The Nitration of Glycyrrhetic Acid

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ONLY a few α-*gem*-dinitro-ketones have been described,[1,2] and were found to be unstable compounds, obtained in small yield. It was surprising, therefore, to find that both glycyrrhetic acid (I) and the corresponding 3-ketone gave the α-*gem*-dinitro-ketone (III) in about 70% yield on treatment with an excess of nitric acid in dioxan or acetic acid, the reaction being completed in a few minutes at 80° or several weeks at room temperature.

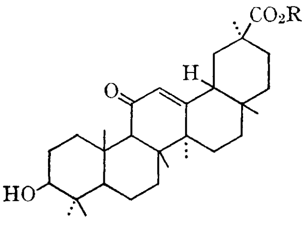
Acetylglycyrrhetic acid was scarcely affected under these conditions, so the reaction was probably confined to ring A. $18\beta\rightarrow18\alpha$-Isomerisation did not take place since the 18α-acid gave a product which could reasonably be assumed to differ from (III) only in the configuration at C-18. Compound (IV) was obtained by nitration of (II) or by esterification of (III) with diazomethane.

Although very stable to acids, (III) was instantly hydrolysed by cold aqueous sodium carbonate to (V). Surprisingly, if methanol was also present, the monomethyl ester (VI) was the major product. The dinitromethyl group formed during these reactions was readily recognised by its behaviour as a strong acid and the characteristic colour of the corresponding nitronitronate anion. Both (V) and (VI) gave, with diazomethane, the same dimethyl ester (VII). In pyridine–acetic anhydride (III) was reformed from (V).

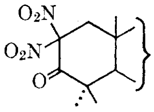
Compounds (III)—(VII) all absorbed strongly in the infrared at 1580 ± 10 cm.$^{-1}$ and 1325 ± 10 cm.$^{-1}$, characteristic[3] of *gem*-dinitro-groups, and they also showed the requisite absorption for the various carbonyl functions [*e.g.*, at 1721, 1695, and 1654 cm.$^{-1}$ for (III) and 1710, 1690, and 1642 cm.$^{-1}$ for (V)].

Whilst these observations, together with supporting analytical data, served strongly to suggest the structures shown, n.m.r. (60 and 100 Mc./sec., $CDCl_3$) confirmed them. The C-1 protons of (IV) gave rise to two doublets at τ 5·8 and 6·9 (J = 17 c./sec.) and the dinitroethyl group of (VII) was revealed by a well defined AMX pattern having three pairs of doublets centred at τ 3·45, 6·45, and 7·74 [J = 17·0 (*gem*), 8·4, and 2·0 c./sec.]. These systems were uncoupled as appropriate under the indicated double resonance conditions.

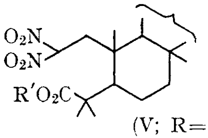
The ultraviolet and light absorption data were of interest since they appeared to reveal an interaction between the enone and the dinitromethyl group. Thus, both (II) and (III) behaved normally (λ_{max} 249 mμ, ϵ_{max} 12,000, in methanol) and the absorption of (II) was unchanged by the addition of alkali [(III) was hydrolysed]. The dimethyl ester, (VIII), however, had λ_{max} 252 mμ, ϵ_{max} 10,500 and, in methanolic alkali, λ_{max} 242 mμ, ϵ_{max} 16,600, and λ_{max} 396 mμ, ϵ_{max} 14,900, this latter wavelength being longer by some 20 mμ than the wavelength of maximum absorption of simple alkyl nitronitronates.



(I; R=H)
(II; R=Me)



(III; R=H)
(IV; R=Me)



(V; R=R'=H)
(VI; R=H, R'=Me)
(VII; R=R'=Me)

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