tilled to yield 2.50 g of a crude yellow solid [95–100° (0.4 mm)], which was further purified by sublimation at atmospheric pressure to afford 1.70 g of product: mp 176–179°; nmr (CCl_4) indicated that the deuterium was located at the C-9 methyl;[15] a mass spectrum showed 11% d_0, 79% d_1, and 10% d_2.

9-Deuterio-10-isobornyl Sultone (1-9-d_1).—9-Deuterio-10-camphorsulfonic acid (9-9-d_1) was prepared in 51% yield according to the procedure of Bartlett and Knox.[16] The sulfonic acid 9-9-d_1 was reduced with sodium borohydride and cyclized with *p*-tolylsulfonyl chloride in pyridine according to our procedure reported earlier in this paper. The desired sultone 1-9-d_1 was contaminated with a small amount (*ca.* 5%) of ethyl tosylate (EtOTs). This mixture was repeatedly washed with hot hexane. The hexane solution was concentrated to afford 0.2 g of 1-9-d_1, still containing *ca.* 2% EtOTs. Its nmr spectrum (CCl_4) showed δ 4.30 (d of d, 1, J = 4 and 7 Hz, HCO), 3.12 (s, 2, $-CH_2SO_2-$), 1.2–2.5 (m, 6, ring protons), 1.11 (s, 3, syn-CH_3), and 0.95 (m, 2, anti-CH_2D).

***exo*-Camphene Sultones (2a and 2b).**—9-Deuterio-10-isobornyl sultone (1-9-d_1) (0.1 g), containing *ca.* 2% EtOTs, was warmed at 140° for 20 min and sublimed (0.4 mm) to afford *ca.* 50 mg of a mushy solid: ir (CCl_4) 1330, 1280, 868 cm^{-1}; nmr (CCl_4) δ 7.21–7.7 (m), 4.08 (q, J = 7 Hz), 3.36 and 2.80 (neq J = 14 Hz), 3.00 (s), 1.50 (s), 1.28 (m). The ratio of exo isomer to endo isomer and to EtOTs in this mixture was 47:35:18, as ascertained by integration of the $-CH_2SO_2-$ resonances of exo sultone (2-d_1) (δ 3.00), the endo sultone (3-d_1) (δ 3.36 and 2.80), and the $-CH_2O$ resonance of EtOTs (δ 4.08). The methyl signal of the sultone 2-d_1 at δ 1.28 was masked by the triplet methyl signal of EtOTs at δ 1.29. A mixture of sultones **2** and **3** and EtOTs in a ratio of 47:34:19 was prepared; the nmr (CCl_4) of this mixture was identical with the deuterated mixture. The integration ratio of the two methyl signal at δ 1.50 and 1.28 (39:27) was also identical with the methyl signal ratio of the deuterated mixture.

An nmr spectrum of a small amount of material which was not sublimed in the above procedure was identical with the nmr spectrum of nondeuterared *exo*-camphene sultone; the impurities of sultone **3** and ethyl tosylate were apparently sublimed out. The great similarity of what is supposed to be deuterated **2** with nondeuterated **2** adds additional support for the deuterium label being spread equally between the two methyl groups. (A content of 40% deuterium in one of three hydrogens of a methyl group may not significantly change the shape of the signal.)

Solution Rearrangement of 10-Isobornyl-3,3-d_2 Sultone.—A solution of 4.0 g of 10-isobornyl-3,3-d_2 sultone (1-3,3-d_2) in approximately 25 ml of *n*-octane was refluxed for 3 hr. The hot octane solution was decanted from the black residue and cooled to give 0.7 g of colorless crystals of *exo*-camphene sultone (2-d_2). A comparison of the integrated areas of **2** with 2-d_2 showed that the latter compound had the following nmr spectrum: δ (CCl_4) 3.00 (s, 2.0, $-CH_2SO_2-$), 1.9–2.4 (m, 2.5, probably C-1, C-4, and syn-C-7 protons), and 1.2–1.7 (m with 2 s at 1.28 and 1.50, 9.5, remaining ring hydrogens and 2 methyls); mass spectrum (70 eV) *m/e* (rel intensity) 39 (19), 41 (25), 42 (18), 43 (100), 44 (17), 67 (31), 68 (41), 69 (50), 84 (25), 85 (16), 111 (27), 148 (29), and 149 (19). The octane filtrate was added to the black residue and evaporated. The resulting residue was extracted several times with hot hexane and cooled to give an additional 1.5 g (55% overall isolated yield) of solid which had the same spectral characteristics as those described above.

Using previously described procedures,[3] the deuterated *exo*-camphene sultone was converted to the deuterated keto sulfone **23**-d_2. A comparison of the nmr spectrum of **23** and **23**-d_2 gave the following results for **23**-d_2: nmr (CCl_4) δ 7.93 (m, 2.00, *o*-H of Ph), 7.57 (m, 3.00, *m*- and *p*-H of Ph), 3.33 (m, 0.96, syn-7 proton), 3.00 (s, 2.00, $-CH_2SO_2-$), 2.50 (m, 0.59, C-1 proton), 1.35–2.18 (m, 4.43, anti-7, C-4, 5 and 6 protons), and 1.30 (s, 3.00, CH_3).

Neat Rearrangement of 10-Isobornyl-3,3-d_2 Sultone.—In a 50-ml round-bottom flask under a N_2 atmosphere 1 g of 10-isobornyl-3,3-d_2 sultone (1-3,3-d_2) was heated at 150° for 30 min. It took about 2 min for the solid to melt and another 2 min for it to turn brown. The dark-colored solid was recrystallized twice from hexane to give 0.44 g of colorless solid, mp 131–133°. The nmr and mass spectra were similar to the other sample of 2-d_2 prepared above. This sultone was converted to the keto sulfone **23**-d_2, which showed an nmr spectrum very similar to the other sample of **23**-d_2 prepared above except that the δ 3.33 and 2.50 multiplets integrated for 0.8 and 0.7 protons, respectively.

Registry No.—**1**, 41348-33-8; 1-9-d_1, 41348-34-9; 1-3,3-d_2, 41348-35-0; 2-d_2, 41348-30-5; **2a**, 41348-36-1; **2b**, 41348-37-2; 3-d_1, 41348-31-6; **9**, 3144-16-9; 9-9-d_1, 41348-39-4; 9-3,3-d_2, 41348-40-7; **10**, 41348-41-8; 10-3,3-d_2, 41348-42-9; 12-9-d_1, 41348-43-0; **13**, 41348-44-1; **14**, 10293-10-4; **15**, 10293-09-1; **23**-d_2, 41348-32-7; **24**, 41348-47-4; **29**, 41523-55-1.

Carbon-13 Nuclear Magnetic Resonance Spectra of Keto Steroids

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Fourier transform C-13 nuclear magnetic resonance spectra have been obtained and assigned for a complete series of keto steroids—the steroid skeletons being those of androstane and cholestane. The assignments were performed by comparing the spectra of these closely related compounds and correlating the shifts due to differences in structure, and by use of off-resonance decoupled spectra. Furthermore, the spectra of a series of specific deuterium-labeled analogs have been obtained for assignment purposes. The assignments show strong internal consistency. It is shown that previous assignments to C-12 and C-16 in these systems is erroneous. The effects of deuterium substitution in the steroid system are described, and the observed deuterium isotope shifts are presented.

While it is now possible to obtain high-resolution carbon-13 nuclear magnetic resonance (cmr) spectra of larger molecules such as steroids within a reasonably short time using pulsed Fourier transform technique, the task of assigning the spectra even of known steroids is still far from routine; day-to-day use of cmr with the purpose of structure elucidation in the steroid field is therefore not yet possible, even though it is quite apparent that cmr spectroscopy has great potential in this respect, as illustrated by the cmr spectra of some 30 steroids investigated by Roberts, *et al.*[2] A few other investigations have dealt with cmr of steroids,[3–6] but a considerable amount of well-documented (empirical) correlations of chemical shifts are needed before it is possible to predict the cmr spectrum of a given ste-

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TABLE I

C-13 CHEMICAL SHIFTS IN 5α-KETO STEROIDS[a]

Steroid	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27
Androstane (A)	38.8	22.3	26.9	29.2	47.1	29.2	32.6[b]	36.0[c]	55.1[b]	36.4	20.9[c]	39.0[b]	40.8[c]	54.7	25.5	20.5[c]	40.5[b]	17.6	12.3								
Cholestane (B)	38.8	22.3	26.9[b]	29.2[c]	47.1	29.2	32.2	35.6	54.9	36.3	20.9	40.2	42.6	56.7	24.2	28.3	56.4	12.2	12.2	35.9	18.7	36.3	24.0	39.6	28.0	22.5	22.8
1-Androstanone (C)	215.8	38.3	28.0	28.0	49.8[b]	28.0	31.5[b]	36.2[c]	47.2	52.0	22.7	38.8	41.0	54.4	25.5	20.4	40.4	17.8	12.3								
2-Cholestanone (D)	54.1[b]	211.7	41.4[b]	28.3[c]	45.4	29.3	31.8	35.0	54.1	40.6[c]	21.0	39.9	42.6	56.4	24.3	28.3	56.4	12.1	12.6	35.8	18.7	36.2	23.9	39.6	28.1	22.5	22.8
3-Androstanone (E)	38.7[c]	38.1[b]	211.0	44.6[b]	46.7	29.0	32.1	35.7	54.1	35.7	21.5	38.8	40.8	54.3	25.5[c]	20.5[b]	40.3[b]	17.5	11.4	35.7	18.7	36.1	23.8	39.5	28.0	22.5	22.8
3-Cholestanone (F)	38.5	38.1	211.2	44.6	46.7	29.0	31.7	35.6	53.8	35.4	21.4	39.9	42.5	56.2	24.2	28.2	56.2	12.1	11.4	35.7	18.7	36.1	23.8	39.5	28.0	22.5	22.8
4-Androstanone (G)	37.8[c]	20.5[b]	41.2[b,c]	212.6	59.3[c]	22.7[b,c]	30.9[b,c]	35.5[c]	54.5	42.6	21.8	38.9	40.8	54.8	25.5	20.5	40.4	17.6	13.8								
4-Cholestanone (H)	37.6	20.5	41.2	212.6	59.2	22.7	30.5	35.1	54.5	42.5	21.7	40.0	42.5	56.3	24.1	28.2	56.3	12.1	13.8	35.8	18.7	36.2	23.9	39.5	28.0	22.7	22.7
6-Androstanone (I)	38.3*	21.5	25.3	20.4	58.8	211.8	47.1	38.3	55.1*	41.8	21.2	38.5*	41.2	54.7*	25.3	20.5	40.2	17.5	13.1								
7-Cholestanone (J)	38.9*	21.8	26.5	29.2	49.1[c]	46.6[b]	211.3	50.1[b]	49.1	36.7	21.3	38.3*	42.5	55.1	25.0	28.5	56.2	12.1	11.6	35.7	18.8	36.2	23.8	39.5	28.0	22.5	22.8
11-Androstanone (K)	37.8	21.9	26.8	28.6*	46.9	28.5*	33.2	37.4	64.9[b]	36.0[c]	210.7	56.9[b]	44.9	54.2	24.9	20.9	39.3	18.2	12.1								
12-Androstanone (L)	38.3	21.9	26.6	28.8	47.0	28.8	31.7	35.0	56.5[c]	36.9	37.5[b]	215.3	54.9	54.6	24.8	19.5	31.9	17.7	11.9								
15-Androstanone (M)	38.7	22.2	26.8	29.0*	47.3	28.6*	30.8	32.5	55.0	36.5	20.4	39.4	39.2	63.4	216.1	35.1*	35.4*	18.3	12.2								
15-Cholestanone (N)	38.7	22.2	26.8	29.0*	47.2	28.7*	30.9	32.1	54.5	36.4	20.5	40.1	42.4	66.1	215.6	42.0	51.7	13.1	12.2	35.4	19.1	36.1	23.9	39.4	28.0	22.5	22.8
16-Androstanone (O)	38.4	22.1	26.8	29.0*	47.0	28.8*	32.4	35.0	54.7	36.5	20.4	38.4	39.2	51.9	39.3[b]	218.3	55.9[b]	18.1	12.3								
17-Androstanone (P)	38.6	22.1	26.7	29.0	47.0	28.8	31.7	35.1	54.9	36.4	20.1	31.0	47.7	51.6	21.7[c]	35.7[b]	220.4	13.8	12.2								

[a] In parts per million relative to TMS. Assignment of chemical shifts for close-lying peaks marked with an asterisk may be reversed. [b] Deuteration at this position causes the peak to "disappear." [c] Isotope shift observed upon deuteration at a neighboring carbon atom.

roidal structure, a necessary prerequisite before applying cmr spectroscopy to routine structural elucidation. This has led us to undertake a systematic investigation of the cmr spectra of steroids, and in this paper we describe the results obtained for steroidal ketones.

Experimental Section

The Fourier transform cmr spectra were recorded using a Varian XL-100-15 spectrometer operating at 25.2 MHz, equipped for pulsed Fourier transformation. The instrument was controlled *via* a Varian 620i computer.

Spectra were obtained in $CDCl_3$ solution with internal TMS as standard. Field frequency lock was established *via* the deuterium resonance of the solvent. Sample concentrations varied from 0.1 to 1.0 *M* solutions. To examine the influence of concentration on chemical shifts, the cmr spectra of 1.0, 0.5, and 0.25 *M* solutions of 7-cholestanone were recorded. The shieldings of all carbons, except the carbonyl carbon, remained within the limits of the experimental reproducibility (less than 0.1 ppm). The chemical shift of the carbonyl carbon exhibited a small but significant concentration dependence, becoming 0.2 ppm more deshielded for each 1:1 dilution. Probe temperature for all experiments was *ca.* 30°.

The steroids used in this investigation were all prepared in this laboratory by already published methods. Most of the labeled compounds studied have been described previously (see Table II). Compounds **7**, **8**, **12**, and **14**–**16** were prepared by base-catalyzed exchange of enolizable hydrogen atoms with MeOD/MeO$^-$ or MeOD/OD$^-$.[7] **2** was prepared by reduction of 17-androstanone to 17-d_1-17-androstanol with lithium aluminum deuteride, conversion to the *N*,*N*,*N*′,*N*′-tetramethylphosphorodiamidate, and reduction of this as given by Ireland, *et al.*[8] Compound **4** was similarly prepared by lithium aluminum hydride reduction of **13** followed by reduction *via* the phosphate.[8,9]

Results

The compounds examined together with their C-13 chemical shift data are presented in Table I, while Table II lists the specific deuterium-labeled steroids for

TABLE II

DEUTERIUM-LABELED STEROIDS EXAMINED

Compd no.	Compd
1	7β-d_1-Androstane[a]
2	17-d_1-Androstane
3	3α-d_1-Cholestane[a]
4	9α,12α-d_2-Androstane
5	5α-d_1-1-Androstanone[b]
6	7-d_1-1-Androstanone[b]
7	1,1,3,3-d_4-2-Cholestanone
8	2,2,4,4-d_4-3-Androstanone
9	16,16-d_2-3-Androstanone[c]
10	2,2,6,6-d_4-4-Androstanone[d]
11	3,3,7,7-d_4-4-Androstanone[d]
12	6,6,8-d_3-7-Cholestanone
13	9α,12α-d_2-11-Androstanone[e]
14	11,11-d_2-12-Androstanone
15	17,17,15,15-d_4-16-Androstanone
16	16,16-d_2-17-Androstanone

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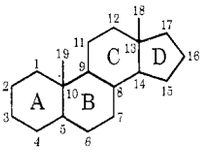
which supporting cmr data have been obtained. In some cases changes in the chemical shifts caused by deuterium substitution were measured; these are discussed below.

Cmr spectra have previously[2] been reported for two of the compounds in Table I, cholestane and 3-cholestanone. The chemical shifts reported earlier differ somewhat from ours, which are all displaced 0.1–0.7 ppm toward lower field, except for the carbonyl carbon in 3-cholestanone, which is 1.8 ppm more shielded. These differences are probably caused by the difference in solvent employed (dioxane–chloroform *vs.* chloroform) and the different instrumentation used.

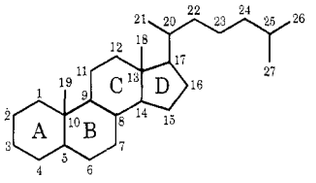
Androstane and Cholestane.—Since androstane and cholestane (Chart I) are the parent hydrocarbons of the

CHART I

STRUCTURES OF THE STEROID SKELETONS EMPLOYED, WITH THE STANDARD NUMBERING SYSTEM



androstane



cholestane

steroids studied in the present investigation, we found it important to establish the assignments of the cmr spectra of those compounds with a great deal of certainty. For androstane, the assignment was greatly facilitated by comparison with the off-resonance decoupled spectrum and with spectra of specifically labeled analogs (see Table II). By substitution of hydrogen by deuterium the intensity of the cmr signal for the carbon bearing the deuterium decreases dramatically.[2,10] This is a consequence of a combination of quadrupolar broadening, spin–spin coupling, and a decrease in the nuclear Overhauser enhancement. As a result the signals for deuterated carbon atoms have a very low intensity; this is the case even for carbon atoms not fully deuterated (see below).

The chemical shift values of the carbons C-1–C-10 and C-19 in androstane are expected to be nearly identical with those of cholestane, which have previously[2] been assigned, and a 1:1 correspondence is also found. These assignments are all in accordance with the off-resonance decoupled spectra and with the cmr data for the deuterated compounds **3**, **1**, and **4**, which allow unambiguous identification of the peaks due to C-3, C-7, and C-9. Furthermore, the isotope shifts often observed at carbons next to a deuterated carbon (see below) also corroborate this assignment. Of the remaining eight peaks in the androstane spectrum, one peak becomes a singlet (C-13), one a doublet (C-14), and one a quartet (C-18) in the off-resonance decoupled spectrum; the last five all become triplets. Among these, the peaks corresponding to C-12, C-16, and C-17 were identified from the spectra of the deuterated compounds **4**, **9**, and **2**. The C-11 position was distinguished from C-15 by comparison with the spectra of 1- and 16-androstanone. The peak assigned to C-11 is virtually unshifted in the spectrum of the 16-keto derivative, but shifts in the spectrum of 1-androstanone, whereas the position of the other peak remains unchanged by introduction of a keto group in the 1 position and changes when the keto group is in the 16 position; the latter is consequently assigned to C-15. The small isotope shift for C-11 observed in *9α,12α-d*$_2$-androstane confirms this assignment.

A comparison of the chemical shifts for the carbon atoms in rings C and D in androstane with those given[2] for cholestane appears to yield some very unusual substituent parameters for introduction of the C-17 side chain. Position 12, which is a γ carbon atom in relation to the 17-alkyl substituent, apparently shifts by -10.7 ppm, and C-16, which is β to the substituent, shifts by -19.7 ppm. Since the chemical shifts of these two atoms in the androstane spectrum have been unequivocally determined by the labeling data, we have reexamined the spectrum of cholestane. It appears that, if the previous[2] assignments for C-12 and C-16 are reversed, more reasonable (from the viewpoint of chemical shift theory) substituent values appear: $+1.2$ ppm for C-12 and $+7.8$ ppm for C-16. This (reversed) assignment for C-12 and C-16 (C-12, 40.2 ppm, and C-16, 28.3 ppm; *cf.* Table I) in cholestane is supported by several observations. For example, the spectrum of 15-cholestanone still retains the peak at 40 ppm while there is one less around 28 ppm, compared to the spectrum of cholestane. Furthermore, the chemical shift value for C-12 is expected to be close to the value for C-1 (which is found to be around 39 ppm), as C-1 and C-12 have very similar geometrical environments; likewise the chemical shift for C-16 should not be far from that of C-15. The argumentation given by Roberts, *et al.*,[2] in support of their assignment of C-12 and C-16 deals with steroids having keto or hydroxyl groups in the 17 position, and the assignments for C-12 and C-16 in those compounds agree very well with the results found in our work. Apparently, the chemical shift values for C-16 (36 ppm) and C-12 (31 ppm) observed in the spectra of 17-keto steroids have been the reason for the assignment of these two carbon resonances in the cholestanes examined, but a detailed argumentation was not given. Furthermore, the suggested assignment requires that the difference in substituent parameters for the side chain and a keto group be small in contrast to previous results.[11–13] We have found, however, that introduction of a keto group in the steroid skeleton shifts a CH_2 β carbon atom about 15 ppm downfield and that a CH_2 γ carbon atom eclipsed to the keto group, as C-12 is to a 17-keto group, is shifted 6–10 ppm upfield, in agreement with the results of Weigert and Roberts[11] for cycloalkanones. These substituent parameters, together with usual[12,13] values for alkyl substitution, provide further evidence for the reversed assignment for C-12 and C-16. The

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reassigned cholestane spectrum has been used as reference for the cholestanones included in Table I. It should be noted that the earlier assignment for C-12 and C-16 in cholestanes has been used in other cmr work on steroids.[3,4,6,14]

Keto Steroids.—The assignment of chemical shift values to specific carbon atoms, as given in Table I, has been based on considerations given below.

In general, we have found that the effect of an oxo group in the steroid skeleton is limited to the chemical shifts of the α, β, γ, and δ carbon atoms (α being the carbonyl carbon), while the rest of the carbon atoms were found to give rise to resonances in essentially the same positions as in the corresponding hydrocarbon. The assignment of carbons remote from the carbonyl group to specific resonances is hence straightforward. Likewise, where labeled analogs were available (see Table II), the assignment of the labeled carbon atoms presents no problem. In many cases shielding effects are observed at carbon atoms that are neighbors to the labeled site (see footnotes to Table I); this effect has been utilized whenever present for assignment purposes.

The carbonyl carbon resonances are unequivocally identified, as they always appear in the lowest field region of the cmr spectra.[15]

Several alkyl-substituted cyclohexanones and cyclopentanones have been examined by Weigert and Roberts.[11] They report that the substituent parameters for the oxo group in these systems range from +11 to +18 ppm for β carbon atoms and from −3 to +3 ppm for γ and δ carbon atoms, except in one case, where a γ-carbon atom is eclipsed to the keto group, in which case a shift of −9 ppm was found. For a number of the steroids, substituent parameters could be extracted directly from the cmr spectra of deuterated analogs and were found to agree well with those found[11] for the simpler systems. These parameters were then used as rough guidelines for assignments in the remaining compounds.

Comparison of the spectra of closely related compounds, *e.g.*, androstanones and cholestanones, with the carbonyl group at the same position, together with data from off-resonance decoupled spectra, data from spectra of labeled compounds, and simple chemical shift considerations, was sufficient to allow complete assignment in all but a few cases. 11-Androstanone is such a case, where differentiation between C-1 and C-17 is not immediately possible. To clarify this point the cmr spectrum of 3β-hydroxy-11-androstanone was obtained, and the unshifted one of the two peaks in question was assigned to C-17. Likewise, in the spectrum of 12-androstanone distinction between the C-9 and C-14 and the C-7 and C-17 resonances was not obvious. A comparison with the spectrum of 5α,12-pregnanone allows the assignment to be made, since only C-14 and C-17 are expected to shift significantly as a result of introduction of the C-17 side chain. Differentiation between close-lying peaks is not always possible, nor always meaningful; such pairs of peaks are designated with asterisks in Table I.

(14) A. Allerhand, D. Doddrell, and R. Komoroski, *J. Chem. Phys.*, **55**, 189 (1971).

(15) See, for example, G. C. Levy and G. L. Nelson, "Carbon-13 Nuclear Magnetic Resonance for Organic Chemists," Wiley-Interscience, New York, N. Y., 1972.

Discussion

The influence of different structural environments on the chemical shift of the carbonyl carbon is well illustrated in this series with keto groups at all possible positions of the steroid skeleton. It has previously[11,16,17] been found that the carbonyl carbon atom frequency in cyclopentanones is shifted about 5 ppm downfield relative to cyclohexanones, and that the effect of alkyl substitution on the carbonyl resonance is relatively small. These observations have been found to hold also for the keto steroids examined in this paper. Steroids with the carbonyl group in positions 2 to 11 all give a constant chemical shift value of 212 ppm (±1). On the other hand, if the carbonyl group is next to one of the two quaternary carbon atoms, as in 1-, 12-, and 17-keto steroids, a further downfield shift of 3–4 ppm is observed. The shielding of carbonyl carbon atoms located in ring D appear to be more sensitive to substitution, as seen, *e.g.*, by the 2.6-ppm difference in chemical shift between the carbonyl carbon atoms in 16-androstanone and 15-androstanone. However, even though some structural information is contained in the small changes of the carbonyl chemical shifts, it should be kept in mind that these shifts are quite sensitive to solvent and concentration changes.[18–20]

The influence of a keto group on the chemical shift of β-carbon atoms varies with the branching at this atom, and the shifts observed are generally smaller when the keto group is located in the five-membered ring than when it is found in one of the three six-membered rings. Average substituent values are 16 ppm for methylene and quaternary carbons and 12 ppm for methine carbon atoms. For keto groups in the five-membered ring these values are reduced by 2–3 ppm except for the quaternary carbon atom, which shows a remarkably low β substituent parameter of only 7 ppm.

The shifts observed at γ-carbon atoms vary greatly in magnitude and direction, covering a range from +6.3 to −9.5 ppm, even though half of the γ shifts observed are within ±2 ppm. The largest upfield shifts appear when the γ-carbon atom is eclipsed or nearly eclipsed to the keto group (*e.g.*, C-4 in 6-androstanone), while the other large up- and downfield γ shifts are observed for bridgehead carbon atoms (*e.g.*, C-10 in 2-cholestanone and C-9 in 7-cholestanone), that are approximately trans to the carbonyl oxygen atom. In a few cases (*e.g.*, C-10 in 11-androstanone) only small upfield shifts are observed at γ-carbon atoms eclipsed to keto groups, but in these cases the γ-carbon atoms are also ring junctions; the smaller upfield shifts for these carbon atoms may be the result of two opposing effects. γ shifts have been found to be caused by 1–4 nonbonded gauche interactions[21] resulting in an upfield shift of the γ-carbon resonance; trans γ-carbon atoms are usually not affected. The large up- and downfield γ shifts observed at (approximately) trans bridgehead carbon atoms probably reflect geometrical changes that take place upon introduction of a carbonyl group in a rigid

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(18) G. E. Maciel and J. J. Natterstad, *J. Chem. Phys.*, **42**, 2752 (1965).

(19) W. H. deJeu, *J. Phys. Chem.*, **74**, 822 (1970).

(20) H. E. Maciel and G. C. Ruben, *J. Amer. Chem. Soc.*, **85**, 3903 (1963).

(21) D. M. Grant and B. V. Cheney, *J. Amer. Chem. Soc.*, **89**, 5315 (1967).

framework as the steroid skeleton as opposed to a more flexible system as, *e.g.*, cyclohexane.

All δ-carbon shifts were found to be within ±2 ppm.

Isotope Effects.—The cmr spectra of the 16 deuterium-labeled compounds included in this study (see Table II) reveal, in accordance with previous reports,[22-26] that the introduction of deuterium atoms influences the chemical shifts of the labeled carbon as well as its neighbors. As noted above, the intensity of the cmr signal due to a deuterated carbon atom is very low; this is especially true when the carbon carries two deuterium atoms [*e.g.*, C-2 and C-6 in **10** (Table II)], since the splitting due to spin–spin coupling then becomes very extensive, and it has not been possible in these cases to measure a direct isotope shift. When a carbon has only one deuterium atom attached (*e.g.*, C-9 and C-12 in **13**), upfield isotope shifts of 0.3–0.5 ppm have been found, with the exception of 5α-d_1-1-androstanone, in which an isotope shift could not be detected.

The shifts observed at carbon atoms adjacent to labeled sites depend on the number of deuterium atoms introduced; a single deuterium atom on an sp^3 carbon atom, as in **1**, causes a geminal isotope shift of 0.1 ppm, while two deuterium atoms (*e.g.*, **9**) give rise to a shift of 0.2 ppm, in both cases toward higher field. These isotope shifts are of the same magnitude and direction as those reported.[22-26] Stothers, *et al.*,[26] have found spin–spin splitting and significantly broadened peaks in the spectra of 3-d_1-camphor and 3-d_1-5,6-dimethylnorbornan-2-ones owing to vicinal ^{13}C–^{2}H couplings. Similar spin–spin splitting, or peak broadenings, have not been observed for any of the labeled steroids examined, even though several compounds (*e.g.*, **1**) are included in which carbon atoms are trans to the deuterium, where the ^{13}C–^{2}H vicinal coupling constant would be expected to have its maximum value.[26] In contrast, upon deuteration we have observed drastic peak intensity changes at carbon atoms other than those deuterated (*e.g.*, C-2 and C-10 in **7**). Generally, the carbonyl carbon signal decreases upon deuterium exchange at the neighboring carbon atoms, rendering it nondetectable under experimental conditions where the undeuterated compound gives a carbonyl peak with a signal to noise ratio of about 15:1. Geminal isotope shifts have therefore not been measured for the sp^2 carbons. The intensity reduction may in these cases be a consequence of the decreased nuclear Overhauser enhancement, since the dipolar interaction between the carbon atom and the nearest hydrogen atoms is distance dependent ($1/r^6$). However, we observe a similarly reduced intensity by up to a factor of 10 relative to the unlabeled compound when introducing only one or two deuterium atoms adjacent to carbon atoms with no directly bonded protons (*e.g.*, C-13 in **2**, C-10 and C-13 in **4**, C-10 in **5**). This would not appear to be a result of simple reduction of the nuclear Overhauser enhancement, since in these cases only one or two out of seven or eight adjacent hydrogens are replaced by deuterium; whether the intensity decrease is then a consequence of peak broadenings caused by a geminal C–D coupling or other effects are involved is currently under investigation.

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Registry No.—Table I: A, 438-22-2; B, 481-21-0; C, 1755-29-9; D, 570-67-2; E, 1224-95-9; F, 566-88-1; G, 13583-70-5; H, 566-51-8; I, 3676-06-0; J, 567-71-5; K, 1755-32-4; L, 3676-09-3; M, 734-68-9; N, 40071-71-4; O, 1032-16-2; P, 963-74-6.

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