoxy-20-methylpregn-17(20)-en-3β-ol (9). A mixture of 420 mg (1.33 mmol) of allylic alcohol **8** and 3.6 mg (14 μmol) of $Mo(CO)_6$ in 50 mL of toluene was stirred at room temperature under N_2. To this mixture was added dropwise 215 μL (2.02 mmol) of 93% *t*-BuOOH. The mixture was stirred at room temperature for 3 days, during which time the progress of the reaction was followed by TLC (40% EtOAc/hexane) and a total of 200 μL (1.88 mmol) additional *t*-BuOOH was added in three portions to drive the reaction to completion. Then the mixture was diluted with ether, washed twice with 10% aqueous Na_2SO_3 and once with brine, and dried over Na_2SO_4. Concentrating the organic solution under reduced pressure provided a residue, which was chromatographed on a 15-mm MPLC column eluting with 30% EtOAc/hexane. This provided 328 mg (74%) of **9**, which was recrystallized from hexane with one reworking of the mother liquor to provide a total of 251 mg (57%), mp 154–161 °C. Anal. Calcd for $C_{22}H_{34}O_2$: C, 79.95; H, 10.37. Found: C, 80.22; H, 10.51.

20-Methylpregn-17(20)-ene-3β,5β-diol (10). To a solution of 211 mg (0.639 mmol) of epoxide **9** in 35 mL of THF at 0 °C under N_2 was added 231 mg (6.09 mmol) of LAH. The mixture was stirred at 0 °C for 1 h and at room temperature for 5 h. The reaction was quenched by the addition of saturated aqueous Na_2SO_4 until a white, granular precipitate was observed. The THF solution was then decanted, and the salts were washed with additional THF. The combined organic solution was dried over Na_2SO_4 and concentrated under reduced pressure to give 211 mg (99%) of **10**. Recrystallization from EtOAc/hexane and reworking the mother liquor provided a total of 131 mg (62%). An analytical sample had a mp of 191–195 °C. Anal. Calcd for $C_{22}H_{36}O_2$: C, 79.46; H, 10.91. Found: C, 79.43; H, 10.77.

3β-Acetoxy-20-methylpregn-17(20)-en-5β-ol (1). A solution of 79.6 mg (0.239 mmol) of diol **10** in 2 mL of pyridine and 1 mL of Ac_2O was stirred at room temperature for 3 days. The mixture was then diluted with ether. The ether solution was washed three times with 10% aqueous $CuSO_4$, twice with saturated aqueous $NaHCO_3$, and once with brine. After drying with Na_2SO_4, the ether solution was concentrated under reduced pressure to provide 89.9 mg (100%) of **1**. Recrystallization from hexane with reworking the mother liquor provided 74.0 mg (83%). An analytical sample had a mp of 154–158 °C: ^1H NMR δ 0.83 (s, 3), 0.98 (s, 3), 1.56 (br s, 3), 1.69 (t, 3, J = 2 Hz), 2.08 (s, 3), 2.98 (br s, 1), 5.22 (m, 1); IR 3640, 1730 cm^{-1}; mass spectrum, m/e 374 (M^+). Anal. Calcd for $C_{24}H_{38}O_3$: C, 76.96; H, 10.23. Found: C, 76.61; H, 10.08.

20-Methylpregna-4,20-dien-3β-ol (12). With a method similar to the one used to prepare **7**, dienol **12** was prepared from 20-methylpregna-4,20-dien-3-one (**11**).[6] The crude product was chromatographed on the MPLC eluting with 20% EtOAc/hexane to provide a 75% yield of product, which was recrystallized from hexane to give a 60% yield of recrystallized material. An analytical sample had a melting point of 124.5–124.8 °C. Anal. Calcd for $C_{22}H_{34}O$: C, 84.02; H, 10.90. Found: C, 84.33; H, 11.03.

4β,5β-Epoxy-20-methylpregn-20-en-3β-ol (13). Epoxide **13** was prepared from **12** by using a method similar to the one used to prepare epoxide **9**. A 77% yield of recrystallized material was obtained, mp 138–140 °C. Anal. Calcd for $C_{22}H_{34}O_2$: C, 79.95; H, 10.37. Found: C, 80.14; H, 10.17.

20-Methylpregn-20-ene-3β,5β-diol (14). Diol **14** was prepared from epoxide **13** by using a method similar to the one used to prepare diol **10**. An 81% yield of recrystallized material was obtained. An analytical sample had a mp of 188–189 °C. Anal. Calcd for $C_{22}H_{36}O_2$: C, 79.46; H, 10.91. Found: C, 79.71; H, 10.94.

3β-Acetoxy-20-methylpregn-20-en-5β-ol (2). Acetate **2** was prepared from diol **14** by using a method similar to the one used to prepare **1**. The crude material was recrystallized from $MeOH/H_2O$ to provide a 67% yield of product, mp 117–118 °C: ^1H NMR δ 0.56 (s, 3), 0.97 (s, 3), 1.75 (br s, 3), 2.08 (s, 3), 2.98 (br s, 1), 4.70 (m, 1), 4.85 (m, 1), 5.23 (m, 1); IR 3610, 1720, 1640, 883 cm^{-1}; exact mass calcd for $C_{24}H_{38}O_3$ m/e 374.28208, found m/e 374.28211. Anal. Calcd for $C_{24}H_{38}O_3$: C, 76.96; H, 10.23. Found: C, 76.66; H, 10.13.

3β-Acetoxy-17,20-dimethyl-18-nor-17α-pregn-13-en-5β-ol (15): (a) From 3β-Acetoxy-20-methylpregn-17(20)-en-5β-ol (1). A solution of 40.2 mg (0.107 mmol) of sterol **1** in 20 mL of CH_2Cl_2, which had been chilled to −20 °C under N_2, was treated with 120 μL (0.976 mmol) of $BF_3{\cdot}Et_2O$. The progress of the reaction was followed by GC (OV-17, 220 °C) analysis of quenched aliquots removed from the mixture. After the mixture had been stirred for 4 h at −20 to −10 °C and at 0 °C for 45 min, GC indicated starting material had been cleanly converted to a product having a shorter retention time. The mixture was quenched by the addition of ether saturated with NH_3 and then diluted with ether, washed with saturated aqueous $NaHCO_3$ and brine, and

dried over Na_2SO_4. The ether solution was then concentrated to give an oil. Attempts at crystallizing this material led only to its partial destruction. The material was thus chromatographed on a 1 mm × 20 cm × 20 cm preparative silica gel TLC plate eluting with 30% EtOAc/hexane, providing 29.7 mg (74%) of product, which was homogenous by TLC (30% EtOAc/hexane) and GC (OV-17, 220 °C). The NMR and IR spectra of this material were identical with spectra obtained for material prepared from steroid **2**.

(b) From 3β-Acetoxy-20-methylpregn-20-en-5β-ol (2). With a procedure similar to the one described above, a 74% yield of rearranged material **15** was obtained from **2**: ^{1}H NMR δ 0.74 (d, 3, J = 7 Hz), 0.84 (d, 3, J = 7 Hz), 0.94 (s, 3), 0.96 (s, 3), 2.08 (s, 3), 5.24 (m, 1); IR 3650, 1740 cm^{-1}; exact mass calcd for $C_{24}H_{38}O_3$ m/e 374.28208, found m/e 374.28153.

17,20-Dimethyl-18-nor-17α-pregn-13-ene-3β,5β-diol (16): (a) Derived from 3β-Acetoxy-20-methylpregn-17(20)-en-5β-ol (1). An 18.9 mg (50.5 μmol) sample of **15**, prepared from **1** as described above, was dissolved in 2 mL of MeOH saturated with NH_3. After being stirred at room temperature overnight, the reaction mixture was partitioned between ether and water. The ether solution was washed with brine, dried over Na_2SO_4, and condensed under reduced pressure to give a residue, which was recrystallized from hexane to give 13.2 mg (79%) of the desired diol **16**, mp 181–185 °C. The NMR and IR spectra of this material were identical with those obtained for the sample of **16** prepared below. Anal. Calcd for $C_{22}H_{36}O_2$: C, 79.46; H, 10.91. Found: C, 79.25; H, 11.08.

(b) Derived from 3β-Acetoxy-20-methylpregn-20-en-5β-ol (2). With a procedure similar to the one described above, a sample of **15** derived from **2** was converted by NH_3/MeOH treatment to **16** in 65% chromatographed yield. Recrystallization from hexane provided a sample which had a mp 179–183 °C: ^{1}H NMR δ 0.73 (d, 3, J = 7 Hz), 0.84 (d, 3, J = 7 Hz), 0.92 (s, 3), 0.96 (s, 3), 2.86 (m, 2), 4.14 (m, 1); IR 3320 cm^{-1}. Anal. Calcd for $C_{22}H_{36}O_2$: C, 79.46; H, 10.91. Found: C, 79.53; H, 10.90.

A mixture of samples of diol **16** derived from sterols **1** and **2** had a melting point of 179–185 °C.

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Reaction of $[Co(CN)_5]^{3-}$ with Alkenyl Halides in an Aprotic Medium

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Activating aryl and vinyl halides toward substitution is one of the oldest uses of transition metals in organic synthesis.[1] Copper has been the metal of choice, but recently several methodologies, some catalytic in metal, have appeared based on nickel,[2] palladium,[3] or cobalt[4] chemistry.

Table I. Reactions of Haloalkenes with $Co(CN)_5^{3-}$

compd	T, °C	t, h	organic prods[a]	yield, %[b]
(*E*)-PhCH=CHBr	40	43	(*E*)-PhCH=CHCN	72
			(*Z*)-PhCh=CHCN	<3
(*Z*)-PhCh=CHBr (90% *Z*)	55	50	(*Z*)-PhCH=CHCN	43
			(*E*)-PhCH=CHCN	28
(*Z*)-PhCH=CHBr (>95% *Z*)	25	18	(*Z*)-PhCH=CHCN	47[c]
			(*E*)-PhCH=CHCN	16
			(*Z*)-PhCH=CHBr	37
(*Z*)-PhCH=CHCl	40	43	(*Z*)-PhCH=CHCN	32
			(*E*)-PhCH=CHCN	13
			(*Z*)-PhCH=CHCl	13
p-$CH_3OC_6H_4Br$	25	24	NR[d]	
$(CH_3)_2C$=CHCl	40	43	$(CH_3)_2C$=CH(CN)	68

[a] Identified by GC and ^{1}H NMR. [b] Determined by GC of ether extracts from aqueous workup unless otherwise indicated. [c] Determined by NMR of reaction mixture, normalized to 100%. [d] Also no reaction after heating 1 h at 60 °C.

Relatively little is known about the mechanisms of these reactions, and there has been some debate over the involvement of concerted exchanges versus organometallic intermediates[5] and between chain and nonchain one- vs. two-electron mechanisms.[6] In the case of the cobalt(II) catalyzed cyanide exchange with vinyl bromides, evidence has recently been presented for a mechanism involving a Co(I)/Co(III) catalytic couple and (σ-vinyl)cobalt cyanide intermediates.[7]

I now report that the reaction of $Co(CN)_5^{3-}$ with β-bromo styrene to give cinnamonitrile occurs under conditions where this mechanism cannot be operative. Reaction of $[(C_2H_5)_3(CH_3)N]_3Co(CN)_5$ with (*E*)-2-bromo-1-phenylethene (1:1 mol ratio) in acetonitrile proceeds slowly at room temperature and more rapidly at 40–80 °C to form a blue solution and solids. Workup with aqueous base and ether extraction gives (*E*)-3-phenylpropenenitrile (Table I). Although the starting cobalt complex is paramagnetic the reaction can be followed by ^{1}H NMR. No evidence for the buildup of an organocobalt intermediate is observed.

Reaction of $Co(CN)_5^{3-}$ with (*Z*)-2-bromo-1-phenylethene is not completely stereospecific: at 25 °C, a 3:1 ratio of (*Z*)- to (*E*)-3-phenylpropenenitrile results at ~60% conversion. At 55 °C, reaction is complete in under 48 h, giving a 71% yield of a 2.3:1 mixture of the *Z* and *E* nitriles (corrected for stereochemical purity of the starting material). Using a 2:1 ratio of $Co(CN)_5^{3-}$ to (*Z*)-2-bromo-1-phenylethene gives reduced stereospecificity and the foormation of significant amounts of (currently unidentified) additional products.

Under the conditions described herein, (*E*)-2-bromo-1-phenylethene is inert to $(C_2H_5)_3CH_3N^+CN^-$ in acetonitrile. Addition of $[(C_2H_5)_3(CH_3)N]_3Co(CN)_5$ to this halide–cyanide mixture does not catalyze the displacement reaction and in fact the presence of excess cyanide appears

(1) (a) Ullman reaction: Fanta, P. E. *Synthesis* **1974**, 9–21. (b) Ullman ether synthesis: Moroz, A. A.; Shvartaberg, M. S. *Russ. Chem. Rev. (Engl. Transl.)* **1974**, *43*, 679–689. (c) Rosenmund–von Braun reaction: Mowry, D. T. *Chem. Rev.* **1948**, *42*, 207–209. (d) Ester synthesis: Cohen, T.; Lewin, A. H. *J. Am. Chem. Soc.* **1966**, *88*, 4521–4522. (e) Application to vinyl halides: Cohen, T.; Poeth, T. *J. Am. Chem. Soc.* **1972**, *94*, 4363–4364. Lapouyade, R.; Daney, M.; Lapenue, M.; Bouas-Laurent, H. *Bull. Soc. Chim. Fr.* **1973**, 720–721.

(2) Some representative reports: Corey, E. J.; Hegedus, L. S. *J. Am. Chem. Soc.* **1969**, *91*, 1233–1234. Hashimoto, J.; Tsuruta, N.; Ryang, M.; Tsutsumi, S. *J. Org. Chem.* **1970**, *35*, 3748–3752. Semmelhack, M. F.; Helquist, P. M.; Jones, L. D. *J. Am. Chem. Soc.* **1971**, *93*, 5909–5310. Zembayashi, M.; Tamao, K.; Yoshida, J.; Kumada, M. *Tetrahedron Lett.* **1977**, 4089–4092. Tamao, K.; Sumitani, Y. K.; Zembayashi, A. F.; Kodama, S.; Nakajima, I.; Minato, A.; Kumada, M. *Bull. Chem. Soc. Jpn.* **1976**, *49*, 1958–1969. Cramer, R.; Coulson, D. R. *J. Org. Chem.* **1975**, *40*, 2267–2273. Cassar, L. *J. Organomet. Chem.* **1973**, *54*, C57–C58.

(3) Inter alia: Yamaura, K.; Murahashi, S.-I. *Tetrahedron Lett.* **1977**, 4429–4430. Negishi, E.; Okukado, N.; King, A. O.; Van Horn, D. E.; Spiegel, B. I. *J. Am. Chem. Soc.* **1978**, *100*, 2254–2256. Takagi, K.; Okamoto, T.; Sakakibara, Y.; Oka, S. *Chem. Lett.* **1973**, 471–474. Heck, R. F. *Pure Appl. Chem.* **1978**, *50*, 691–701. Kim, J.-I. I.; Patel, B. A.; Heck, R. F. *J. Org. Chem.* **1981**, *46*, 1067–1073.

(4) (a) Dodd, D.; Johnson, M. D.; Meeks, B. S.; Titchmarsh, D. M.; Duong, K. N. V.; Gaudemer, A. *J. Chem. Soc., Perkin Trans. 2* **1976**, 1261–1267. (b) Funabiki, T.; Yoshida, S.; Tarama, K. *J. Chem. Soc., Chem. Commun.* **1978**, 1059–1061.

(5) Cohen, T.; Wood, J.; Dietz, A. G., Jr. *Tetrahedron Lett.* **1974**, 3555–3558.

(6) Kochi, J. K. "Organometallic Mechanisms and Catalysis"; Academic Press: New York, 1978; pp 168–173.

(7) Funabiki, T.; Hosomi, H.; Yoshida, I.; Tarama, K. *J. Am. Chem. Soc.* **1982**, *104*, 1560–1568.

0022-3263/85/1950-3934$01.50/0