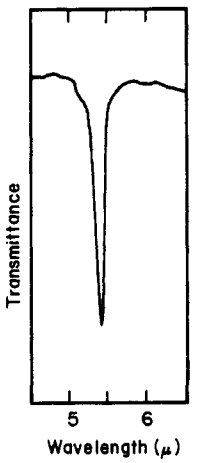
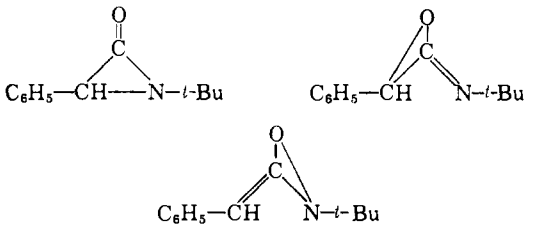


Fig. 1.—Infrared spectrum of 1-*t*-butyl-3-phenylaziridinone (in pentane solution).

as noted previously, the evidence accumulated to date cannot eliminate the alternative structures



(valence tautomers) or some more highly delocalized structure.[1,6] Probably no chemical technique would suffice to distinguish between the valence tautomers (if they exist independently as such) because of the ever-present possibility of interconversion prior to or during reaction. Nevertheless, the isolation of III of analytical and spectroscopical purity encourages one to think that its structure may be more rigorously defined by more sophisticated physical techniques (*e.g.*, X-ray analysis). The latter as well as the preparation and reactions of analogs of III are under study.

(6) See A. W. Fort, *J. Am. Chem. Soc.*, **84**, 2620 (1962), for references to the related problem of the structure of the intermediate in the Favorski reaction.

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RECEIVED NOVEMBER 5, 1962

C(19)-SUBSTITUTED STEROIDS. IV.[1] STUDIES OF LONG RANGE SHIELDING BY THE CARBONYL GROUP WITH NUCLEAR MAGNETIC DOUBLE RESONANCE AND NUCLEAR MAGNETIC TRIPLE RESONANCE AT 100 MC.

Sir:

We wish to report the examination of 3,3-dimethoxy-2β,19-epoxy-5α-androstan-17β-ol[1] I, 2β,-17β-dihydroxy-3,3-dimethoxy-5α-androstan-19-oic acid 2,19-lactone II,[1] and 2β,19-epoxy-5α-cholestan-3-one[1] III by n.m.r. spectrometry and the demonstration of long range shielding effects of the carbonyl

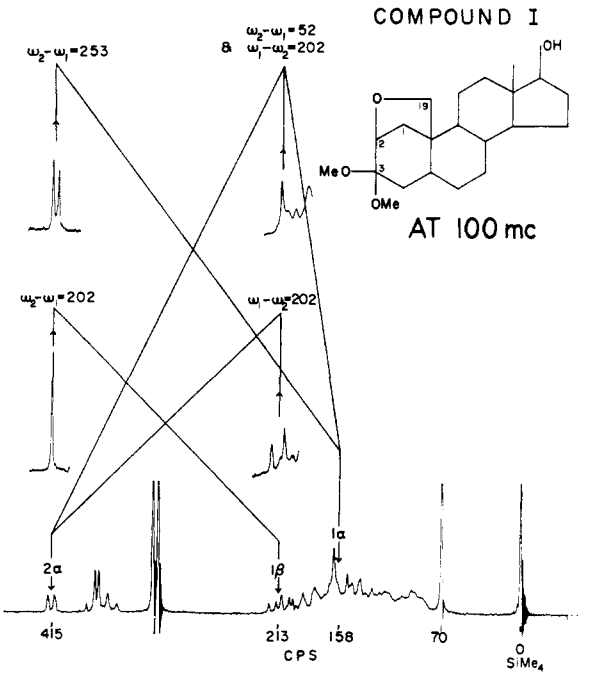

Fig. 1a.

group[2] in II and III by double resonance (n.m.d.r.)[3 a-f] and triple resonance (n.m.t.r.) techniques using Varian HR-100 spectrometer. These experiments were performed by modifying[4] the Varian-3521 integrator by breaking connection between modulation output and the probe sweep coils and inserting a 0.01 μfd capacitor, then the modulation index of 1.8 is reduced to a much lower number. Ordinary absorption spectra then are obtained by using either upper or lower 2 kc. (ω_1) sideband. By connecting an audio-oscillator to either the r.f. unit or the sweep coils additional field modulation at a variable frequency (ω_2) can make a portion of the r.f. power available for selective nuclear saturation and hence spin–spin decoupling or double resonance (n.m.d.r.). Similarly triple resonance (n.m.t.r.) was accomplished by using an additional oscillator. When operating on the lower 2 kc. sideband, protons whose chemical shifts are at higher applied field than those to which they are coupled may be decoupled by getting $\omega_2 - \omega_1$ approximately equal to the separation of the signals being decoupled. The frequency difference between ω_2 and ω_1 is not exactly equal to the chemical shift difference of the two groups of spin-coupled nuclei[5] although in general this discrepancy is small. The n.m.r. spectra are shown in Fig. 1 and the pertinent resonance values and coupling are given in Table I. All the samples were run as $CDCl_3$ solutions with tetramethylsilane added to act as an internal reference.

(1) Paper III in this series: R. Kwok and M. E. Wolff, *J. Org. Chem.*, in press. This investigation was supported in part by a PHS research grant (A-5016) from the National Institute of Arthritis and Metabolic Diseases, United States Public Health Service.

(2) Y. L. Crombie and J. W. Lown, *Proc. Chem. Soc.*, 299 (1961).

(3) (a) A. L. Bloom and J. N. Shoolery, *Phys. Rev.*, **97**, 1261 (1955). (b) W. A. Anderson, *ibid.*, **102**, 151 (1956). (c) J. D. Baldeschwieler, *J. Chem. Phys.*, **36**, 152 (1961). (d) J. P. Maher and D. F. Evans, *Proc. Chem. Soc.*, 208 (1961). (e) V. Royden, *Phys. Rev.*, **96**, 534 (1954). (f) R. Freeman and D. H. Whiffen, *Mol. Phys.*, **4**, 321 (1961).

(4) Varian Technical Information Bulletin, Vol. III, No. 3, ins. 1471.

(5) W. A. Anderson and R. Freeman, *J. Chem. Phys.*, July 1 (1962).

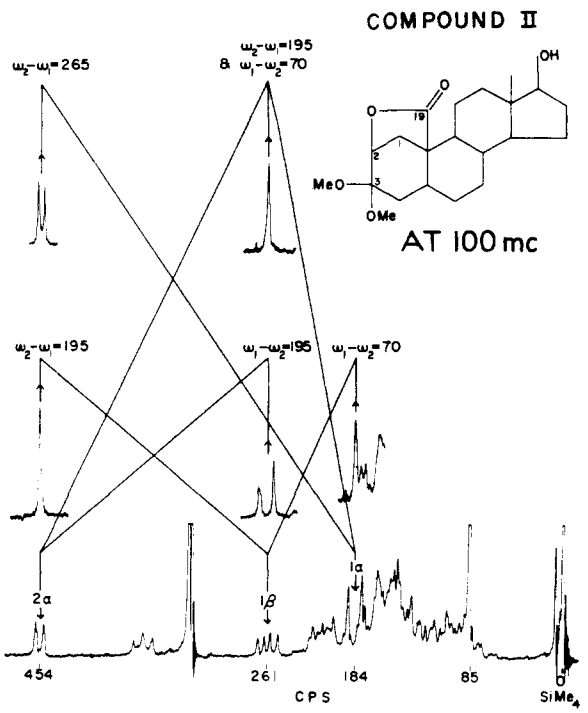

Fig. 1b.

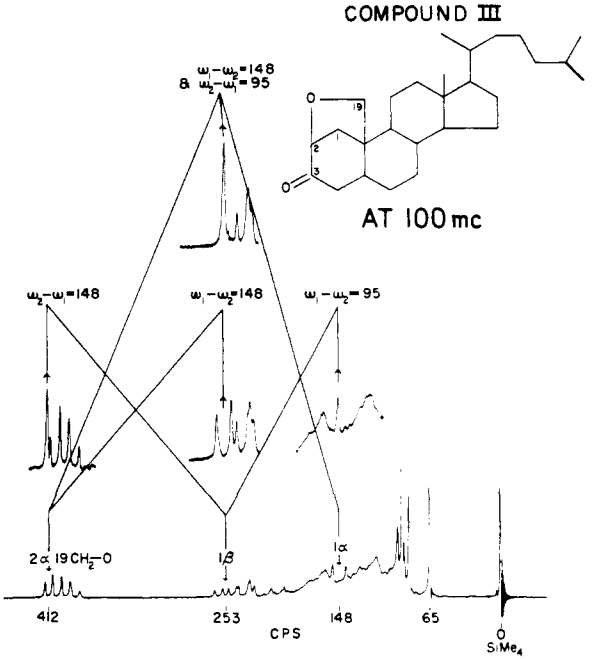

Fig. 1c.

Three principal regions are of interest. The signals at $\delta = 4.12$ in the spectrum of Compound III arise from the 2α-H spin coupled to the 1β-H as shown by n.m.d.r.; the 1α-H is virtually uncoupled from the 2α-H owing[6] to a dihedral angle

TABLE I

CHEMICAL SHIFT (P.P.M.) VALUES AND SPIN COUPLINGS (C.P.S.) FOR STEROID DERIVATIVES

Compound	2α-H	1β-H	1α-H	C.P.S. $J_{2\alpha \text{ and } 1\beta}$	C.P.S. $J_{2\alpha \text{ and } 1\alpha}$	C.P.S. $J_{1\alpha \text{ and } 1\beta}$
I	4.15	2.13	1.58	7	1	12
II	4.54	2.61	1.84	7	1	12
III	4.12	2.53	1.48	7	..	12

of approximately 90° (Courtauld models) between the atoms. In the case of Compounds I and II this proton appears as a pair of doublets at $\delta = 4.15$ and 4.54, respectively. Here the dihedral angle between 2α-H and 1α-H is somewhat greater than in III. A pair of doublets at $\delta = 2.13$, 2.61 and 2.53 in the spectra of Compounds I, II, and III, respectively, is due to the 1β-H spin-coupled to both the 1α-H and the 2α-H. This multiplet collapsed to a doublet on double irradiation at the 1α-H frequency, whereas a singlet resulted in the n.m.t.r. experiment.

The position of the 1α-H resonance was uncertain because of nearby signals from other protons. However, its location was uniquely determined by double irradiation at the frequency of the 2α-H, which caused the 1α-H doublet to degenerate to a singlet. The chemical shift between the 1α-H and the 1β-H in II and III is too large to be explained in terms of the axial and equatorial conformations of these protons, but this is not the case in I, in which $\delta\beta$ is of the expected magnitude for such a pair. These data indicate that the carbonyl group at C(19) or C(3) exerts a long range negative shielding effect on the equatorial 1β-H, and the axial 1α-H, in Compound II, but not on axial 1α-H in Compound III. This phenomenon is in harmony with the previously described[7] approximation of the long range shielding effect of the carbonyl group. In conventional steroids, the methyl protons at C(19) are located in an approximately geometrically equivalent position relative to the C(3) carbonyl group as the 1β-H in Compound III. And therefore the displacement of the resonance due to the C(19) protons in a 3-oxosteroid to lower field by 0.15 p.p.m.[8] can be explained in a similar way.

(9) M. Karplus, *J. Chem. Phys.*, **30**, 11 (1959).

(7) L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon, New York, N. Y., 1959, p. 124.

(8) J. N. Shoolery and M. T. Rogers, *J. Am. Chem. Soc.*, **80**, 5121 (1958).

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RECEIVED SEPTEMBER 17, 1962

THE STABILIZATION TOWARD TEMPERATURE OF THE HELICAL CONFORMATION OF COPOLYPEPTIDES OF L-GLUTAMIC ACID AND L-LEUCINE: AN INVERSE TEMPERATURE EFFECT

Sir:

The investigation of the forces responsible for conformational stability of proteins and polypeptides has, in recent years, led to the hypothesis that hydrophobic forces play an important role in