Acknowledgments. We appreciate stimulating discussions with Dr. Louis P. Hammett, Dr. Herbert C. Brown, and Dr. Robert W. Taft. Samples of several of the compounds used in the study were donated by Dr. Herbert C. Brown, Dr. Saul G. Cohen, Dr. Thomas DeVries, Dr. George C. Fraenkel, Dr. J. J. Norman, and Dr. Paul J. Ricca. We are grateful for their generosity. We are indebted to the National Science Foundation and the National Aeronautics and Space Administration for generous support of this work.

Mass Spectrometry in Structural and Stereochemical Problems. XCIII.[1] Further Observations on the Importance of Interatomic Distance in the McLafferty Rearrangement. Synthesis and Fragmentation Behavior of Deuterium-Labeled 12-Keto Steroids[2,3]

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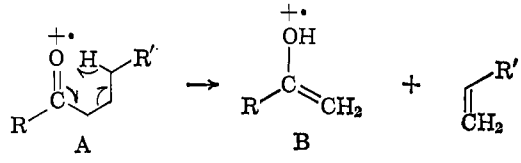
Contribution from the Department of Chemistry, Stanford University, Stanford, California. *Received September 13, 1965*

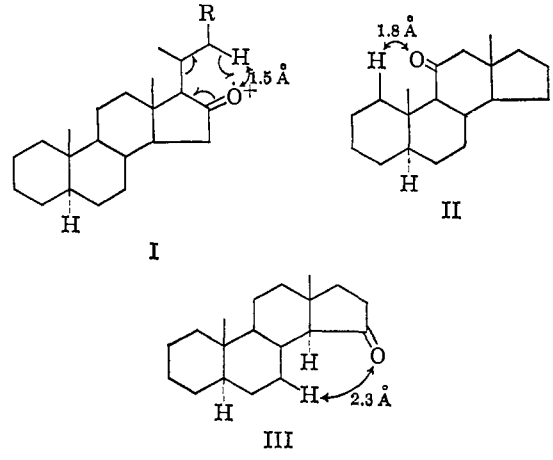
Abstract: Earlier work with deuterium-labeled 11-, 15-, and 16-keto steroids had indicated that the McLafferty rearrangement of ketones (β-cleavage with concomitant transfer of a γ-hydrogen atom) proceeds only if the interatomic distance between the itinerant hydrogen and the receptor oxygen is less than 1.8 Å. 12-Ketopregnanes, therefore, should not undergo a McLafferty rearrangement with transfer of a C-20 hydrogen atom, because the interatomic distance in the *intact* steroid is approximately 3.0 Å. Deuterium labeling has shown that the C-20 hydrogen atom is, in fact, transferred and this apparent discrepancy is rationalized by the assumption that the 13–17 bond is broken *prior* to hydrogen transfer, thus permitting close approach of the C-12 oxygen and the C-20 hydrogen atoms. The nature of all of the significant peaks in the high mass range of the mass spectrum of 5α-pregnan-12-one could be explained through the concept of charge localization by means of appropriate deuterium labeling, which also uncovered a reciprocal double hydrogen transfer involved in the genesis of the *m/e* 246 peak.

The electron impact induced fission of a β bond with simultaneous transfer of a γ-hydrogen atom (A → B) in carbonyl compounds appears to be of wide generality. Its recognition is due to McLafferty[4] and the experimental evidence, principally based on deuterium labeling, has already been summarized in various forms.[5–8]



A B

Recent studies in our laboratory with isotopically labeled ketones have shed considerable light on some of the more subtle factors affecting the McLafferty rearrangement such as the preference for abstraction of a secondary over a primary hydrogen atom,[1,9] the operation of restricted rotation,[10] and the existence of an appreciable deuterium isotope effect.[11] Through the use of suitably labeled steroids, it could be shown that the specific transfer of a γ-hydrogen did occur (see arrows in I) in 16-keto steroids (I),[9] where the γ-



I II III

(1) Paper XCII: H. Budzikiewicz, C. Fenselau, and C. Djerassi, *Tetrahedron*, in press.

(2) Financial assistance by the National Institutes of Health (Grant No. CA-07195) of the U. S. Public Health Service is gratefully acknowledged.

(3) Taken from part of the Ph.D. Dissertation of L. T., Stanford University, 1965.

(4) F. W. McLafferty, *Anal. Chem.*, **31**, 82 (1959).

(5) K. Biemann, "Mass Spectrometry," McGraw-Hill Book Co., Inc., New York, N. Y., 1962, Chapter 3.

(6) S. Meyerson and J. D. McCollum in "Advances in Analytical Chemistry and Instrumentation," C. N. Reilly, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, pp. 184–199.

(7) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1964, Chapter 1.

(8) G. Spiteller and M. Spiteller-Friedmann, *Monatsh.*, **95**, 257 (1964).

(9) C. Beard, J. M. Wilson, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, **86**, 269 (1964).

(10) H. Fritz, H. Budzikiewicz, and C. Djerassi, *Ber.*, in press.

(11) D. H. Williams, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, **86**, 284 (1964).

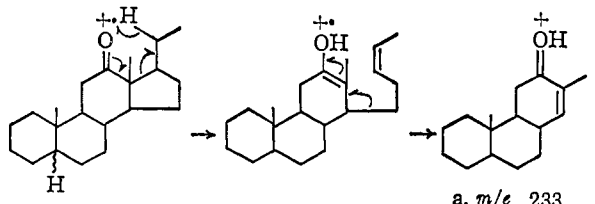
Table I. Shifts[a] of Principal Mass Spectral Peaks of Deuterated Analogs of 5α-Pregnan-12-one (IV)

5α-Pregnan-12-ones	Isotopic purity, %	M^+	M − CH_3	M − H_2O	M − C_2H_5	M − (H_2O + CH_3)	M − (H_2O + C_2H_5)	M − C_4H_8	M − C_5H_9	M − (C_5H_9 + H_2O)	M − C_9H_{17}
d_0 (IV)	...	302	287	284	273	269	255	246	233	215	177
8β-d_1 (XXIX)	4 d_0 85 d_1 11 d_2	303	288	285	274	270	256[b]	247	234	216	178
9α-d_1 (XXVIII)	5 d_0 93 d_1 2 d_2	303	288	285	274		256[b]	247	234	216	177
11,11-d_2 (XVII)	6 d_1 94 d_2	304	289	286	275	271	257	248	235	217	177
20-d_1 (XXIV)	12 d_0 84 d_1 4 d_2	303	288	285 (65%) 284 (35%)	273	270 (~70%) 269 (~30%)	255	246 (~50%) 247 (~50%)	233 (66%) 234 (44%)	215[b]	178
20,20-d_2 (XXV)	7 d_0 15 d_1 54 d_2 20 d_3 4 d_4	304	289	285[b]	273	271[b]	255	247	234 (~90%)	215[b]	178
20,20,21,21,21-d_5 (XIX)	6 d_1 23 d_2 16 d_3 21 d_4 31 d_5 3 d_6	307	292		273		255	247	234 (~90%)	215[b]	182

[a] Reported shifts are corrected for isotopic impurity as well as ^{13}C contributions and are greater than 90% unless indicated otherwise. Blank spaces indicate that no unambiguous assignment could be made. [b] Mainly at indicated *m/e* value, but exact calculation was impossible because of isotopic contaminants or low intensity of peak.

hydrogen atom can approach the oxygen to within 1.5 Å., but not in 11-keto (II)[12] or 15-keto (III)[13] steroids, where the interatomic distance ranges between 1.8 and 2.3 Å. Interatomic distance is thus another factor which must be taken into consideration in a mechanistic evaluation of the McLafferty rearrangement.

Several years ago, before the importance of interatomic distance in the McLafferty rearrangement had been recognized, we observed[14] that 12-keto steroids possessing a C-17 side chain with a C-20 hydrogen atom (12-ketopregnanes, -ergostanes, and -cholanates) exhibited in their mass spectra a very strong peak (see for instance *m/e* 233 in Figure 1), which could be attributed to a McLafferty rearrangement with transfer of a C-20 hydrogen atom as illustrated below for 5α- (IV) and 5β-pregnan-12-one (V). Measurements with Dreiding models,[15] however, show that the distance between the carbonyl oxygen and the C-20 hydrogen atom approaches 3 Å., which on the basis of the results[12,13] with II and III should preclude operation of the conventional McLafferty transfer of hydrogen.



IV, 5α
V, 5β

a, *m/e* 233

Deuterium labeling among 12-keto steroids was thus clearly indicated and the present paper describes the successful accomplishment of this work and the conclusions derived from it.[16]

Synthesis of 12-Keto Steroids. Since we wished to concentrate on the mass spectrometric fragmentation triggered by the 12-keto group without complications caused by the presence of other functional groups, it was necessary to prepare the hitherto undescribed "naked" steroids,[17] 5α-pregnan-12-one (IV) and 5α-androstan-12-one (XXXII), together with the appropriately labeled deuterium analogs. We found it most convenient to employ one common starting material for all of the synthetic transformations and hence chose the readily available sapogenin hecogenin (VI). Lithium aluminum hydride reduction of its tosylate effected the desired deoxygenation[18] of ring A as well as reduction of the 12-keto function to a readily separable mixture of 12α (VIII) and 12β alcohols (IX).[19] The acetate X of 5α-spirostan-12β-ol (IX) was subjected to the usual Marker side-chain degradation employing the octanoic anhydride modification.[20] The resulting Δ[16]-5α-pregnen-12β-ol-20-one acetate (XII) was catalytically hydrogenated to 5α-pregnan-12β-ol-20-one (XIII). Wolff–Kishner reduction followed by chromium trioxide oxidation of the 12-hy-

(12) D. H. Williams, J. M. Wilson, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 2091 (1963); D. H. Williams and C. Djerassi, *Steroids*, **3**, 259 (1964).

(13) C. Djerassi, G. von Mutzenbecher, J. Fajkos, D. H. Williams, and H. Budzikiewicz, *J. Am. Chem. Soc.*, **87**, 817 (1965).

(14) H. Budzikiewicz and C. Djerassi, *ibid.*, **84**, 1430 (1962).

(15) A. S. Dreiding, *Helv. Chim. Acta*, **42**, 1339 (1959).

(16) A preliminary report of some of the results was contained in a lecture by C. D. at the Third International Symposium on the Chemistry of Natural Products, Kyoto, Japan, April 1964; see C. Djerassi, *Pure Appl. Chem.*, **9**, 172 (1964).

(17) 5β-Pregnan-12-one (V) has been described by A. Ruff and T. Reichstein, *Helv. Chim. Acta*, **34**, 70 (1951). We are grateful to Professor Reichstein for a gift of this valuable substance.

(18) M. E. Wall and S. Serota, *J. Am. Chem. Soc.*, **78**, 1747 (1956).

(19) For leading references to the stereochemical course of reduction of 12-keto steroids see C. R. Engel, S. Rakhit, and W. W. Huculak, *Can. J. Chem.*, **40**, 921 (1962), as well as M. Alauddin and M. Martin-Smith, *J. Org. Chem.*, **28**, 886 (1963).

(20) A. F. B. Cameron, R. M. Evans, J. C. Hamlet, J. C. Hunt, P. G. Jones, and A. G. Long, *J. Chem. Soc.*, 2807 (1955).

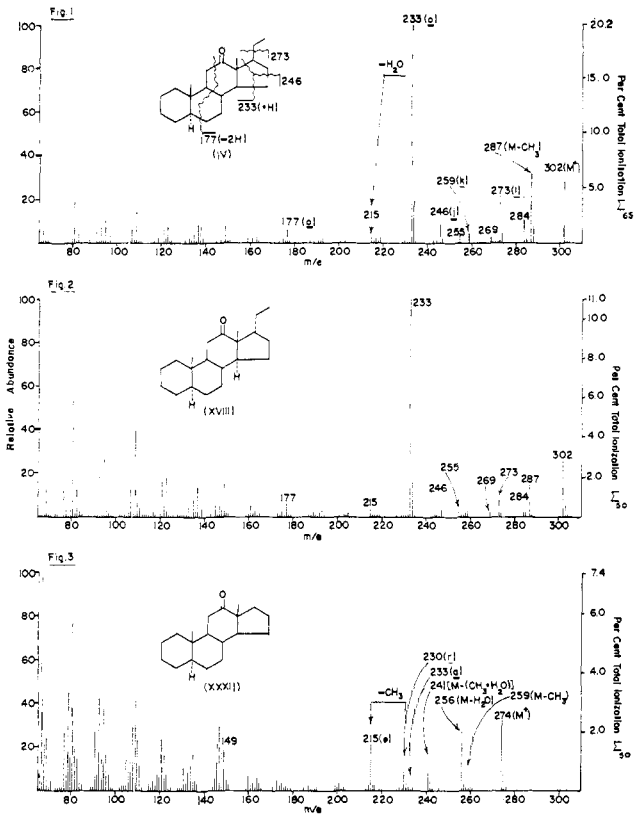


Figure 1. Mass spectrum of 5α-pregnan-12-one (IV).
Figure 2. Mass spectrum of 5α,17-isopregnan-12-one (XVIII).
Figure 3. Mass spectrum of 5α-androstan-12-one (XXXII).

droxy group led to 5α-pregnan-12-one (IV) accompanied by a small amount of the 17α isomer XVIII, which was also required for the mass spectrometric work and which could be obtained in a pure state by thin layer chromatography of the mother liquors. The stereochemistry at C-17 of IV (and hence of XVIII) was established by conversion to the known hydrocarbon 5α-pregnane. The usual base-catalyzed exchange[21] of IV in deuteriomethanol led to the 11,11-d_2 analog XVII of high isotopic purity (see Table I).

The most important labeled substrate for the present mass spectrometric studies was the one with deuterium attached to C-20. While desulfurization of mercaptals with deuterated Raney nickel catalyst frequently leads to isotopic scrambling,[21] this is not always the case. Consequently, Δ^{16}-5α-pregnen-12β-ol-20-one was hydrogenated to the alcohol XIV, transformed to the 20-ethylene mercaptal XV, desulfurized with deuterated Raney nickel catalyst, and then oxidized at C-20. As shown in Table I (see M − C_2H_5 column), extensive scrambling of deuterium occurred, the principal constituent of the mixture being the d_5 analog XIX rather than the desired 20,20-d_2-5α-pregnen-20-one (XXV).

As an alternate approach to the 20,20-d_2 ketone XXV, the 12β-acetoxy-20-ketone XIII was converted into the 20-tosylhydrazone XVI and then reduced[22] with sodium borodeuteride in deuteriomethanol, followed by reoxidation of the concomitantly produced 12-hydroxyl group. The resulting product (see Table I) contained 54% of the desired 20,20-d_2 12-ketone XXV together with 20% of a d_3 contaminant (evidently formed by exchange of the tosylhydrazone prior to reduction) and smaller quantities of d_1 and d_0 species.

Monodeuteration at C-20 was effected in the following fashion. 5α-Pregnan-12β-ol-20-one (XIV) was oxidized to the 12,20-diketone (XX) and the 12-keto function protected by ketalization with ethylene glycol.[23] Reduction of the remaining 20-keto group with lithium aluminum deuteride followed by dehydration of the alcohol XXII and cleavage of the 12-ketal grouping furnished a mixture of $\Delta^{17(20)}$- and Δ^{20}-5α-pregnen-12-one-20-d_1 (XXIII), which was then catalytically hydrogenated to the 20-d_1-labeled 5α-pregnan-12-one (XXIV). The relatively high isotopic purity (84% d_1; see Table I) is due to the fact that vinylic hydrogen (or deuterium) is not readily exchanged on a catalyst surface.

Introduction of deuterium into the tertiary 8β (XXIX) and 9α (XXVIII) positions was accomplished through one common intermediate, namely $\Delta^{9(11)}$-5α-pregnen-12-one (XXVI), which was obtained by selenium dioxide oxidation[24] of 5α-pregnan-12-one (IV). Catalytic deuteration[25] of the α,β-unsaturated ketone XXVI, followed by back exchange with hydroxide of the exchangeable 11-deuterium atom, led to 9α-d_1-5α-pregnan-12-one (XXVIII), while base-catalyzed exchange of XXVI in deuteriomethanol provided the 8β,11-d_2-$\Delta^{9(11)}$-5α-pregnen-12-one (XXVII), which was catalytically hydrogenated and then back exchanged with hydroxide to 8β-d_1-5α-pregnan-12-one (XXIX).

In order to examine the effect of the 17-ethyl side chain in 12-ketopregnanes upon the mass spectral fragmentation pattern, it was necessary to have available the spectrum of the hitherto unreported 5α-androstan-12-one (XXXII). For this purpose the oxime XXX of 5α-pregnan-12β-ol-20-one acetate (XIII) was subjected to Beckmann rearrangement[26] and the resulting 17-ketone XXXI reduced by the Wolff–Kishner procedure and reoxidized at C-12. Deuterium labeling at C-11 (XXXIII) was accomplished in the usual fashion[21] by base-catalyzed exchange in deuteriomethanol. 8β-d_1-5α-Androstan-12-one (XXXVI) was synthesized *via* $\Delta^{9(11)}$-5α-androsten-12-one (XXXIV) and its 8β-11-d_2 derivative XXXV as described above for the pregnane analog XXIX, while introduction of deuterium into C-17 (XXXIX) was effected by desulfurization of the mercaptal XXXVII with deuterated Raney nickel catalyst and thus resulted in the expected[21] isotopic scrambling (see Table II).

Discussion of Mass Spectra. The mass spectrum of 5α-pregnan-12-one (IV) is reproduced in Figure 1, while the shifts of the principal peaks in the deuterated analogs are listed in Table I. By far the most intense

(21) For review see H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Structure Elucidation of Natural Products by Mass Spectrometry," Vol. I, Holden-Day, Inc., San Francisco, Calif., 1964, Chapter 2.

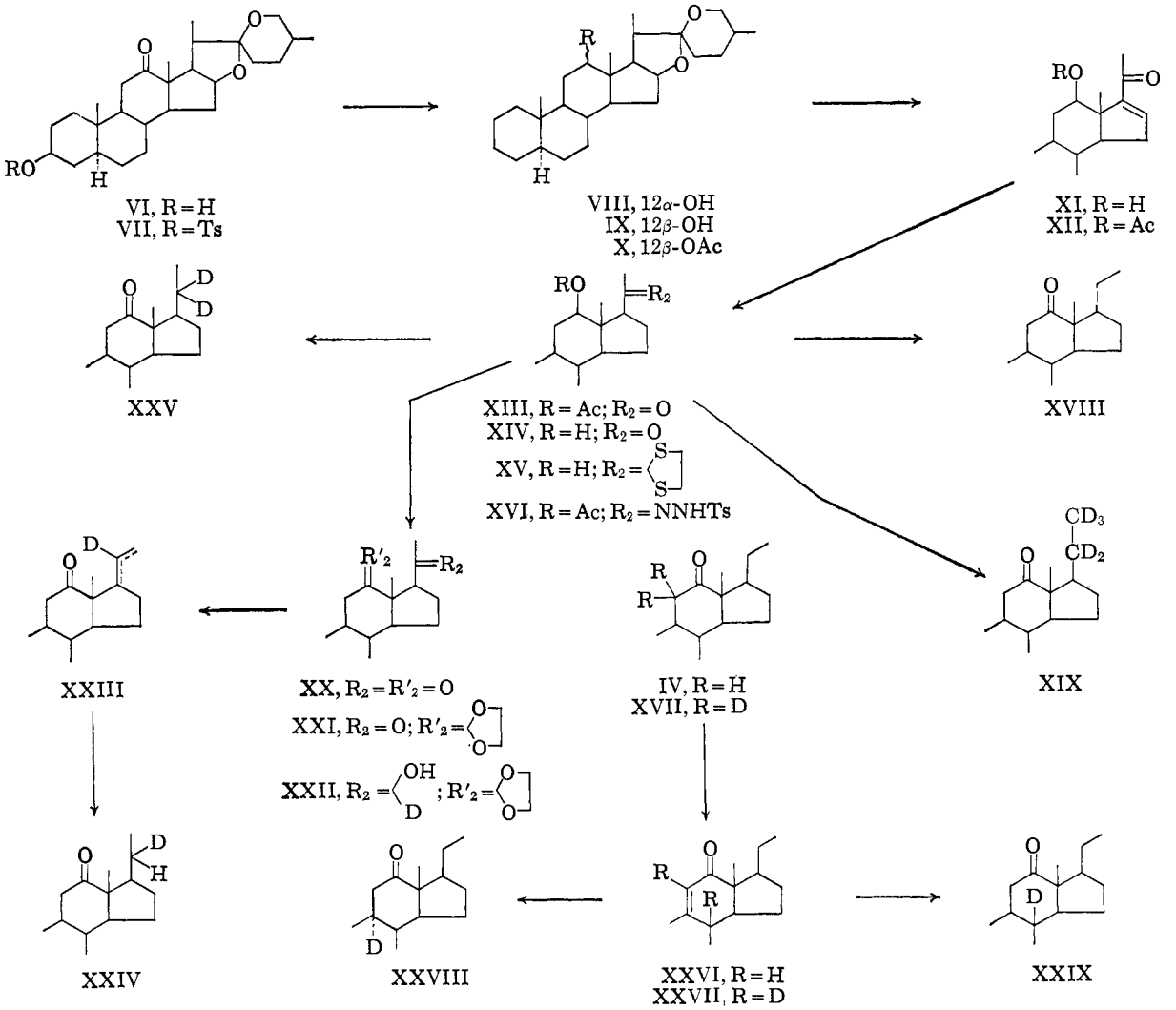
(22) L. Caglioti and P. Grasselli, *Chem. Ind.* (London), 153 (1964); L. Caglioti, *Chim. Ind.* (Milan), **46**, 1492 (1964); *Ric. sci.*, **34** [I], 41 (1964); M. Fischer, Z. Pelah, D. H. Williams, and C. Djerassi, *Ber.*, **98**, 3236 (1965).

(23) For another example of selective ketalization at C-12 in 12,20-diones see D. N. Kirk, D. K. Patel, and V. Petrow, *J. Chem. Soc.*, 1046 (1957).

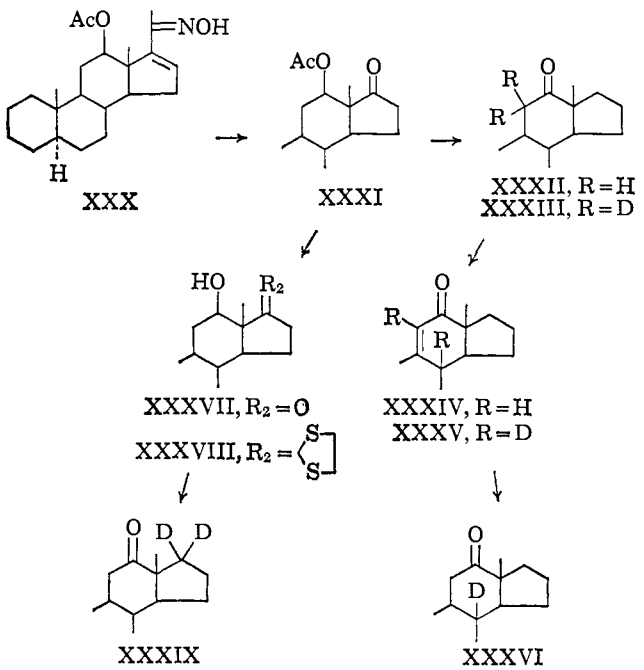
(24) For leading references see R. Owyang in "Steroid Reactions," C. Djerassi, Ed., Holden-Day, Inc., San Francisco, Calif., 1963, Chapter 5.

(25) In contrast to the catalytic deuteration of olefins, that of α,β-unsaturated ketones is accompanied by only little scrambling of isotope.

(26) For complete literature survey of this approach to 17-keto steroids see D. M. Feigl in "Steroid Reactions," C. Djerassi, Ed., Holden-Day, Inc., San Francisco, Calif., 1963, Chapter 10.



peak in the spectrum, amounting to 20% of the total ionization (Σ_{65}), occurs at *m/e* 233 and corresponds formally to loss of ring D (fission of the 13–17 and 14–15 bonds) and the gain, by the charged moiety, of one hydrogen atom. It should be noted that such a cleavage is very characteristic of steroids in general[27] but that in the absence of a 12-keto function, it is accompanied by the loss, rather than gain, of one hydrogen atom.



Inspection of Table I shows that approximately 90% of the migrating hydrogen originates from C-20, which would seem to support the operation of the standard McLafferty rearrangement as outlined in the introduction in terms of the process IV → a. In view of the prohibitively large distance (3 Å.) between the oxygen and C-20 hydrogen atoms, we suggest the following alternate explanation for the production of the ion of mass 233.

The virtually ubiquitous ring D fission with loss of a hydrogen atom in most steroids is best rationalized through the intervention of a molecular ion of type b.[27,28] Such an ion would not be favored in 12-keto steroids since the positive charge would be located next to a carbonyl group and it is more reasonable, therefore, to assume charge retention on oxygen (see IV). Homolytic fission of the 13–17 bond now yields a species, c, in which the strain inherent in the *trans*-hydrindane system is released. Hydrogen transfer to the oxygen atom, thus satisfying its radical site, would be expected

(27) H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Structure Elucidation of Natural Products by Mass Spectrometry," Vol. II, Holden-Day, Inc., San Francisco, Calif., 1964, Chapter 21.

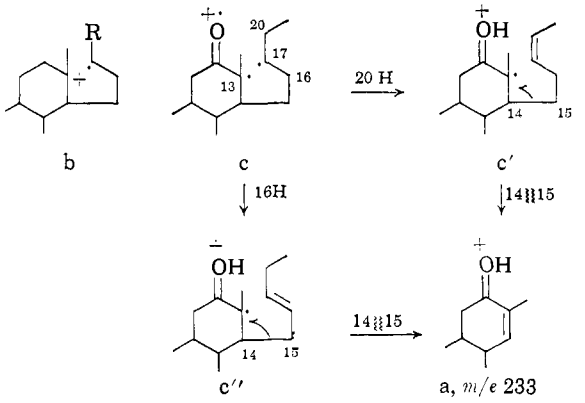
(28) See ref. 16, p. 166 as well as M. Spiteller-Friedmann, S. Eggers, and G. Spiteller, *Monatsh.*, **95**, 1740 (1964).

Table II. Shifts[a] of Principal Mass Spectral Peaks of Deuterated Analogs of 5α-Androstan-12-one (XXXII)

5α-Androstan-12-ones	Isotopic purity, %	M+	M − CH_3	M − H_2O	M − (H_2O + CH_3)	M − C_3H_5	M − C_2H_4O	M − (C_2H_4O + CH_3)
d_0 (XXXII)	...	274	259	256	241	233	230	215
8β-d_1 (XXXVI)	3 d_0 97 d_1	275	260	256 (~33%) 257 (~67%)	241 (~35%) 242 (~65%)	234	230	215
11,11-d_2 (XXXIII)	8 d_1 92 d_2	276	261	258	243	235	230	215
17,17-d_2 (XXXIX)	10 d_1 40 d_2 39 d_3 11 d_4	276	261		243[b]		232[b]	217
9α-d_1 (3β-OH)[c]	7 d_0 83 d_1 10 d_2	291	276			250[b]	247[b]	232[b]

[a] See footnote *a* in Table I. [b] See footnote *b* in Table I. [c] The preparation of this substance is described by R. H. Shapiro, D. H. Williams, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, **86**, 2837 (1964).

to occur from either C-20 or C-16, since a $\Delta^{17(20)}$ (c′) or Δ^{16} (c″) olefinic linkage would be produced at the same time. Homolysis of the 14–15 bond then leads to the stable conjugated oxonium ion a of mass 233.



With ring C in the chair form, the C-20 hydrogen atom in c can approach the oxygen atom to within 1.7 Å., while the C-16 hydrogen can only come within 3.8 Å. However, if ring C "flips" into one of the flexible forms, the C-20 hydrogen can approach the carbonyl group to within any desired distance; indeed even the distance between the C-16 hydrogen and the oxygen atom can be reduced to 1.5 Å. We believe, therefore, that it is the possibility for closer approach of the C-20 hydrogen atom, which is responsible for its transfer to the extent of 90% and that the remainder probably originates from C-16. Further comment on this point will be made below in a discussion of the mass spectrum of 5α-androstan-12-one (XXXII) in which the C-20 hydrogen is lacking.

On the basis of the intermediacy of species c, one would predict that the fragmentation process leading to the ion a would be independent of the stereochemistry at C-17 and this is demonstrated in Figure 2 by 17-iso-5α-pregnan-12-one (XVIII), whose mass spectrum is very similar to that of IV even though the distance between the C-20 hydrogen atom and the oxygen function in the intact steroid is only 1.65 Å.

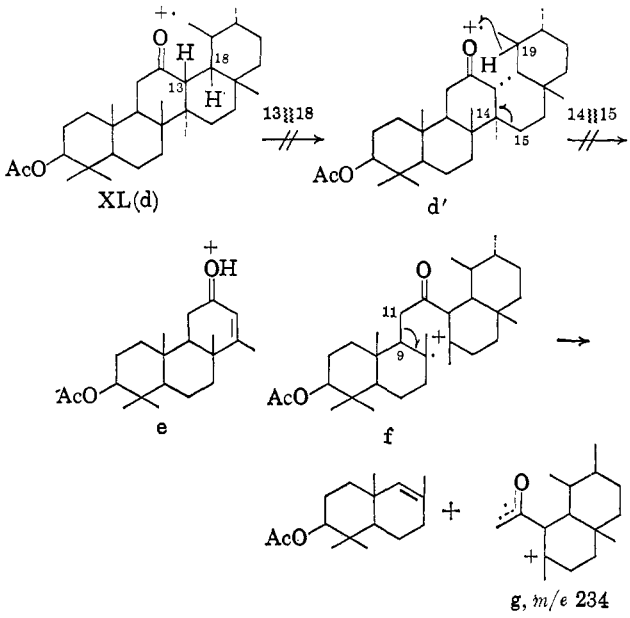
If the first step is indeed fission of the 13–17 bond (c), then the interatomic distance in the intact steroid should, of course, not have any important effect. The mass spectrum (not reproduced) of 5β-pregnan-12-one (V)[17] is, as expected, very similar to that of the 5α isomer IV.

The significance of charge localization in triggering given fragmentation paths is illustrated in two other compounds which are related to pregnan-12-one, but where ions analogous to a are not observed. One of these is hecogenin (VI), which possesses all of the structural requirements for such a cleavage, yet whose mass spectrum[29] does not exhibit any significant peak at *m/e* 249 (ion a with additional hydroxyl group), because charge retention on the spiroketal oxygen atoms is favored and thus leads to completely different fragments involving largely the side chain.[30]

The other substance is 3β-acetoxy-12-oxoursane (XL), where cleavage of the 13–18 bond in the molecular ion d to d′ followed by transfer of the C-19 hydrogen and finally fission of the 14–15 linkage should yield e, which would be completely analogous to ion a in 20-keto steroids. In point of fact, no such peak is observed in the mass spectrum[31] of this triterpene, the most intense one being at *m/e* 234 which is associated with rings C, D, and E, rather than A, B, and C. A reasonable explanation for this apparent discrepancy is that the absence of the angular methyl group at C-13 in the triterpene and the lower strain of its C–D ring system lessens the driving force for rupture of the 13–18 bond as compared to the situation in the steroids. On the other hand, the presence of additional quaternary centers through the methyl groups at positions 8 and 14 offers serious competition to the carbonyl group for charge localization and it is not unreasonable to expect that ion f may be an important contributor to the molecular ion. Fission of the 9–11 bond would then produce a neutral olefin and the ion radical g (corresponding to the base peak at *m/e* 234) with the favorable tertiary carbonium ion and a resonance-stabilized radical site.

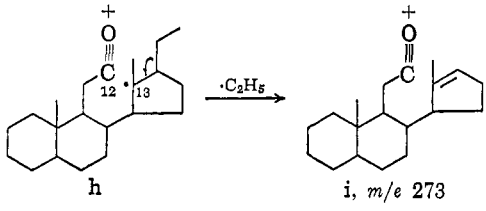
Charge localization is also a convenient concept to rationalize the remaining significant peaks in the high mass range of the mass spectrum (Figure 1) of 5α-pregnan-12-one (IV). The M − CH_3 peak at *m/e* 287 is due to expulsion of an angular methyl group,

(29) H. J. M. Fitches *Advan. Mass Spectry.*, **2** 451 (1963).
(30) H. Budzikiewicz, J. M. Wilson, and C. Djerassi, *Monatsh.*, **93**, 1033 (1962), as well as Chapter 22 in ref. 27.
(31) H. Budzikiewicz, J. M. Wilson, and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 3688 (1963).

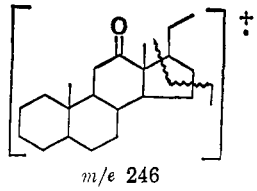


rather than the C-21 methyl substituent as demonstrated by the spectrum (Table I) of the side-chain d_5-labeled analog XIX. Loss from C-21 could have been rationalized from a molecular ion such as b, which, however, would not be favored in the presence of a 12-keto group. Expulsion of the C-21 methyl group from a species such as c would satisfy the radical site at C-17 through formation of a 17–20 olefin, but there would remain in ring C a diradical ion without any opportunity for resonance stabilization.

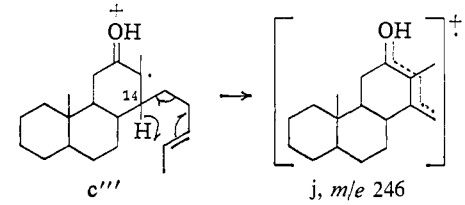
Of interest is the observation that the M − C_2H_5 ion of mass 273, due to loss of the ethyl side chain (see Table I), is much more intense in the 12-ketones IV and V as compared to the hydrocarbon pregnane.[32] Charge localization on the carbonyl group offers a ready explanation for this observation, since the well-known[7] α cleavage of ketones involving the more highly substituted 12–13 bond would then lead to species h, whose C-13 radical site could then be readily satisfied by expulsion of an ethyl radical with production of ion i (*m/e* 273).



The peak at *m/e* 246 is due to the loss of the elements of C_4H_8. In the absence of deuterium labeling, it would be depicted formally as follows without implicating any hydrogen migrations.

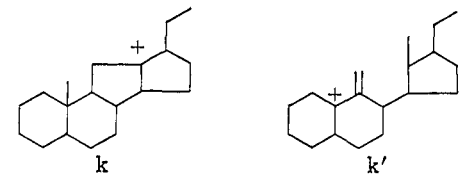


The results summarized in Table I, show, however, that a hydrogen atom is transferred from C-20, and since the 246 value implies no net loss or gain of hydrogen, another hydrogen atom must be shifted back from the charge-retaining moiety. The simplest explanation is to assume again the intermediacy of species c and c', except that the latter now undergoes concerted transfer of the C-14 hydrogen atom (c''') to yield the resonance-stabilized ion radical j (*m/e* 246).



The more or less random loss of water from ketones has been observed frequently[7,33] and hence is not diagnostic of hydroxyl-containing substances. In the present instance, it occurs not only from the molecular ion ($M^+ \rightarrow$ *m/e* 284) but is also implicated in the peaks found at *m/e* 269 [M − (H_2O + CH_3)], *m/e* 255 [M − (H_2O + C_2H_5)], and *m/e* 215 (a − H_2O, confirmed by high-resolution mass measurements[34]). As shown in Table I, one of the C-20 hydrogen atoms seems to be involved to a considerable extent in these electron-impact induced "dehydrations."

The availability of the labeled substrates sheds light on the nature of two additional peaks in the mass spectrum (Figure 1) of 5α-pregnan-12-one (IV). The small peak at *m/e* 259 was shown by high-resolution mass measurements[34] to consist of two ions, $C_{18}H_{27}O$ (30%) and $C_{19}H_{31}$ (70%). The low abundance does not permit any definite assignment to the oxygen-containing peak (M − C_3H_7), but the hydrocarbon portion corresponds to the loss of carbon monoxide and a methyl radical. A plausible representation for this ion may be k or k'.



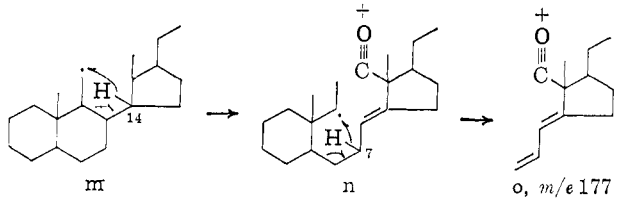
The high-resolution mass measurements[34] demonstrated that over 90% of the *m/e* 177 peak corresponded to an oxygen-containing fragment. If one takes into consideration the deuterium-labeling results (Table I) which show that the side chain and C-8 are retained, but C-9 and C-11 lost, then an energetically plausible reaction path and structure for the resulting ion can be put forward. Charge retention on oxygen and α fission of the 11–12 rather than 12–13 bond (see h) would yield m, which upon successive hydrogen transfers and bond fissions *via* n would produce ion o (*m/e* 177). While labeling at C-14 and C-7 would be required to support the postulated mechanism, it should be noted that each step involves the generation of an energetically progressively more favored species and that the reactions are very similar to the isotopically documented fissions of ethylene ketals.[35]

(32) L. Tökés, unpublished observation.

(33) *Cf.* E. Lund, H. Budzikiewicz, J. M. Wilson, and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 941 (1963).

(34) Performed by Dr. D. Goldsmith on an A. E. I. MS-9 double-focusing mass spectrometer.

(35) Ref. 27, Chapter 18.

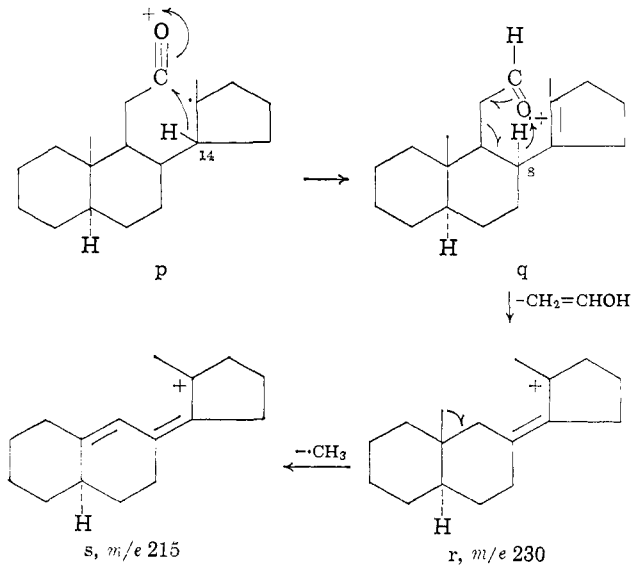


m n o, *m/e* 177

The most significant difference between the mass spectrum (Figure 1) of 5α-pregnan-12-one (IV) and that (Figure 3) of the corresponding androstane XXXII is the absence of an intense *m/e* 233 peak (a). This is completely consistent with the earlier postulated mechanism for 5α-pregnan-12-one (IV) which involves initial fission of the 13–17 bond (c). This is much more favored in steroids with a C-17 substituent as demonstrated in related work[32] with hydrocarbons (androstane *vs.* pregnane *vs.* cholestane). The weak 233 ion in the 5α-androstan-12-one spectrum (Figure 3) probably owes its genesis to transfer of a C-16 hydrogen atom (see c → c″ → a).

The peaks at *m/e* 259 (loss of angular methyl group), 256 (loss of water), and 241 (combined loss of methyl radical and water) are unexceptional and require no further comment. The ion of mass 149 should correspond to the *m/e* 177 species o of the pregnane series. However, it is also isobaric with $C_{11}H_{17}$, which is found in many ring A and B deoxy steroids,[27] and high-resolution mass measurements[34] demonstrated a 2:1 ratio for $C_{11}H_{17}$ and $C_{10}H_{13}O$. The complexity of the *m/e* 145–149 region in Figure 3 does not permit an evaluation of peak shifts in the spectra of the deuterated species, but it is likely that the $C_{10}H_{13}O$ component of the *m/e* 149 peak arises in a fashion analogous to that postulated above for ion o in the pregnane series.

Two peaks are present in the high mass range of Figure 3 which structurally have no counterpart in the pregnane series. The first is the *m/e* 230 peak which involves the loss of the elements of C_2H_4O, the deuterium labels at C-8 and C-11 having been lost, but that at C-9 retained (see Table II). A plausible sequence is depicted below, starting with the α-cleavage product p, which probably stabilizes itself through transfer of the C-14 hydrogen. The analogous α-fission product h in the pregnane series behaves differently



p q

$-CH_2=CHOH$

$-\cdot CH_3$

s, *m/e* 215 r, *m/e* 230

since it has available another path for satisfying the electron deficiency at C-13, namely, expulsion of the ethyl side chain. The fragmentation is then completed by the documented (see Table II) transfer of the C-8 hydrogen with concomitant elimination (see q) of acetaldehyde (in its enol form) and production of the resonance-stabilized ion radical r (*m/e* 230). This assignment also explains the origin of the second peak under consideration, *m/e* 215, which must be attributed to the further loss of a methyl radical. On the basis of structure r for the ion of mass 230, it would be predicted that it is the C-19 methyl group which is lost with formation of the conjugated carbonium ion s (*m/e* 215).

Experimental Section[36]

12α- (VIII) and 12β-Hydroxy-5α,22αO-spirostan (IX). Hecogenin (VI)[37] was transformed into its tosylate (VII)[18] and then reduced[18] with lithium aluminum hydride in tetrahydrofuran solution. Chromatography on neutral alumina (activity II) and elution with benzene afforded 66% of 5α,22αO-spirostan-12β-ol (IX), which exhibited m.p. 191.5–192.5°, $[\alpha]^{25}D$ −67° (*c* 1.2) after recrystallization from methanol. *Anal.* Calcd. for $C_{27}H_{44}O_3$: C, 77.83; H, 10.65. Found: C, 77.87; H, 10.38.

Further elution of the column with benzene–ether (9:1) gave 22% of 5α,22αO-spirostan-12α-ol (VIII), m.p. 203–204°, $[\alpha]^{24}D$ −42° (*c* 0.99) after recrystallization from methanol. *Anal.* Calcd. for $C_{27}H_{44}O_3$: C, 77.83; H, 10.65. Found: C, 77.90; H, 10.51.

Acetylation of the alcohols by warming for 1 hr. at 60° with acetic anhydride–pyridine and keeping at room temperature overnight yielded the appropriate acetates, which were recrystallized from ethanol. The **12α-acetate** had m.p. 170–172°, $[\alpha]^{23}D$ −2° (*c* 1.0), λ_{max}^{Nujol} 5.74 and 8.06 μ. *Anal.* Calcd. for $C_{29}H_{46}O_4$: C, 75.94; H, 10.11. Found: C, 75.69; H, 9.95. The **12β-acetate** (X) had m.p. 183–183.5°, $[\alpha]^{26}D$ −71° (*c* 1.0), λ_{max}^{Nujol} 5.74 and 8.06 μ. *Anal.* Calcd. for $C_{29}H_{46}O_4$: C, 75.94; H, 10.11. Found: C, 75.93; H, 10.09.

Side-Chain Degradation of 5α,22αO-Spirostan-12β-ol Acetate (X). The conversion of the spirostan X to the corresponding furosten was accomplished by heating 24 g. of X with a mixture of octanoic acid and octanoic anhydride according to the procedure of Cameron, *et al.*,[20] while the subsequent oxidation and alkaline hydrolysis (potassium hydroxide in *t*-butyl alcohol) was performed under the conditions recommended by Wall and collaborators[38] for similar transformations. Chromatography of the crude reaction product on 1.1 kg. of neutral alumina (activity II) gave the following three products. Elution with benzene–hexane mixtures removed 1.1 g. of unreacted starting material (X), while with benzene containing 10 and 20% of ether there was obtained 4.7 g. of Δ16-5α-pregnen-12β-ol-one acetate (XII), which exhibited the following constants after recrystallization from ethanol: m.p. 182.5–183°, $[\alpha]^{25}D$ +28° (*c* 1.3), λ_{max}^{EtOH} 234 mμ (ε 8700), $\lambda_{max}^{CHCl_3}$ 5.80, 5.97, 6.28, and 8.0 μ. *Anal.* Calcd. for $C_{23}H_{34}O_3$: C, 77.05; H, 9.56. Found: C, 77.32; H, 9.72.

By increasing the proportion of ether to 20–50%, there was isolated 1.8 g. of Δ16-5α-pregnen-12β-ol-20-one (XI), which was

(36) Melting points (uncorrected) were determined on the Kofler block. Optical rotations and infrared spectra were measured in chloroform solution and ultraviolet absorption spectra in ethanol. Optical rotatory dispersions, performed by Mrs. Ruth Records, were obtained with a Durrum-JASCO Model ORD-5 spectropolarimeter. Thin-layer chromatography (t.l.c.) was performed on silica gel H (E. Merck, A. G., Darmstadt) followed by spraying with a 2% ceric sulfate solution in 2 *N* sulfuric acid and heating for optimum development of the colored spots. In preparative t.l.c. experiments, the appropriate fractions were detected by exposure to ultraviolet light or by spraying with iodine vapor. All mass spectra were determined by Mr. John Smith or Dr. H. Budzikiewicz with a CEC Model 21-103C mass spectrometer using an all-glass inlet system heated to 200° with the isatron temperature maintained at 270°, while the ionizing energy was kept at 70 e.v. and the ionizing current at 50 μa. All microanalyses were by Messrs. E. Meier and J. Consul.

(37) Kindly supplied by Dr. Pierre Crabbé, Syntex S. A., Mexico City, Mexico.

(38) M. E. Wall, H. E. Kenney, and E. S. Ruthman, *J. Am. Chem. Soc.*, 77, 5665 (1955).

recrystallized from ethanol, m.p. 167–168°, $[\alpha]^{26}D$ −10° (*c* 1.0), λ_{max}^{EtOH} 243 mμ (ε 8200), $\lambda_{max}^{CHCl_3}$ 2.96, 6.10, and 6.32 μ. *Anal.* Calcd. for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found: C, 79.76; H, 10.30.

In agreement with related observations in the literature,[39] we were unsuccessful in effecting acetylation of the hydroxyl group of XI by warming with acetic anhydride in pyridine solution at 60° for 1 hr.

5α-Pregnan-12β-ol-20-one (XIV) and Acetate (XIII). Hydrogen uptake was complete within 40 min. when a solution of 2.0 g. of Δ16-5α-pregnen-12β-ol-20-one acetate (XII) in 200 ml. of ethanol was shaken at room temperature and atmospheric pressure in an atmosphere of hydrogen with 0.15 g. of 5% palladized charcoal catalyst. Filtration of the catalyst, evaporation of the filtrate to dryness, and recrystallization from ethanol yielded 1.65 g. of 5α-pregnan-12β-ol-20-one acetate (XIII, m.p. 149–149.5°, $[\alpha]^{26}D$ +56° (*c* 0.85), λ_{max}^{EtOH} 5.76, 5.85, and 8.06 μ, ORD in dioxane (*c* 0.17) $[\phi]_{312}^{peak}$ +3750°, $[\phi]_{285}^{trough}$ +1100°. *Anal.* Calcd. for $C_{23}H_{36}O_3$: C, 76.62; H, 10.07. Found: C, 76.62; H, 10.09.

A similar hydrogenation of the unsaturated alcohol XI proceeded in 90% yield to give after recrystallization from hexane 5α-pregnan-12β-ol-20-one (XIV), m.p. 118–118.5°, $[\alpha]^{26}D$ +4° (*c* 1.0), $\lambda_{max}^{CHCl_3}$ 2.95 and 5.92 μ, ORD in dioxane (*c* 0.10) $[\phi]_{318}^{peak}$ +2830°, $[\phi]_{270}^{trough}$ −2150°. *Anal.* Calcd. for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76. Found: C, 79.30; H, 10.67.

When a sample of the acetate XIII was subjected to saponification (1 hr. reflux with 5% ethanolic potassium hydroxide) there was obtained a mixture of the alcohol XIV and its **17α isomer**, which could be isolated in pure form by slow recrystallization from hexane, m.p. 138–139.5°, $[\alpha]^{24}D$ −32°, ORD[40] in dioxane (*c* 0.26) $[\phi]_{305}^{trough}$ −1150°, $[\phi]_{268}^{peak}$ +859°. *Anal.* Calcd. for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76. Found: C, 79.10; H, 10.76.

17β- (IV) and 17α-5α-Pregnan-12-one (XVIII). A mixture of 145 mg. of the acetate XIII, 4 ml. of ethylene glycol, 2 ml. of *n*-butyl alcohol, and 1.5 ml. of hydrazine hydrate (95%) was heated under reflux for 1 hr.; the solution was cooled to 100°, followed by the addition of 300 mg. of potassium hydroxide, and was heated (without condenser) until the temperature reached 200°. After subsequent heating under reflux at 215° for 4 hr., the reaction mixture was poured into water, extracted with ether, washed with water, dried over anhydrous magnesium sulfate, and evaporated to dryness. Recrystallization from methanol provided 62 mg. of the 17β isomer IV (m.p. 138–141°), while thin layer chromatography of the mother liquors yielded an additional 34 mg. of IV as well as 13 mg. of the 17α isomer XVIII, which after recrystallization melted at 106–108° (for mass spectrum see Figure 2). The pure 17β isomer IV after recrystallization from methanol exhibited m.p. 141–142°, $[\alpha]^{25}D$ +120° (*c* 1.0), $\lambda_{max}^{CHCl_3}$ 5.88 μ, ORD in methanol (*c* 0.15) $[\phi]_{307}^{peak}$ +5160°, $[\alpha]_{255}^{trough}$ −1840°. *Anal.* Calcd. for $C_{21}H_{34}O$: C, 83.38; H, 11.33. Found: C, 83.38; H, 11.48.

Deuteration at C-11 was effected by heating under reflux for 22 hr. a solution of 4 mg. of 5α-pregnan-12-one (IV) in 1.5 ml. of deuteriomethanol containing 2 drops of 20% sodium deuterioxide solution in deuterium oxide. Extraction with ether, washing with water, drying, evaporation, and recrystallization from deuteriomethanol afforded 2.5 mg. of 11,11-d_2-5α-pregnan-12-one (XVII) of 94% isotopic purity (see Table I).

20,20,21,21,21-d_5-5α-Pregnan-12-one (XIX). A mixture of 150 mg. of 5α-pregnan-12β-ol-20-one (XIV), 0.5 ml. of ethane dithiol, and 0.5 ml. of boron trifluoride etherate was kept at room temperature for 8 min., diluted with ether, washed several times with dilute sodium hydroxide solution and water, and then dried and evaporated. Chromatography on a silica gel H plate (benzene development) and recrystallization from methanol provided 98 mg. of the **ethylene mercaptal** XV, m.p. 167–168°, $[\alpha]^{29}D$ −10° (*c* 0.92), which lacked carbonyl absorption in the infrared. *Anal.* Calcd. for $C_{23}H_{38}OS_2$: C, 69.99; H, 9.71. Found: C, 69.91; H, 9.54.

Desulfurization of 15 mg. of the mercaptal XV was effected by heating under reflux with stirring for 4 hr. with 2.5 ml. of deuteriomethanol and 0.5 g. of freshly prepared[41] deuterium-containing Raney nickel catalyst. The crude deuterated 12β alcohol[42] (12 mg.) was obtained by filtration of the catalyst and evaporation of the filtrate and was subjected without further purification to Jones oxidation[43] to give 8 mg. of the side chain labeled 5α-pregnan-12-one (XIX), m.p. 138–140°, whose isotopic composition is listed in Table I.

20,20-d_2-5α-Pregnan-20-one (XXV). A solution of 200 mg. of 5α-pregnan-12β-ol-20-one acetate (XIII) and 200 mg. of *p*-toluenesulfonylhydrazide in 12 ml. of methanol containing 1 drop of sulfuric acid was heated under reflux for 2 hr., then concentrated under reduced pressure; crystallization was induced by addition of a small amount of water. The resulting tosylhydrazone XVI (296 mg., m.p. 155–163° dec.) was collected and the crude material (50 mg.) was dissolved in 1 ml. of deuteriomethanol[44] and heated under reflux with 50 mg. of sodium borodeuteride. After 2 hr., an additional 50 mg. of sodium borodeuteride was added and heating was continued for 8 hr. Dilution with ether and successive washing with dilute hydrochloric acid and water, followed by evaporation and t.l.c. purification (benzene containing 10% ether), left 48 mg. of unreacted tosylhydrazone (XVI) (a result in agreement with subsequent reports[22,44]) and only 2 mg. of slightly impure deuterated 5α-pregnan-12β-ol, which was oxidized directly by the Jones procedure[43] to give 0.8 mg. of 20,20-d_2-5α-pregnan-12-one (XXV). The isotopic composition of this ketone (m.p. 132–137°) is given in Table I.

20-d_1-5α-Pregnan-12-one (XXIV). Jones oxidation[43] of 5α-pregnan-12β-ol-20-one (XIV) proceeded in nearly quantitative yield to provide **5α-pregnane-12,20-dione** (XX), which exhibited m.p. 148.5–150°, $[\alpha]^{27}D$ +175° (*c* 0.85), after recrystallization from methanol. *Anal.* Calcd. for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found: C, 79.38; H, 10.12.

A solution of 185 mg. of the 12,20-diketone XX in 0.7 ml. of methylene chloride was mixed with 0.25 ml. of ethylene glycol and an equal quantity of boron trifluoride etherate.[23] After being in the dark at room temperature for 3 days, the mixture was diluted with ether, washed with sodium bicarbonate solution and water, dried, and evaporated. Crystallization from methanol containing 1 drop of pyridine gave 107 mg. of the **12-monoketal** XXI, m.p. 179–180°, $[\alpha]^{26}D$ +124° (*c* 1.0), $\lambda_{max}^{CHCl_3}$ 5.90 μ, ORD in methanol (*c* 0.21) $[\phi]_{305}^{peak}$ +7460°, $[\phi]_{267}^{trough}$ −4970°. *Anal.* Calcd. for $C_{23}H_{36}O_3$: C, 76.62; H, 10.06. Found: C, 76.57; H, 9.97.

A sample (100 mg.) of the 12-monoketal XXI was reduced with lithium aluminum deuteride (40 mg.) in 10 ml. of tetrahydrofuran (2 hr. at room temperature), the excess reagent was decomposed with water, the slurry was filtered, and the filtrate was evaporated to dryness. Purification of the residue by t.l.c. (benzene–ether–methanol 8.5:10:5) and recrystallization from methanol led to 84 mg. of 20α-d_1-5α-pregnan-20β-ol-12-one ethylene ketal (XXII), m.p. 127–129°, which exhibited no carbonyl absorption in the infrared. *Anal.* Calcd. for $C_{23}H_{37}DO_3$: C, 75.98; H, 10.53. Found: C, 75.92; H, 10.41.

The above alcohol XXII (70 mg.) was dehydrated by keeping at room temperature for 18 hr. with 1 ml. of pyridine and 0.2 ml. of freshly distilled phosphorus oxychloride. After concentration under reduced pressure, water was added and the product (XXIII) was extracted with ether. Cleavage of the ketal grouping had already occurred during that reaction as shown by the infrared band at 5.87 μ. The olefin mixture was hydrogenated overnight at room temperature and atmospheric pressure with 50 mg. of 10% palladized charcoal and worked up in the usual manner (see preparation of XII). Recrystallization from methanol yielded 22 mg. of 20-d_1-5α-pregnan-12-one (XXIV), m.p. 140–141°, of 84% isotopic purity (see Table I).

Δ9(11)-5α-Pregnen-12-one (XXVI). The selenium dioxide dehydrogenation[24] was performed under acid-catalyzed conditions[19] by heating under reflux overnight a solution of 177 mg. of 5α-pregnan-12-one (IV) in 5 ml. of acetic acid (6 × 10⁻⁴ *N* in hydrochloric acid) with 130 mg. of selenium dioxide. The filtered solution was concentrated under reduced pressure and the product was extracted with ether. Purification by preparative t.l.c. in benzene containing 5% of ether and recrystallization from methanol provided 155 mg. of the unsaturated ketone XXVI, m.p. 132–134°, $[\alpha]^{26}D$ +98°

(39) W. J. Adams, D. N. Kirk, D. K. Patel, V. Petrow, and I. A. Stuart-Webb, *J. Chem. Soc.*, **870** (1955).

(40) The Cotton effect of 17α and 17β isomers of 20-ketopregnanes is of opposite sign: C. Djerassi, *Bull. Soc. Chim. France*, 741 (1957).

(41) See D. H. Williams, J. M. Wilson, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, **85**, 2091 (1963).

(42) In a model experiment with ordinary (hydrogen-containing) Raney nickel, 5α-pregnan-12β-ol was isolated in 88% yield and recrystallized from methanol, m.p. 156–157.5°, $[\alpha]^{28}D$ + 27° (*c* 1.0).

(43) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).

(44) This experiment was performed prior to Caglioti's report[22] on the advantages of dioxane over methanol in such sodium borohydride reductions and was prompted by the observation (unpublished results from this laboratory) that the presently described conditions worked very well in the sodium borodeuteride reduction (in deuteriomethanol) of the tosylhydrazone of 5β-pregnan-3α-ol-20-one.

(*c* 1.0), λ_{max}^{EtOH} 240 mμ (ε 13,300), $\lambda_{max}^{CHCl_3}$ 6.02 and 6.25 μ. *Anal.* Calcd. for $C_{21}H_{32}O$: C, 83.94; H, 10.73. Found: C, 83.84; H, 10.80.

Introduction of deuterium was effected by heating 29 mg. of XXVI under reflux for 3 days with 5 ml. of deuteriomethanol which was saturated with a 20% solution of sodium deuterioxide in deuterium oxide. The 8β,11-d_2 analog XXVII (m.p. 132–134°) was isolated in nearly quantitative yield and according to mass spectrometry was of excellent isotopic purity (6% d_1, 94% d_2).

9α-d_1-5α-Pregnan-12-one (XXVIII). A suspension of 30 mg. of 10% palladized charcoal catalyst in 5 ml. of cyclohexane was stirred for 30 min. in an atmosphere of deuterium, followed by the addition of 14 mg. of $\Delta^{9(11)}$-5α-pregnen-12-one (XXVI) dissolved in 5 ml. of cyclohexane. After continued stirring for 2 hr., the total crude product was heated under reflux for 36 hr. with methanol containing a few drops of dilute sodium hydroxide solution in order to back exchange the 11-deuterium atom. Ether extraction and t.l.c. purification gave 9 mg. of 9α-d_1-5α-pregnan-12-one (XXVIII), m.p. 137–138° of 93% isotopic purity (see Table I).

8β-d_1-5α-Pregnan-12-one (XXIX). Catalytic hydrogenation in the usual manner (see preparation of XIII) of 27 mg. of 8β,11-d_2-$\Delta^{9(11)}$-5α-pregnen-12-one (XXVII) in methylcyclohexane solution followed by back exchange (10 hr. of reflux with methanolic sodium hydroxide solution) produced after t.l.c. purification and recrystallization from ethanol 19 mg. of XXIX, m.p. 140–141° (for isotopic purity see Table I).

5α-Androstan-12β-ol-17-one Acetate (XXXI). Δ^{16}-5α-Pregnen-12β-ol-20-one acetate (XII) was converted in 77% yield into the oxime XXX (m.p. 150–166° by direct crystallization from the diluted reaction mixture) by heating for 30 min. with hydroxylamine hydrochloride in ethanol–pyridine. The crude oxime (364 mg.) was subjected directly to Beckmann rearrangement[26,45] giving 266 mg. of the acetate XXXI with m.p. 137–140°. The analytical specimen crystallized from methanol and exhibited m.p. 142–143°, $[\alpha]^{23}D$ +35° (*c* 1.0). *Anal.* Calcd. for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.84; H, 9.48.

Saponification of the acetate XXXI with methanolic potassium hydroxide and recrystallization from methanol gave 5α-androstan-12β-ol-17-one (XXXVII), m.p. 156–157°, $\lambda_{max}^{CHCl_3}$ 2.80 and 5.75 μ. *Anal.* Calcd. for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41. Found: C, 78.18; H, 10.12.

5α-Androstan-12-one (XXXII). Wolff–Kishner reduction (see preparation of IV) of 5α-androstan-12β-ol-17-one acetate (XXXI) proceeded in 87% yield to afford 5α-androstan-12β-ol, m.p. 128–129°, $[\alpha]^{25}D$ +3° (*c* 1.2) after recrystallization from methanol. *Anal.* Calcd. for $C_{19}H_{32}O$: C, 82.54; H, 11.66. Found: C, 82.27; H, 11.39.

Jones oxidation[43] of the 12-alcohol and recrystallization from ethanol give the required ketone XXXII, m.p. 107–108.5°, $[\alpha]^{24}D$ +64° (*c* 1.0), $\lambda_{max}^{CHCl_2}$ 5.88 μ, ORD in methanol (*c* 0.14) $[\phi]_{307}^{peak}$ +4160°, $[\phi]_{265}^{trough}$ −2240°. *Anal.* Calcd. for $C_{19}H_{30}O$: C, 83.15; H, 11.01. Found: C, 83.22; H, 10.89.

Base-catalyzed equilibration at C-11 was performed in the same manner as described for XVII to give 11,11-d_2-5α-androstan-12-one (XXXIII), m.p. 104–105°, of 92% isotopic purity (see Table II).

8β-d_1-5α-Androstan-12-one (XXXVI). The conversion of 5α-androstan-12-one (XXXII) into $\Delta^{9(11)}$-5α-androsten-12-one (XXXIV) was accomplished in 88% yield by base-catalyzed (pyridine in *t*-butyl alcohol) treatment[46] (10 days of reflux) with selenium dioxide. Recrystallization from methanol led to colorless leaflets of XXXIV possessing m.p. 115–116°, λ_{max}^{EtOH} 238 mμ (ε 12,500), $\lambda_{max}^{CHCl_3}$ 6.00 and 6.25 μ. *Anal.* Calcd. for $C_{19}H_{28}O$: C, 83.77; H, 10.36. Found: C, 83.37; H, 10.15.

Deuterium was introduced into the 8β and 11 positions of XXXIV in the same manner as described above for the pregnene derivative XXVII and afforded 8β,11-d_2-$\Delta^{9(11)}$-5α-androsten-12-one (XXXV) consisting of 96% d_2 and 4% d_1 species. Catalytic hydrogenation with palladized charcoal catalyst and back exchange with methanolic sodium hydroxide as recorded above for the corresponding pregnane XXIX gave in 65% over-all yield the desired 8β-d_1-5α-androstan-12-one (XXXVI) (m.p. 103–104°) of 97% isotopic purity (see Table II).

17,17-d_2-5α-Androstan-12-one (XXXIX). The conversion of 5α-androstan-12β-ol-17-one (XXXVII) into the 17-ethylene mercaptal XXXVIII was accomplished in 83% yield by exactly the same procedure employed for the preparation of XV. After recrystallization from aqueous methanol, the mercaptal XXXVIII exhibited m.p. 119–120° and lacked carbonyl absorption in the infrared. *Anal.* Calcd. for $C_{21}H_{34}OS_2$: C, 68.79; H, 9.35. Found: C, 68.66; H, 9.11.

The desulfurization was performed in the same manner as described for the analogous transformation in the pregnane series (XV → XIX) and was also accompanied by extensive isotopic scrambling as shown in Table II for the ketone XXXIX (m.p. 105–106° after t.l.c. purification and recrystallization from methanol) which resulted from Jones oxidation[43] of the intermediate 5α-androstan-12β-ol.

(45) See D. N. Kirk and V. Petrow, *J. Chem. Soc.*, 2091 (1961).

(46) A. Bowers, E. Denot, M. B. Sanchez, F. Neumann, and C. Djerassi, *ibid.*, 1859 (1961).

The Reactions of Triplet NH with Olefins

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Abstract: Reactions of several hydrocarbons (ethylene, ethane, methane, butene-1, heptene-3, and 2,3-dimethylbutene-2) with triplet NH were studied. The NH was produced by both flash and steady photolysis of HN_3; DN_3 also was used. Both flash kinetic absorption spectroscopy and product analysis were used to establish the mechanism of the reaction of triplet NH with olefins. The principal nitrogen-containing product (aside from N_2 itself) was CN, then HCN when the reaction conditions were adiabatic, and HCN and alkylnitriles when the conditions were isothermal. In the latter case, the reaction apparently involves a vibrationally equilibrated alkylnitrene. A rough estimate of the rate constant for bimolecular addition of $NH(^3\Sigma^-)$ to C_2H_4 is 10^7 l./mole sec.

The reactions of NH with ethylene and other simple olefins offer a tantalizing means for the study of simple gas-phase reactions. This applies both to the specific study of imine and nitrene formation and to the more general problem of skeletal bond formation. The NH can be prepared readily by steady or flash photolysis. With the latter procedure, the absorption spectrum of NH itself becomes a convenient detection probe; conceivably one can also observe spectra of

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