Table I. ^{13}C Chemical Shifts of the Polycyclic Hydrocarbons 1–5

Registry no.	Compd	C_1	C_2	Others
280-33-1	1	24.0[a]	26.0[a]	
279-23-2	2	36.6[b]	30.0[b]	C_7 38.6[b]
285-86-9	3	39.5	26.3[c]	C_5 39.0[c]
277-10-1	4	47.3	47.3	
287-13-8	5	5.6	40.0	C_3 20.8
				C_4 21.3

[a]For literature values see ref 1. [b]For literature values see ref 2. [c]Shifts may be interchanged.

Table II. One-Bond ^{13}C–H Coupling Constants in the Polycyclic Hydrocarbons 1–5

Compd	$'J(^{13}C_1$–H)	% s character	$'J(^{13}C$–H) others	% s character
1	134.3	26.9	C_2 125.7	25.1
2	140.1[a,b]	28.0	C_2 130.3[b]	26.1
			C_7 131.3[b]	26.3
3	150.5	30.1	C_2 132.5[d]	26.5
			C_5 135.1[d]	27.0
4	153.8	30.8		
5	200.3[c]	40.0	C_2 154.2[c]	30.8
			C_3 126.2[c]	25.4
			C_4 126.2[c]	25.4

[a]For literature values see ref 3a. [b]For literature values see ref 3b. [c]For literature values see ref 4. [d]Coupling constants may be interchanged.

coupled spectra, and by relative intensities in the proton-decoupled spectra. Coupling constants of directly bonded ^{13}C–H are displayed in Table II. As expected there is a pronounced increase in the magnitude of the bridgehead carbon–proton coupling with increased strain at the bridgehead. Thus, the value of $'J(^{13}C_1$–H) in the relatively strain-free molecule, 1, is essentially identical with that in adamantane (133.5 Hz).[3a] On the other hand, the highly strained hydrocarbons such as cubane (4) and tricyclo[4.1.0.$0^{2,7}$]heptane (5) show markedly higher values. The calculated fractional s characters of the C–H bonds are also included in Table II. Clearly, in both 4 and 5, the bridgehead skeletal angles are substantially smaller than those in 1, resulting in an increase in the p character of the endocyclic hybrid orbitals of the bridgehead carbon atom with a corresponding increase in the s component of the exocyclic hybrid orbital.

Experimental Section

^{13}C NMR spectra were measured on a Bruker Scientific Inc. WH-270 Fourier transform NMR spectrometer operating at 67.89 MHz, or, in a few instances, on a WH-90 spectrometer operating at 22.625 MHz. Samples were ca. 3 M in deuteriochloroform with Me_4Si added as an internal reference. Chemical shifts are estimated to be accurate to ±0.1 ppm, and coupling constants to ±0.6 Hz. Bicyclo[2.2.2]octane, norbornane, and cubane were obtained from the corresponding bridgehead-substituted bromides by reaction with tributyltin hydride under ultraviolet irradiation as described.[8] Tricyclo[4.1.0.$0^{2,7}$]heptane was synthesized by the improved procedure reported by Gassman and Richmond.[9]

Bicyclo[2.1.1]hexane. Bicyclo[2.1.1]hexan-2-one[10] (1.0 g, 10.4 mmol) and *p*-toluenesulfonylhydrazine (2.4 g, 13.0 mmol) in ethanol (70 mL) were boiled under reflux for 20 h. The solution was cooled and the crystalline deposit was recrystallized from ethanol to give bicyclo[2.1.1]hexan-2-one *p*-toluenesulfonylhydrazone (1.9 g, 70%) as needles, mp 184–185 °C.

Anal. Calcd for $C_{13}H_{16}N_2O_2S$: C, 59.07; H, 6.10; N, 10.60; S, 12.13. Found: C, 59.35; H, 6.34; N, 10.57; S, 11.9.

The hydrazone (1.8 g, 6.8 mmol) was dissolved in 1:1 DMF/sulfolane (32 mL), heated to 110 °C, and then treated with three portions each containing sodium cyanoborohydride (1.7 g, 27.4 mmol) and *p*-toluenesulfonic acid (0.3 g) added every 3 h as outlined by Hutchins and co-workers.[11] The product which distilled and was collected in a cold trap (−40 °C) was shown (VPC) to be practically pure and was identified as bicyclo[2.1.1]hexane by comparison of its physical and spectral properties (MS, IR, NMR) with those of the authentic material

Acknowledgment. This work was supported in part by a grant made available by the Australian Research Grants Committee.

Registry No.—Bicyclo[2.1.1]hexan-2-one, 5164-64-7; *p*-toluenesulfonylhydrazine, 1576-35-8; bicyclo[2.1.1]hexan-2-one *p*-toluenesulfonylhydrazone, 62708-51-4.

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Synthesis of 4-Spiro[cyclopropanecholestan-3β-ol]

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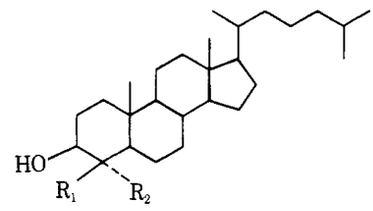
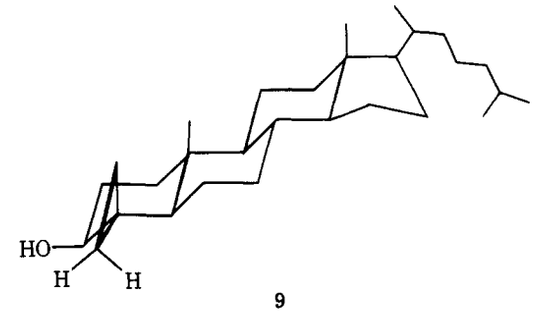
Previous studies of the interaction of rat liver enzyme preparations with cholestane derivatives having various substituents at C4 have indicated that there is a high degree of substrate specificity in the biological demethylations at that position during the conversion of lanosterol to cholesterol.[1–3] Specifically, steroids 1–5 are converted to cholestan-3β-ol by



1, R_1, R_2 = CH_3
2, R_1 = H; R_2 = CH_3
3, R_1 = CH_3; R_2 = CH_2OH
4, R_1 = CH_3; R_2 = CHO
5, R_1 = CH_3; R_2 = COOH
6, R_1 = CH_2OH; R_2 = CH_3
7, R_1 = CH_3; R_2 = CH_2CH_3
8, R_1 = CH_2CH_3; R_2 = CH_3

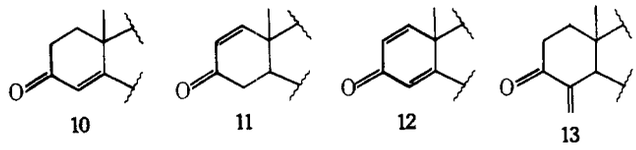


9

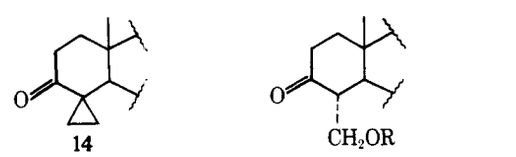
the same enzymes which convert lanosterol to cholesterol, whereas steroids **6–8** are unaffected by that enzyme system.[1-3] In order to probe further the geometric requirements of substrates for enzymic C4 oxidative demethylation, it was decided to study the spirocyclopropyl alcohol **9**. If **9** were unchanged by an active rat liver homogenate, it might suggest that the key initial biochemical hydroxylation of the 4α methyl group[1-4] occurs at a carbon–hydrogen bond with a geometry different from those depicted in **9**. This note describes the synthesis of **9**; the results of incubation of **9** will be reported subsequently.

Direct cyclopropanation by bisalkylation at C4 using a 1,2-dihaloethane seemed the simplest route to **9**, and such a reaction has been successfully performed on 17α-methyltestosterone.[5] However, attempts to effect cyclopropanation of cholest-4-en-3-one (**10**) using a variety of bases followed by 1,2-dibromoethane or 1,2-diiodoethane failed. Similar alkylations were also attempted on cholest-1-en-3-one[6] (**11**), which can form an enolate anion only at C4. Aside from recovered **11**, the only identified product obtained was a small amount of dienone **12**[7] from a reaction using 1,2-diiodoethane. Formation of **12** presumably occurred via iodination at C4 followed by elimination of hydrogen iodide. It is not clear why this precedented[5] method of cyclopropanation was unsuccessful in our hands.

Attention was then turned to the synthesis of **9** via 4-methylenecholestan-3-one (**13**). If **13** could be prepared, its reaction with a methylene transfer reagent, such as dimethylsulfoxonium methylide, would presumably produce spirocyclopropyl ketone **14**.[8] Hydride reduction would then be expected to afford **9** without difficulty. Synthesis of **13** was first attempted by application to **10** of the method of Stork and d'Angelo,[9] involving reaction of the trimethylsilyl enol ether of a kinetically generated C4 enolate anion with methyllithium followed by treatment with formaldehyde. If successful, this procedure would lead to **15**, which presumably would be easily convertible to **13**. Unfortunately, efforts to prepare trimethylsilyl enol ether **16** failed. The major product (48%) from treatment of **10** with lithium and ammonia, followed by trimethylsilyl chloride,[9] was the monotrimethylsilyl ether of **17**, a pinacol which is well known as the unwanted product of dissolving metal reduction of **10**.[10,11] Isolation of only the monoether is probably a consequence of steric hindrance to introduction of a second trimethylsilyl group.

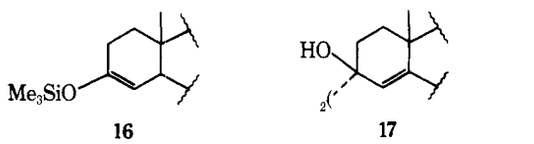


10 **11** **12** **13**



14

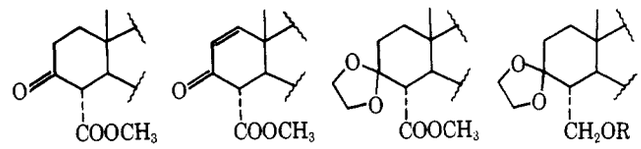
15, R = H
24, R = Ms



16 **17**

Hajos and co-workers have studied the synthesis of α-methylene ketones,[12] and essentially one of their methods was used in a successful preparation of **13**, starting with the familiar β-keto ester **18**.[1,10,13] Preparation of **18** by reductive carbomethoxylation of **10** is much less effective than preparation of other β-keto esters by this procedure, owing to formation of **17**,[10] so a more efficient route to **18** was sought. Carboxylation of enone **11** with methylmagnesium carbonate,[14,15] followed by treatment with diazomethane, afforded **19** in 82% yield, and hydrogenation of **19** to **18** was essentially quantitative. The overall yield of **18** from cholesterol by this route in six steps is ca. 45%, whereas the overall yield of **18** from cholesterol via **10** is only ca. 15%.

For the synthesis of **13**, **18** was converted in the usual manner in 77% yield to ketal **20**, which was then reduced with $LiAlH_4$ to afford 93% of **21**. Conversion of **21** to **13** was first accomplished by the reaction of acetate **22** with *p*-toluenesulfonic acid in benzene. However, treatment of mesylate **23** with dilute methanolic hydrochloric acid in methylene chloride, followed by heating of the resulting mixture (containing principally **13** and **24**) with 1,5-diazabycyclo[5.4.0]undec-5-ene (DBU) in toluene,[16] proved to be a more reliable synthesis of **13**, affording 59% overall yield from **21**. Enone **13** [ν 1690 cm^{-1}, λ_{max}(cyclohexane) 225 nm (ϵ 4000), and δ 5.0 and 5.8 ppm] tended to decompose on standing to an unidentified compound, mp 228–235 °C dec, so it was used soon after preparation.



18 **19** **20**

21, R = H
22, R = Ac
23, R = Ms

Dimethylsulfoxonium methylide[8] gave a complex mixture of products upon reaction with **13**. Effective cyclopropanation was achieved when **13** was treated with diazomethane in the presence of palladium acetate,[17] which afforded 70% of **14**, mp 100–101 °C, ν 1710 cm^{-1}. Reduction of **14** with either $LiAlH_4$ or $NaBH_4$ readily produced the desired 4-spiro[cyclopropanecholestan-3β-ol] (**9**), mp 173–174 °C. The 3β configuration was assigned to the hydroxyl group of **9** on the basis of the NMR signal of the 3αH[10] and the known stereochemistry of hydride reduction of other 4,4-disubstituted cholestan-3-ones.[10]

Experimental Section

Melting points were determined in open capillaries in a Thomas-Hoover apparatus and are uncorrected. Elemental analyses were performed by Spang Microanalytical Laboratory, Ann Arbor, Mich. Infrared (IR) spectra were recorded on a Perkin-Elmer Model 137 or 337 spectrometer. Unless otherwise specified, IR spectra were taken as KBr pellets. Ultraviolet (UV) spectra were recorded on a Unicam SP 800B spectrometer. Nuclear magnetic resonance (NMR) spectra were recorded on a Perkin-Elmer R-24 instrument, equipped with a spin-decoupler unit, using $CDCl_3$ as solvent unless otherwise noted. Tetramethylsilane was used as an internal standard. Mass spectra were determined by Dr. Catherine Costello at the MIT Mass Spectra Facility sponsored by the USPHS Division of Research Resources through Grant RR 00317. Preparative thin layer chromatography (TLC) was performed on 20 × 20 cm plates coated with 1.45-mm thick layers of silica gel $PF_{(254+366)}$ (Brinkmann Instruments Inc., Westbury, N.Y.) which had been mixed with 0.002% Rhodamine 6G dye (Eastman Kodak Co., Rochester, N.Y.). UV light was used to visualize TLC plates. Qualitative plates (0.25-mm thick layers of silica gel $PF_{(254+366)}$) were sprayed with a 5% methanol–water (70:30) solution of phosphomolybdic acid (Eastman Kodak) and heated briefly at 110 °C. Brine refers to saturated aqueous sodium chloride solution. Bicarbonate refers to saturated aqueous $NaHCO_3$ solution. The term "ether workup" refers to the following procedure: the material was dissolved in ~50 mL of ether which was washed twice with 25-mL portions of water. The combined aqueous layers were reextracted with 25 mL of ether. The combined ethereal layers were washed with 25 mL of water, dried ($MgSO_4$), and concentrated in vacuo.

Attempted Preparation of 4-Spiro[cyclopropanecholest-1-

en-3-one] by Bisalkylation of 11 with 1,2-Diiodoethane. Cholest-1-en-3-one (**11**) was prepared from 2α-bromocholestan-3-one essentially by the procedure of Green and Long[6] in 75% yield after recrystallization from ethanol as white needles: mp 96–97 °C (lit.[6] mp 98 °C); IR 1680 cm^{-1}; NMR δ 0.70 (s, 3, H_3C_{18}–), 0.81 (s, 3, H_3C_{19}–), 5.85 (d, 1, J = 8 Hz, HC_2=), and 7.1 ppm (d, 1, J = 8 Hz, HC_1=). 2α-Bromocholestan-3-one was prepared essentially by the procedure of Nace and Iacona,[18] except that the crude product was dissolved in benzene, washed twice with bicarbonate and twice with water, dried ($MgSO_4$), and evaporated to give a solid which was recrystallized from hexane to afford 80% of 2α-bromocholestan-3-one (free of cholestan-3-one by TLC) as fine needles, mp 171–173 °C (lit.[18] mp 174–174.5 °C).

Various combinations of bases (NaH, KH, NaO-*t*-Bu, KO-t-Bu, LICA) and solvents (Me_2SO, THF, DME, PhH, *t*-BuOH) were used with **11**, followed by either 1,2-dibromo- or 1,2-diiodoethane. In a representative experiment, an oven-dried flask was charged with 40 mL of dry DME, 1 drop of *t*-BuOH, and 0.150 g (0.40 mmol) of **11** under an N_2 atmosphere. This solution was brought to reflux and 0.050 g (1.0 mmol) of 50% NaH suspension in mineral oil was added. This mixture was allowed to reflux for 2 h, at which time 2 mL of DME containing 0.170 g (0.6 mmol) of 1,2-diiodoethane was added, and refluxing was continued for an additional 4 h. Ether workup gave 0.200 g of yellow oil. Preparative TLC (3:1 hexane–ether) gave 0.016 g of unidentified solid, 0.110 g (82%) of **11**, and 0.008 g (6%) of a more polar component, assigned structure **12**: mp 97–100 °C (lit.[7] mp 108–110 °C); IR 1690 cm^{-1}; NMR δ 0.71 (s, 3, H_3C_{18}–), 0.82 (s, 3, H_3C_{19}–), 6.2 (bs, HC_4= and HC_2=), 6.34 (d, $J \cong 2$ Hz, HC_2=), and 7.1 ppm (d, 1, J = 11 Hz, HC_1=), a pattern in the vinyl proton region of the spectrum characteristic of steroidal 1,4-dien-3-ones.[19]

Attempted Preparation of Trimethylsilyl Enol Ether 16. According to the procedure of Stork and d'Angelo,[9] 5.00 g (0.013 mol) of **10** afforded 5.502 g of orange oil. Chromatography on silica gel afforded 2.61 g (48%) of the monotrimethylsilyl ether of **17** as a yellow oil which cyrstallized on standing. Further elution gave 1.24 g of cholestan-3-one. The 2.61 g of the Me_3Si derivative of **17** was recrystallized, with difficulty, from pentane to give 1.76 g of white solid: mp 124–128 °C; further recrystallization from ether–methanol raised the mp to 128–134 °C; IR 3580 cm^{-1}; NMR (benzene-d_6) δ 0.20 [s, 9, $(CH_3)_3Si$–], 0.70 (s, 3, H_3C_{18}–), 3.78 (s, 1, HO–, exchangeable with D_2O), 5.48 (s, 1, HC_4=), and 5.58 ppm (s, 1, HC_4=).

Anal. Calcd for $C_{57}H_{98}O_2Si$: C, 81.17; H, 11.71. Found: C, 81.06; H, 11.74.

When 163 mg (0.193 mmol) of this substance dissolved in 50 mL of 1:1 ether–methanol was treated with 1 mL of 1 N NaOH solution for 1.5 h at room temperature, followed by an ether workup, there was obtained 160 mg of white solid, which was recrystallized from hexane to afford 137 mg (92%) of **17**, mp 208–211 °C dec, which was identical (TLC, IR, NMR, and mixture melting point) with an authentic sample of **17**.[10]

4α-Carbomethoxycholest-1-en-3-one (19). To a solution of 1.000 g (2.60 mmol) of **11** in 20 mL of DMF was added 30 mL (60 mmol) of freshly prepared methylmagnesium carbonate[14] in DMF, and the mixture was heated at 120 °C for 36 h under a slow stream of carbon dioxide. The resulting yellow solution was cooled to 5 °C, mixed with 100 mL of 10% sulfuric acid, and poured into 200 mL of ether. The aqueous layer was extracted with an additional 100 mL of ether. The combined organic layers were washed with water (2 × 100 mL), and then added dropwise to a freshly prepared ethereal diazomethane[20] solution. After 1 h, ether workup afforded 1.117 g of yellow solid. Preparative TLC (3:1 hexane–Et_2O, twice) afforded 0.147 g of **11** and 0.940 g (82%) of **19** as a white solid. Recrystallization from ether afforded 0.860 g (75%) of pure **19** as white flakes: mp 124–125 °C; IR 1735 and 1680 cm^{-1}; NMR δ 0.69 (s, 3, H_3C_{18}–), 3.38 (1, d, J = 12 Hz, HC_4), 3.79 (s, 3, H_3COOC–), 6.02 (1, d, J = 10 Hz, HC_2=), and 7.25 ppm (1, d, J = 10 Hz, HC_1=); M^+ m/e 442.3449 (calcd for $C_{29}H_{46}O_3$, 442.3447).

Preparation of 4α-Carbomethoxycholestan-3-one (18) by Hydrogenation of 19. A solution of 1.672 g (3.78 mmol) of **19** in 200 mL of cyclohexane and 50 mL of THF was hydrogenated over 250 mg of 10% palladium on carbon for 45 min. Removal of the catalyst by filtration and concentration in vacuo afforded 1.669 g (99%) of solid **18**. Recrystallization from ether afforded 1.525 g (91%) of **18** as white prisms: mp 171–172 °C (lit.[13] mp 171–172 °C); IR 1740 and 1710 cm^{-1}; NMR δ 0.67 (s, 3, H_3C_{18}–), 1.03 (s, 3, H_3C_{19}–), 3.23 (d, J = 12 Hz, 1, HC_4–), and 3.73 ppm (s, 3, H_3COOC–).

4α-Carbomethoxycholestan-3-one Ethylene Ketal (20). A solution of 300 mg (0.69 mmol) of **18** in 40 mL of benzene containing 0.02 mL (3.23 mmol) of ethylene glycol and one small crystal of *p*-toluenesulfonic acid was refluxed for 12 h with azeotropic removal of water. The solution was cooled, washed with 50 mL of bicarbonate and 50 mL of water, dried ($MgSO_4$), and concentrated in vacuo to give 325 mg of yellow solid. Preparative TLC (1:1 hexane–Et_2O) afforded 310 mg (94%) of **20** as a white solid which was recrystallized from ether to give 252 mg (77%) of pure **20**: mp 195–196 °C; IR 1720 cm^{-1}; NMR δ 0.78 (s, 3, H_3C_{18}–), 2.80 (d, 1, J = 12 Hz, HC_4–), 3.70 (s, 3, H_3COOC–), and 3.95 ppm (bs, 4, $-OCH_2CH_2O$–); M^+ m/e 488.3866 (calcd for $C_{31}H_{52}O_4$, 488.3880).

4α-Hydroxymethylcholestan-3-one Ethylene Ketal (21). To a solution of 125 mg (0.26 mmol) of **20** in 20 mL of ether was added 100 mg of $LiAlH_4$. This mixture was allowed to stir for 10 h. An ether workup using bicarbonate for all aqueous washings afforded 120 mg of white solid. Preparative TLC (ether) gave 110 mg (93%) of **21**, which was recrystallized from ether to afford 101 mg (86%) of **21** as white prisms: mp 182–184 °C; IR 3600 cm^{-1}; NMR δ 0.68 (s, 3, H_3C_{18}–), 0.85 (s, 3, H_3C_{19}–), and 3.95–3.80 (6, bs and m, $-OCH_2CH_2O$– and 4α-CH_2O–); M^+ m/e 460.3966 (calcd for $C_{30}H_{52}O_3$, 460.3916).

Acetate (22) of 4α-Hydroxymethylcholestan-3-one Ethylene Ketal. A solution of 100 mg (0.216 mmol) of **21** and 100 mg (0.98 mmol) of freshly distilled acetic anhydride in 3 mL of pyridine was stirred at room temperature for 5 h. An ether workup afforded 112 mg of solid which was purified by preparative TLC (3:2 ether–hexane) to afford 104 mg (95%) of **22**. Recrystallization from hexane–ether afforded 91 mg (84%) of pure **22** as white plates: mp 177–179 °C; IR 1740 cm^{-1}; NMR δ 0.67 (s, 3, H_3C_{18}–), 2.00 (s, 3, H_3COO–), 3.94 (bs, 4, $-OCH_2CH_2O$–), and 4.13 ppm (d, 2, 4α-CH_2O–); M^+ m/e 502.4022 (calcd for $C_{32}H_{54}O_4$, 502.4022).

Mesylate (23) of 4α-Hydroxymethylcholestan-3-one Ethylene Ketal. According to the procedure of Crossland and Servis,[21] a mixture of 100 mL of methylene chloride, 1.746 g (3.79 mmol) of **21**, and 0.500 g (4.95 mmol) of triethylamine was cooled to 0 °C. Freshly distilled methanesulfonyl chloride (0.500 g, 4.35 mmol) was added and the solution was allowed to warm to room temperature and stirred for an additional 1 h. An ether workup using bicarbonate for the aqueous washings afforded 2.005 g (98%) of a white solid, which was homogeneous by TLC. Attempted recrystallization of this material from isopropyl alcohol–chloroform gave a gel, which after collection by filtration and drying in vacuo afforded 1.716 g (84%) of white, chalky solid **23**: mp 143–146 °C dec; IR 1340 and 1160 cm^{-1}; NMR δ 0.64 (s, 3, H_3C_{18}–), 2.98 (s, 3, H_3CSO_3–), 3.98 (bs, 4, $-OCH_2CH_2O$–), and 4.31 ppm (m, 2, 4α-CH_2O–); M^+ m/e 443.3780 (calcd for $C_{30}H_{50}O_2$ = **23** − CH_3SO_3H, 443.3810).

4-Methylenecholestan-3-one (13). To a solution of 0.360 g (0.67 mmol) of **23** in 50 mL of methylene chloride was added 20 mL of a mixture of 25 mL of MeOH and 5 mL of concentrated HCl and then 5 mL of methanol to restore homogeneity. This mixture was stirred for 16 h at room temperature and then concentrated in vacuo. The residue was mixed with 50 mL of ether and 25 mL of water and the aqueous layer was made basic by slow addition of solid sodium bicarbonate. Ether workup afforded 0.295 g of oil, which was dissolved in 20 mL of toluene containing 1 mL of DBU[22] and refluxed for 24 h. An ether workup gave 0.223 g of solid which was purified by preparative TLC (3:1 hexane–ether) to afford 0.210 g (78%) of **13** and 0.002 g of 4-methylcholest-4-en-3-one (TLC mobility in several solvent systems identical with that of an authentic sample[23]). Recrystallization of the **13** from 9:1 95% ethanol–methanol gave 0.186 g (70%) of pure **13** as white prisms: mp 99–100 °C; IR 1690 cm^{-1}; NMR δ 0.65 (s, 3, H_3C_{18}–), 5.00 (bs, 1 HC=), and 5.80 ppm (bs, 1, HC=); UV λ_{max} (cyclohexane) 225 nm (ε 4000); M^+ m/e 398.3568 (calcd for $C_{28}H_{46}O$, 398.3549).

When the crude product before treatment with DBU from a comparable experiment was purified by preparative TLC (3:1 hexane–ether) there was obtained 55% of **13**, 3% of 4-methylcholest-4-en-3-one, and 41% of **24**: mp 110–115 °C; IR 1710 cm^{-1}; NMR δ 0.65 (s, 3, H_3C_{18}–), 0.80 (s, 3, H_3C_{19}–), 3.30 (s, 3, H_3CSO_3–), and 3.65 ppm (bt, 2, 4α-CH_2O–).

4-Spiro[cyclopropanecholestan-3-one] (14). According to the procedure of Mende et al.,[17] an excess (8 mmol) of freshly prepared ethereal diazomethane[20] was added dropwise to a mixture of 240 mg (0.61 mmol) of **13**, 25 mg (1.5 mmol) of $Pd(OAc)_2$,[24] and 50 mL of ether cooled to 0 °C. The resulting mixture was stirred for 1 h at room temperature. The black solid was removed by filtration and the yellow solution was concentrated in vacuo to afford 281 mg of yellow oil. Preparative TLC (5:1 hexane–ether) afforded 192 mg (78%) of **14**, which had the same R_f as **13**. Recyrstallization from methanol gave 174 mg (70%) of pure **14** as white plates: mp 100–101 °C; IR 1710 cm^{-1}; NMR δ 0.68 (s, 3, H_3C_{18}–) and 0.81 ppm (s, 3, H_3C_{19}–); M^+ m/e 412.3738 (calcd for $C_{29}H_{48}O$, 412.3705).

Anal. Calcd for $C_{29}H_{48}O$: C, 84.40; H, 11.72. Found: C, 84.53; H, 11.59.

4-Spiro[cyclopropanecholestan-3β-ol] (9). A solution of 51 mg (0.12 mmol) of **14** and 25 mg (0.68 mmol) of $NaBH_4$ in 25 mL of methanol was stirred at room temperature for 1 h. Concentration in vacuo and an ether workup afforded 50 mg of white solid. Preparative TLC (2:1 hexane–ether) gave 48 mg (94%) of **9** and recrystallization from methanol gave 39 mg (76%) of pure **9** as silky needles: mp 173–174 °C; IR 3400 cm^{-1}; NMR δ 0.68 (s, 3, H_3C_{18}–), 0.84 (s, 3, H_3C_{19}–), and 3.5–3.9 ppm (bm, $3\alpha H^{25}$); M^+ *m/e* 414.3955 (calcd for $C_{29}H_{50}O$, 414.3861).

Anal. Calcd for $C_{29}H_{50}O$: C, 83.99; H, 12.15. Found: C, 84.08; H, 12.10.

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Registry No.—**9**, 62742-97-6; **10**, 601-57-0; **11**, 601-55-8; **12**, 566-91-6; **13**, 62742-98-7; **14**, 62742-99-8; **17** Me_3Si ether, 62743-00-4; **18**, 38367-88-3; **19**, 62743-01-5; **20**, 62743-02-6; **21**, 62743-03-7; **22**, 62743-04-8; **23**, 62743-05-9; **24**, 62743-06-0; ethylene glycol, 107-21-1.

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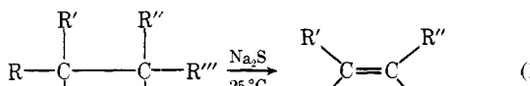
Communications

The Synthesis of Functionalized Tetrasubstituted Olefins. Calcium Amalgam—a Novel Reducing Agent

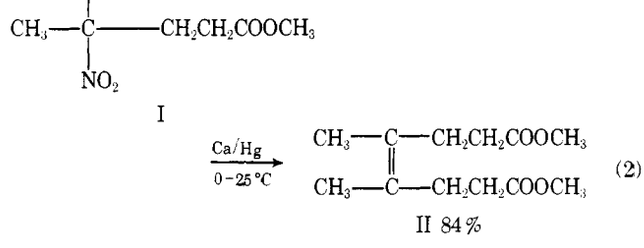
Summary: A general synthesis of symmetrical and unsymmetrical functionalized tetrasubstituted olefins is described.

Sir: In 1971 a synthesis of tetrasubstituted olefins was described which is noteworthy for its simplicity and which gives pure symmetrical and unsymmetrical olefins in high yields.[1] Since then several other very useful procedures for the synthesis of tetrasubstituted olefins have been reported.[2-7] However, except for two methyl ethers, none of the olefins prepared by these procedures contains a functional group. We now describe a simple method for the synthesis of symmetrical and unsymmetrical tetrasubstituted olefins bearing cyano, keto, ester, and ether groups. A further point of interest is the use of a novel reducing agent—calcium amalgam.

In our earlier olefin synthesis[1] vicinal dinitro compounds were treated with sodium sulfide (or sodium thiophenoxide), eq 1. Attempts to extend the reaction of eq 1 to the synthesis of functionalized olefins soon revealed that neither sodium sulfide, nor sodium thiophenoxide, was likely to prove satisfactory.[8] In contrast, amalgamated calcium, which is readily available and inexpensive,[9] is effective in bringing about elimination of vicinal nitro groups without attacking other functions. Equation 2 is illustrative.



(1)



(2)

Table I lists the olefins obtained from vicinal dinitro compounds by the action of calcium amalgam. It should be noted that yields refer to pure, isolated, products which, when the possibility exists, contain both the cis and trans forms. Also, the yields of unsymmetrical olefins are lower than for the symmetrical compounds because the unsymmetrical dinitro compounds employed were not fully purified.

The general procedure is illustrated by the preparation of nitro ester (I) and its conversion to the olefin (II). Lithium methoxide (1.52 g, 40 mmol) in 40 mL of DMF is allowed to