# Nuclear Magnetic Resonance for the Reversible Stereospecific Protonation of Steroidal α-Diazo-ketones

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MOHRIG and KEEGSTRA[1] recently reported the $^1H$ and $^{19}F$ n.m.r. spectra of 2,2,2-trifluoroethyldiazonium ion in $FSO_3H$ solution at −60°. On warming the solution to −20°, they observed evolution of nitrogen and disappearance of the signal due to the diazonium ion.

We performed similar experiments with 2-diazo-5α-cholestan-3-one (Ia)[2,3] and 2-diazo-4,4-dimethyl-5α-cholestan-3-one (Ib),[4] in order to check by physical methods the results we obtained chemically.[3,4] In the mixture $FSO_3H$–$CDCl_3$–$SO_2$, both (Ia) and (Ib) exhibit a new signal at *ca.* 93 p.p.m. (corresponding to one proton), which may be ascribed to the protonated diazo-ketone system.

At −70°, the half-band width is about 5 Hz [4 Hz for the deuteriated ketone (Ic)]. On warming the solution, the signal becomes broader to the point that it is hardly detectable at −30°.

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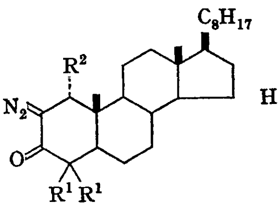
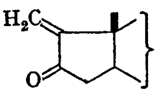
(Figure 1). There is, however, *no* nitrogen evolution, and the signal is restored to its original shape on cooling to −70°. By careful neutralisation of the solutions with potassium carbonate in methanol, both diazo-ketones (Ia) and (Ib) can be recovered quantitatively. These results clearly indicate that protonation of the diazo-ketones is reversible under these conditions, and agree with the conclusions derived from kinetic measurements by Dahn and Gold[5] for α-diazo-ketones, and by Zwanenburg and Engberts[6] for α-diazo-sulphones. Jugelt and Schmidt[7] and Engberts, Bosch, and Zwanenburg[8] described kinetic evidence for a rate-determining protonation in the hydrolysis of PhC⁚N:N·CO·Ph and of 2-diazoacenaphthenone, but their substrates are obviously very different from ours.





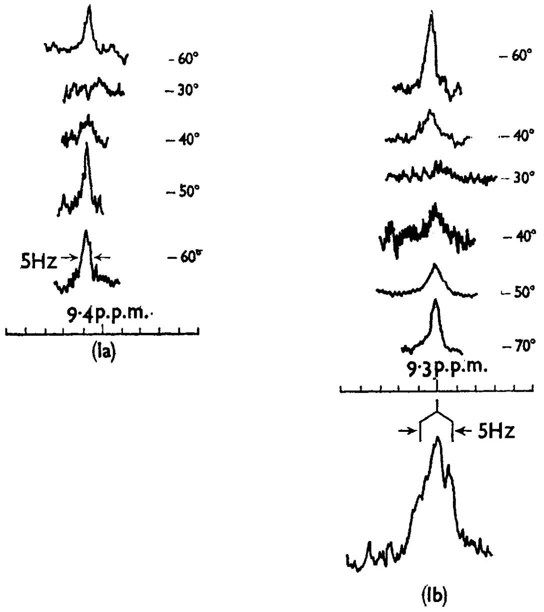
(II)

(I) a; $R^1$=$R^2$=H
b; $R^1$=Me,$R^2$=H
c; $R^1$=Me,$R^2$=D

Three protonation sites can be envisaged: oxygen, carbon, or terminal nitrogen. Oxygen can probably be excluded because the new proton shows up at much higher field (9·3 p.p.m.) than expected[10] for a proton linked to a carbonyl oxygen (15 p.p.m.).‡

Protonation on nitrogen was not observed by Mohrig and Keegstra[1] in the case of $CF_3CHN_2$. In the present case, the signal at 9·3 p.p.m. becomes broader as the temperature is raised from −70° to −30°; this is taken as an indication that proton exchange is slow at −70°, but fast at −30° (*cf.* ref. 10). This broadening is exactly opposite to what has been observed for protons linked to nitrogen,[11] and makes it unlikely that protonation should occur on nitrogen.

Moreover, the half-band width (5 Hz) at −70° is much smaller than that expected from $^{14}N$ quadrupolar relaxation. The fact that the chemical shift (9·3 p.p.m.) closely approximates to that of an immonium ion (*ca.* 9·7 p.p.m.)[12]§ might well be a coincidence, because in immonium ions, nitrogen is $sp^2$ hybridized, whereas it is $sp$ hybridized in diazo-ketones protonated on nitrogen. In the view of the well known difference in chemical shift between ethylene and acetylene,[13] a nitrogen-protonated species would be expected to give a signal at higher field.



FIGURE

*Left: Signal of the* C-2 *proton of* (Ia) (*sweep width:* 0·5 *Hz/mm. at* 60 *MHz*) *from* −60° (*bottom*) *to* −30° *and back to* −60° (*top*).

*Right: Signal of the* C-2 *proton of* (Ib) (*sweep width:* 0·5 *Hz/mm. at* 60 *MHz*) *from* −70° (*bottom*) *to* −30° *and back to* −60° (*top*).

*Bottom right: Signal of the* C-2 *proton of* (Ib) (*sweep width:* 2 *Hz/mm. at* 60 *MHz*) *showing the triplet shape.*

If these arguments are accepted, the half band width of the signal (5 Hz) in both (Ia) and (Ib), at −70°, means that protonation occurs from the α-side (protonation from the β-side would be expected to give a doublet of doublets with *J ca.* 3 and 12 Hz). This is in full agreement with what is known about the kinetic bromination of enols in these series.[14–16]

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‡ With diazo-ketone (Ia), an additional allylic coupling with the C-4 protons would be expected[10] to broaden further the signal at 9·4 p.p.m. As this signal has the same half-band width in the spectra of both (Ia) and (Ib), protonation on oxygen is regarded as unlikely at −60°.

§ We thank a referee for bringing to our attention this possible objection.

At higher temperatures (−30°) fast proton exchange may lead partly to the thermodynamically more favourable $\beta$-protonation, thus accounting for the products.[3,4]

At low temperature, the protonation thus seems both reversible and highly stereoselective. Chemical evidence pertaining to this conclusion will be published later.[4]

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