from methylene chloride–ether to give 6.5 g (34.5%) of yellow crystals: mp 118–118.5°; ir 1595 cm^{-1}; uv 228 nm (log ϵ 4.29); nmr δ 2.42 (s, 3 H, $ArCH_3$), 5.62 (d, 1 H, J = 2.5 Hz, C_4 H), 6.11 (s, 1 H, C_1 H), 6.88 (d, 1 H, J = 2.5 Hz, C_3 H), 7.3–7.55 (m, 6 H, aromatic), 7.9–8.05 (m, 2 H, aromatic). *Anal.* Calcd for $C_{17}H_{14}Br_2N_2O_2S$: C, 43.43; H, 3.00; Br, 34.00. Found: C, 43.72; H, 3.29; Br, 34.32.

4-Bromo-1-cyano-3-ethoxy-2-*p*-toluenesulfonyl-1,2,3,4-tetrahydroisoquinoline (5). A mixture of 2.0 g of **2** and 20 ml of absolute ethanol was stirred under reflux for 4 hr. The clear solution obtained was evaporated to dryness. Addition of ether and filtration yielded 1.1 g (59.4%) of colorless crystals of **5**: mp 163°, raised to 169° by recrystallisation from methylene chloride–hexane; ir 1600 cm^{-1}; uv 230 nm (log ϵ 4.32); nmr ($CDCl_3$) δ 1.20 (t, 3 H, CCH_3), 2.38 (s, 3 H, $ArCH_3$), 3.80 (q, 2 H, OCH_2), 5.28 (d, 1 H, J = 2.5 Hz, C_4 H), 5.70 (s, 1 H, C_1 H), 5.82 (d, 1 H, J = 2.5 Hz, C_3 H), 7.22–7.40 (m, 6 H, aromatic H), and 7.88–8.05 (m, 2 H, aromatic H).

Anal. Calcd for $C_{19}H_{19}BrN_2O_3S$: C, 52.42; H, 4.39; N, 6.44. Found: C, 52.20; H, 4.49; N, 6.72.

4-Bromo-1-cyano-3-isopropoxy-2-toluenesulfonyl-1,2,3,4-tetrahydroisoquinoline (6). A mixture of 3 g of **2** and 20 ml of 2-propanol was stirred under reflux for 4 hr. The clear solution was worked up under conditions described for **5** to give 2.2 g (76.8%) of colorless crystals of **6**: mp 162°, raised to 166° by recrystallisation from 2-propanol; ir and uv were similar to those of **5**; nmr ($CDCl_3$) δ 1.22 (t, 3 H, CCH_3), 2.40 (s, 3 H, $ArCH_3$), 4.12 (m, 1 H, OCH) 5.21 (d, 1 H, J = 2.5 Hz, C_4 H) 5.72 (s, 1 H, C_1 H) 5.90 (d, 11 H, J = 2.5 Hz, C_3 H), 7.22–7.40 (m, 6 H, aromatic H), and 7.88–8.05 (m, 2 H, aromatic H).

Anal. Calcd for $C_{20}H_{21}BrN_2O_3S$: C, 53.46; H, 4.71; N, 6.24. Found: C, 53.29; H, 4.91; N, 6.03.

4-Bromo-1-cyano-3-hydroxy-2-*p*-toluenesulfonyl-1,2,3,4-tetrahydroisoquinoline (7). To a solution of 2 g of **2** dissolved in 50 ml of chloroform was added 10 ml of a saturated aqueous solution of sodium bicarbonate and the solution was stirred overnight at room temperature. The chloroform layer was separated, dried over Na_2SO_4, and evaporated. After trituration with methylene chloride–ether the colorless crystals obtained were filtered to give 0.2 g (11.5%) of **7**: mp 177–178° (recrystallization from 2-propanol raised the melting point to 184°); ir (Nujol) 3350 and 1700 cm^{-1}; uv λ_{infl} 226 nm (log ϵ 4.32); nmr ($CDCl_3$, CD_3SOCD_3)[8] δ 2.35 (s, 3 H, $ArCH_3$), 5.25 (d, 1 H, J = 2.5 Hz, C_4 H), 5.85 (s, 1 H, C_1 H), 6.08 (d, 1 H, J = 2.5 Hz, C_3 H), 7.22–7.40 (m, 6 H, aromatic H), 7.75–8.00 (m, 2 H, aromatic H). *Anal.* Calcd for $C_{17}H_{15}BrN_2O_3S$: C, 50.14; H, 3.71; N, 6.88. Found: C, 50.14; H, 3.69; N, 7.15.

4-Bromo-1-cyano-2-*p*-toluenesulfonyl-1,2-dihydroisoquinoline (4). A. By Base Treatment of 2. A solution of 2.35 g (0.005 mol) of **2** in 30 ml of dioxane containing 0.44 g (0.005 mol) of morpholine was stirred for 6 hr at room temperature. The solution was evaporated to dryness under reduced pressure. Dilution with water and filtration gave 1.12 g (57.5%) of **4**: mp 161° (recrystallization from methylene chloride–ether raised the melting point to 164°); ir 1598 cm^{-1}; uv 232 nm (log ϵ 4.31) and 298 (3.99); nmr ($CDCl_3$) δ 2.35 (s, 3 H, $ArCH_3$), 6.15 (d, 1 H, J = 0.5 Hz, C_1 H), 7.15 (d, 1 H, J = 0.5 Hz, C_3 H), 7.22–7.45 (m, 6 H, aromatic H), 7.65–7.85 (m, 2 H, aromatic H). *Anal.* Calcd for $C_{17}H_{13}BrN_2O_2S$: C, 52.46; H, 3.37; N, 7.20. Found: C, 52.72; H, 3.70, N, 7.03.

B. By Reissert Reaction. To a suspension of 20.8 g (0.1 mol) of 4-bromoisoquinoline in methylene chloride (60 ml) containing 19.5 g (0.3 mol) of potassium cyanide in 48 ml of water was added gradually under vigorous stirring 57.0 g (0.3 mol) of *p*-toluenesulfonyl chloride in 40 ml of methylene chloride and stirring was continued for 6 hr. The methylene chloride layer was separated and washed with 10% aqueous hydrochloric acid, 5% aqueous sodium hydroxide, and finally water. It was dried over Na_2SO_4 and evaporated. On trituration of the residue with ether 22.5 g (57.85%) of **4** was obtained which was identical in all respects with the product obtained by procedure A.

1-Cyano-4-bromoisoquinoline (9). A solution of 2.35 g (0.005 mol) of **2** in 70 ml of dioxane containing 1.29 g (0.015 mol) of morpholine was refluxed for 4 hr. The solution was evaporated to dryness under reduced pressure. The residue was treated with sodium bicarbonate solution followed by water. Trituration with 2-propanol gave 0.92 g (78.9%) of **9**, mp 123°. Recrystallization from hexane afforded pure crystals of **9**: mp 125° (lit.[6] mp 122–123°); ir 1605 and 1550 cm^{-1}; uv 233 nm (log ϵ 4.62) and 339 (3.92). *Anal.* Calcd for $C_{10}H_5BrN_2$: C, 51.53; H, 2.16; N, 12.02. Found: C, 51.74; H, 2.27; N, 12.19.

Registry No.—**1**, 3340-68-9; **2**, 51270-04-3; **4**, 51270-05-4; **7**, 51270-06-5; **9**, 27224-09-5; bromine, 7726-95-6; 4-bromoisoquinoline, 1532-97-4; *p*-toluenesulfonyl chloride, 98-59-9; morpholine, 110-91-8.

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(8) Drops of CD_3SOCD_3 were added to the compound suspended in $CDCl_3$ until a homogenous solution was formed.

Medium-Ring Systems.[1] IV. Synthesis of Spiro[2.*n*]alkan-5-ones. Neighboring Hydroxyl in a Hofmann Elimination

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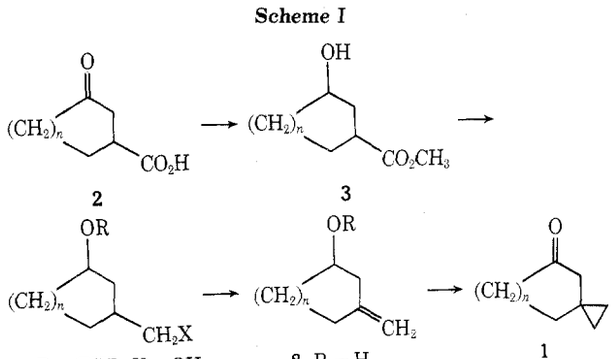
As a part of a study of the properties of medium-ring systems,[1] we have prepared spiro[2.7]decan-5-one (**1a**) and spiro[2.9]dodecan-5-one (**1b**) by the general route indicated in Scheme I. The appropriate 3-carboxycycloalkanones[1a] (**2**) were converted to the corresponding methyl 3-hydroxycycloalkanecarboxylates (**3**) by a reported procedure.[1b] The alcohol group was protected as the tetrahydropyranyl ether,[3] and the ester functionality was reduced to the alcohol level (**4**) with equimolar amounts of lithium aluminum hydride.[4] Attempts to directly dehydrate these alcohols using phosphorus oxychloride[5] or thionyl chloride[6] led to recovery of unreacted starting material.

Work[7] with cyclohexylmethanol and cyclooctylmethanol suggested that bromination with phosphorus tribromide in pyridine and benzene[8] followed by dehydrobromination with potassium *tert*-butoxide in dimethyl sulfoxide[9] might be the method of choice, but the bromination reaction

Scheme I



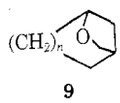
2 **3**

4, R = THP; X = OH
5, R = THP; X = OTs
6, R = H; X = $N(CH_3)_2$
7, R = H; X = $N^+(CH_3)_3{}^-OH$
11, R = CH_3; X = $N(CH_3)_2$

8, R = H
10, R = CH_3

1

a, $n = 4$
b, $n = 6$



9

a, $n = 4$
b, $n = 6$

with alcohol **4a** produced a multicomponent mixture containing none of the desired bromide. Conversion of the alcohols **4** to the tosylate esters **5** proceeded in high yield, but elimination using refluxing pyridine[10] failed. However, the tosylates reacted cleanly with dimethylamine to produce the unprotected amino alcohols **6a** and **6b**, thereby setting the stage for elimination by the Cope or Hofmann procedures.[11] Quaternization with methyl iodide followed by conversion to the hydroxide over Rexyn 201 (OH)[12] provided the required quaternary ammonium hydroxide.

The Hofmann elimination of quaternary salt **7a** at 10 mm produced 56% of the desired alkenol (**8a**), 8% of bicyclic ether **9a**, and a small amount of methoxyalkene **10a**. Hofmann elimination of **7b** under analogous conditions produced 13% of the desired alkenol (**7b**), 33% of bicyclic ether **9b**, 3% of methoxyalkene **10b**, and a small amount of methoxyamine **11b**. While these Hofmann eliminations in compounds containing nearby hydroxy functions appear to be unprecedented, all of the products are reasonable based on the usual mechanistic picture for this reaction.

In each series, the alkenol **8** was treated with Simmons–Smith reagent,[13] and the resulting spiro alcohol was then oxidized with modified Collins reagent[14] to complete the synthetic route.

Experimental Section

Melting points and boiling points are uncorrected. Nmr spectra were recorded on a Varian A-60A instrument using 10% solutions in deuteriochloroform unless otherwise noted, and are reported in parts per million downfield from tetramethylsilane as an internal standard. Only distinct absorptions will be listed herein. Infrared spectra were determined with a Beckman IR-10 spectrophotometer on 5–7% solutions in chloroform unless otherwise specified. Only major absorptions are listed herein. Ultraviolet spectra were measured with a Cary 15 spectrophotometer. Elemental analyses were performed by Alfred Bernhardt Mikroanalytisches Laboratorium, Elbach, West Germany.

Tetrahydropyranyl Ether of Methyl 3-Hydroxycyclooctanecarboxylate. A solution of 28 ml of 2,3-dihydropyran (freshly distilled over NaOH pellets), 3.44 g (18.5 mmol) of methyl 3-hydroxycyclooctanecarboxylate (**3d**),[1b] and 2 drops of concentrated HCl was treated according to the procedure of Dauben and Bradlow,[3] yielding 4.10 g (82.5%) of a viscous, clear, and colorless oil: ir 1730 cm^{-1}; nmr δ 3.17–4.15 (m, 5), 4.65 (broad s, 1).

Anal. Calcd for $C_{15}H_{26}O_4$: C, 66.64; H, 9.69. Found: C, 66.69; H, 9.78.

Tetrahydropyranyl Ether of Methyl 3-Hydroxycyclodecanecarboxylate. This compound was prepared by the above procedure[3] from 1.96 g (9.15 mmol) of methyl 3-hydrocyclodecanecarboxylate (**3b**),[1b] 13 ml of 2,3-dihydropyran, and 2 drops of concentrated HCl. After distillation, a quantitative yield (2.75 g) of a viscous, clear, and colorless oil was obtained: bp 114–120° (0.2 mm); ir 1730 cm^{-1}; nmr δ 4.24–3.27 (m, 6), 4.69 (broad s, 1).

Anal. Calcd for $C_{17}H_{30}O_4$: C, 68.42; H, 10.13. Found: C, 68.29; H, 9.97.

1-Tetrahydropyranyl Ether of 1-Hydroxy-3-hydroxymethylcyclooctane (4a). A solution of 2.70 g (10.0 mmol) of the tetrahydropyranyl ether of methyl 3-hydroxycyclooctanecarboxylate in 8 ml of ethyl ether was added[4] to 0.38 g (10.0 mmol) of $LiAlH_4$, yielding 2.42 g (99.5%) of a clear and colorless oil: ir 3400 cm^{-1} (broad); nmr δ 2.55 (s, 1), 3.00–4.15 (m, 5), 4.61 (broad s, 1).

Anal. Calcd for $C_{14}H_{26}O_3$: C, 69.38; H, 10.81. Found: C, 69.20; H, 10.72.

1-Tetrahydropyranyl Ether of 1-Hydroxy-3-hydroxymethylcyclodecane (4b). This compound was prepared[4] from 185.15 g (623 mmol) of the tetrahydropyranyl ether of methyl 3-hydroxycyclodecanecarboxylate and 23.05 g (607 mmol) of $LiAlH_4$ to yield 156 g (93.5%) of a viscous, clear, and colorless oil: ir 3400 cm^{-1} (broad); nmr δ 2.78 (s, 1), 3.20–4.20 (m, 6), 4.70 (broad s, 1).

Anal. Calcd for $C_{16}H_{30}O_3$: C, 71.07; H, 11.18. Found: C, 70.98; H, 11.06.

1-Tetrahydropyranyl Ether of 1-Hydroxy-3-tosyloxymethylcyclooctane (5a). A solution of **4a** (84 g, 347 mmol) in 121 ml of pyridine at 0° was combined with 73.5 g (386 mmol) of *p*-toluenesulfonyl chloride[15] to give a heavy oil (133 g, 97% yield), nmr δ 2.60 (s, 3, $ArCH_3$), 3.70–4.20 (m, 5), 4.63 (m, 1), 7.56 (d of d, 4, ArH).

1-Tetrahydropyranyl Ether of 1-Hydroxy-3-tosyloxymethylcyclodecane (5b). This compound was prepared[15] from 73 g (302 mmol) of alcohol **4b** and 60 g (315 mmol) of *p*-toluenesulfonyl chloride. The resulting product was 115 g (96.5% yield) of the desired **5b**, nmr δ 2.43 (s, 3, $ArCH_3$), 3.70–4.30 (m, 5), 4.63 (m, 1), 7.61 (d of d, 4, ArH).

Anal. Calcd for $C_{23}H_{36}O_5S$: C, 65.06; H, 8.55. Found: C, 65.12; H, 8.54.

3-Hydroxy-1-dimethylaminomethylcyclooctane (6a). Tosylate **5a** was converted to **6a** in three batches which were combined. Wet dimethylamine was generated by adding 750 g (9.2 mol) of dimethylamine hydrochloride in 500 ml of water dropwise to 1500 g of a stirred 50% NaOH solution. The temperature in the generator rose to 37° by the end of the addition, after which time it was slowly heated to reflux. The wet dimethylamine was bubbled as generated into a flask containing 115 g of tosylate **5a** in 600 ml of dimethylformamide, during which time an exothermic process occurred (temperatures up to 55°). When bubbling ceased, the generator was disconnected and the reaction flask refluxed for 2 hr. Benzene (500 ml) was added, and the mixture was extracted with three 500-ml portions of 10% NaOH solution. The aqueous layers were back-extracted with 500 ml of benzene, and the combined benzene layers were dried (Na_2SO_4) and concentrated under reduced pressure.

A total of 356 g of **5a** treated in the above manner was combined and vacuum distilled. The main fraction (123 g, 61% yield) was a clear liquid, bp 132–148° (4–6 mm), corresponding to the desired hydroxy amine **6a**: ir 3400 cm^{-1} (broad); nmr δ 2.00 (broad, 2, CH_2N), 2.20 (s, 6, NCH_3), 3.50–4.15 (m, 2, **CHOH**); mass spectrum molecular ion m/e 185.

Anal. Calcd for $C_{11}H_{23}NO$: C, 71.30; H, 12.51; N, 7.56. Found: C, 71.27: H, 12.46; N, 7.71.

3-Hydroxy-1-dimethylaminomethylcyclodecane (6b). The above procedure was used to convert 115 g of tosylate **5b** to 37.9 g (65.5% yield) of the desired hydroxy amine **6b**: bp 124° (0.6 mm); ir 3400 cm^{-1} (broad); nmr δ 1.95–2.15 (broad, 3, CH_2N, OH), 2.23 (s, 6, NCH_3), 3.40–3.90 (m, 1, **CHOH**); mass spectrum molecular ion m/e 213.

Anal. Calcd for $C_{13}H_{27}NO$: C, 73.18; H, 12.76; N, 6.56. Found: C, 72.97; H, 12.70; N, 6.65.

Methiodide of Amine 6a. Amine **6a** (123 g, 665 mmol) was quaternized[11] with methyl iodide (492 g, 3.47 mol) to produce 186 g (85.3% yield) of the desired salt: mp 159–164° dec; nmr (D_2O) δ 3.16 (s, 9, NCH_3), 3.28–3.40 (m, 2, CH_2N), 3.73–4.13 (m, 1, **CHOD**); mass spectrum m/e 185, 142.

Anal. Calcd for $C_{12}H_{26}NOI$: C, 44.04; H, 8.00; N, 4.28. Found: C, 43.94; H, 8.05; N, 4.23.

Methiodide of Amine 6b. Amine **6b** (37.9 g, 178 mmol) was quaternized[11] with methyl iodide (75.7 g, 534 mmol) to yield 50.0 g (79.5% yield) of the desired methiodide: ir 3480 cm^{-1} (broad); nmr δ 3.48 (s, 9, NCH_3), 3.70–4.33 (broad, 2, **CHOH**); mass spectrum m/e 213, 142.

Anal. Calcd. for $C_{14}H_{30}NOI$: C, 47.33; H, 8.57; N, 3.94. Found: C, 47.15; H, 8.46; N, 4.05.

***N*-(3-Hydroxycyclooctylmethyl)trimethylammonium Hydroxide (7a).** The methiodide of amino alcohol **6a** (127 g, 388 mmol) was converted to the corresponding quaternary ammonium hydroxide (**7a**) in two batches, by a modification of the procedure of Coke and Mourning.[12] Prewashed Rexyn 201 (OH) (220 g) was added to a magnetically stirred solution of the salt in 500 ml of water. After 15 hr of stirring, the reaction mixture was filtered and the residue was washed twice with hot water. The filtrate and the washes were combined and concentrated under reduced pressure to 117 g of material containing an indeterminate amount of water.

***N*-(3-Hydroxycyclooctylmethyl)trimethylammonium Hydroxide (7b).** The above procedure was used to convert 50.0 g (141 mmol) of the methiodide of amine **6b** to the corresponding hydroxide **7b** using a threefold excess of Rexyn 201 (OH).

3-Methylenecyclooctanol (8a). A portion of quaternary hydroxide **7a** corresponding to 43 g of methiodide was heated under vacuum with stirring. Remaining water was removed at 25° (15 mm). At 40–45° (15 mm) vigorous bubbling ensued and trimethylamine was produced. The pressure was lowered to 7 mm and the heating was continued. At 75–80° (7 mm) crystalline material sublimed in the distillation head. Heating was discontinued so that this material could be removed as an ethereal solution. The ethereal solution as washed with water, dried ($MgSO_4$), and con-

centrated under reduced pressure. The resulting solid (1.6 g) contained two components, which were separated by column chromatography on neutral alumina. The faster moving material (1.18 g) appeared pure, but melted over a 6° range. A 140-mg portion was sublimed to give 55 mg of bicyclic ether **9a**: mp 54.5–56°; nmr δ 2.25–2.83 (m, 2), 3.60–4.50 (m, 3, CH_2OCH); mass spectrum molecular ion m/e 140.

Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.05; H, 11.59.

The distillation was resumed and a fraction was collected at 110–125° (8–9 mm), dissolved in ether, washed three times with water, dried (Na_2SO_4), and concentrated. The resulting material (11.5 g, 56% yield) was found to be the desired enol **8a** contaminated with a small amount of methoxyalkene **10a** (nmr δ 3.35, sharp singlet). Column chromatography on neutral alumina permitted the desired separation of pure 3-methylenecyclooctanol (**8a**): ir 3350, 3090, 1640 cm^{-1}; nmr δ 2.00 (s, 1, OH), 2.10–2.80 (m, 4, allylic), 3.86 (m, 1, CHO), 4.90 (m, 2, vinylic); mass spectrum molecular ion m/e 140.

Anal. Calcd for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.22; H, 11.43.

3-Methylenecyclodecanol (8b). Hofmann elimination of quaternary hydroxide **7b** was performed by the above procedure and was accompanied by serious foaming problems. After removal of water and trimethylamine, a 6.68-g fraction was obtained at 105–122° (4 mm), and another fraction (5.96 g) was obtained at 125–135° (4 mm). The first fraction consisted of approximately 85% bicyclic ether **9b** and about 15% methoxyalkene **10b**. Sequential column chromatography and preparative tlc permitted isolation of the methoxyalkene **10b** in about 90% purity: ir 1650, 3100 cm^{-1}; nmr δ 2.00–2.80 (m, 4, allylic), 3.30 (s, 3, OCH_3), 3.40–3.80 (m, 1, CHO), 4.88 (m, 2, vinylic).

The second fraction, approximately 50% of hydroxyalkene **8b**, 13% of methoxy amine **11b**, and 35% of bicyclic ether **9b**, was separated by column chromatography on neutral alumina. Approximately 600 mg of 3-methoxy-1-dimethylaminomethylcyclodecane (**11b**) was recovered and purified by vacuum distillation, nmr δ 2.07 (broad, 2, CH_2N), 2.20 (s, 6, NCH_3), 3.31 (s, 3, OCH_3), 3.40–3.80 (m, 1, CHO).

Anal. Calcd for $C_{14}H_{29}NO$: C, 73.95; H, 12.85. Found: C, 74.17; H, 12.83.

The desired 3-methylenecyclodecanol (**8b**, 1.78 g) was obtained in later chromatography fractions. A 380-mg sample was further purified by preparative tlc. Approximately one-third of the 300 mg of material recovered was vacuum distilled to give a clear liquid: ir 3200–3500 and 1650 cm^{-1}; nmr δ 1.66 (s, 1, OH), 2.10–2.75 (m, 4, allylic), 4.25 (m, 1, CHO), 4.95 (m, 2, vinylic); mass spectrum molecular ion m/e 168.

Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.42; H, 12.08.

Spiro[2.7]decan-5-ol. The Simmons–Smith procedure[13] was used for the cyclopropanation of 3-methylenecyclooctanol (**8a**). A 9.52-g (68 mmol) sample of slightly impure **8a** was treated twice with methylene iodide and Zn–Cu couple to produce 4.7 g of a liquid estimated to contain about 85% of the desired spiro alcohol (by nmr), nmr δ 0.10–0.70 (m, 4, cyclopropyl), 2.60 (s, 1, OH), 3.03–4.13 (broad m, 1, CHO).

Spiro[2.9]dodecan-5-ol. The Simmons–Smith procedure[13] was applied to 1.4 g (83.3 mmol) of 3-methylenecyclodecanol (**8b**) to give 500 mg of a crude oil which crystallized on standing. A 430-mg sample of this material was purified by preparative tlc followed by vacuum distillation to give pure spiro alcohol: mp 41–44°; nmr δ 0.10–0.46 (m, 4, cyclopropyl), 4.00 (m, 1, CHO).

Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 78.99; H, 12.10.

Spiro[2.7]decan-5-one (1a). The Collins oxidation as modified by Ratcliffe and Rodehorst[14] was used to oxidize 0.46 g (3 mmol) of spiro[2.7]decan-5-ol to the corresponding ketone. The resulting 0.39 g (85.5% yield) of product was distilled at 70–78° (0.9 mm): ir 1705 cm^{-1}; uv λ_{max} (EtOH) 280 nm (ϵ 44.5); nmr δ 0.29–0.70 (m, 4, cyclopropyl), 2.25 (s, 2, c-Pr($CH_2C{=}O$), 2.33–2.66 (m, 2, $CH_2C{=}O$); mass spectrum molecular ion m/e 152.

Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 78.74; H, 10.65.

Spiro[2.9]dodecan-5-one (1b). The Ratcliffe–Rodehorst procedure[14] was used to oxidize 80 mg (4.4 mmol) of spiro[2.9]dodecan-5-ol. A 73-mg sample of crude ketone was vacuum distilled to give 60 mg (75.8% yield) of pure ketone **1b**: ir 1700 cm^{-1}; uv λ_{max} (EtOH) 282 nm (ϵ 120); nmr δ 0.20–0.60 (m, 4, cyclopropyl), 2.33 (s, 2, c-Pr$CH_2C{=}O$), 2.50–2.80 (m, 2, $CH_2C{=}O$); mass spectrum molecular ion m/e 180.

Anal. Calcd for $C_{12}H_{20}O$: C, 79.94; H, 11.18. Found: C, 79.96; H, 11.26.

Registry No.—1a, 51364-58-0; **1b,** 51364-59-1; **4a,** 51364-60-4; **4b,** 51364-61-5; **5a,** 51364-62-6; **5b,** 51364-63-7; **6a,** 51364-64-8; **6a** methiodide, 51364-65-9; **6b,** 51364-66-0; **6b** methiodide, 51364-67-1; **7a,** 51364-68-2; **7b,** 51364-69-3; **8a,** 51364-70-6; **8b,** 51364-71-7; **9a,** 18417-66-8; **9b,** 24995-59-3; **10b,** 51364-72-8; **11b,** 51364-73-9; methyl 3-hydroxycyclooctanecarboxylate tetrahydropyranyl ether, 51364-74-0; methyl 3-hydroxycyclodecanecarboxylate tetrahydropyranyl ether, 51364-75-1; spiro[2.7]decan-5-ol, 51364-76-2; spiro[2.9]dodecan-5-ol, 51364-77-3.

References and Notes

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Quantitative Conversion of Carboxylic Acids and Phenols to Esters and Ethers by Reaction of Their Salts with Alkyl Halides

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Recently we reported that carboxylic acids can be quantitatively converted to esters by reaction of their salts with alkyl bromides or iodides in hexamethylphosphoramide (HMPA) at room temperature.[1] We now wish to report results of further studies which extend the scope of this reaction. These include the rapid reaction of ethyl iodide with salts of hindered acids, the use of anhydrous potassium carbonate as base to prevent decarboxylation of certain acids, the use of geminal dihalides as the alkylating agent, and the quantitative O-alkylation of phenoxide ions.

Reaction of mesitoic acid and triethylacetic acid with sodium hydroxide (aqueous 25% NaOH) in HMPA followed by addition of ethyl iodide (4 equiv) gave the ethyl esters in quantitative yield. In each case the time required for alkylation was less than 5 min at room temperature. The short reaction time, simple procedure, and quantitative yield of this reaction make it a valuable method for preparing ethyl esters.[2] Other solvent systems such as dimethyl sulfoxide and dimethylformamide required the use of longer reaction times. Reaction of sodium triethylacetate with ethyl iodide at room temperature was only two-