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NOVEL RING FRAGMENTATION PRODUCTS VIA DIAZIRINES AND ITS CONVERSION TO A-NOR STEROIDS

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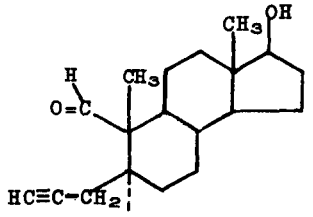
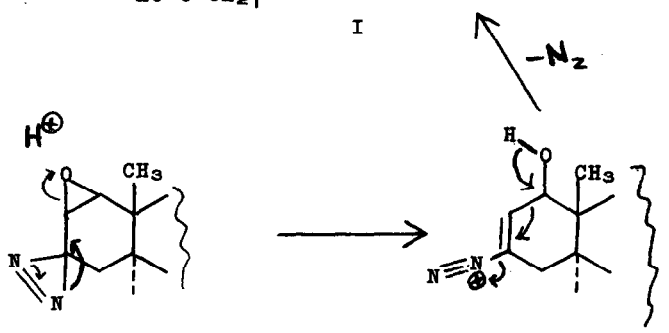
The recent reports on epoxyketone ring openings to form acetylenic ketones[1] prompts us to report our findings on steroid diazirine derivatives.[2]

When 1,2-epoxy-3-diazirine-5α-androstan-17-β-ol [mp 134-136° (d)] was treated with iodide-acetic acid[3] conditions for removal of the oxide protective function,[4] a crystalline substance (I, mp 132-136°) containing no nitrogen was obtained in about 60% yield. The substance was also obtained just after solution of the 1,2-epoxy-3-diazirine compound in acetic acid or refluxing in ethanol. Subsequent analysis (C = 78.95%, H = 9.83%, $C_{18}H_{28}O_2$) by IR [1725 cm^{-1}, 2110 cm^{-1}, and 2690 cm^{-1}) and NMR [44(18-H,s) 56(19-H,s) 220(17-H,t) 558(aldehydic H,s)cps] indicated structure to be the aldehyde acetylene derivative II, possibly resulting by a cationic process as shown below.

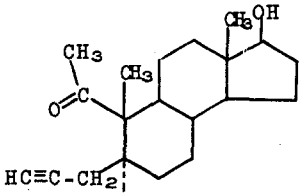


I

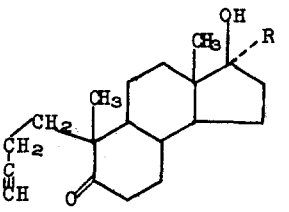


It is known that pyrolytic treatment of 3-diazirines yields the corresponding Δ^2-steroids[5] probably via the carbene.

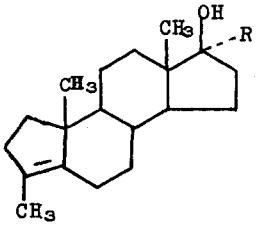
Similarly, 1-methyl-1,2-epoxy-3-diaziridine-5α-androstan-17β-ol (mp 178-181°) under acidic oxidation conditions and 4,5-epoxy-3-diazirine-17α-methyl-androstan-17β-ol [mp 120-122° (d)] upon treatment for oxide removal or acetic acid alone provided the corresponding ketones II {mp 161-163°; IR (1725 cm^{-1}, 2110 cm^{-1}, 3300 cm^{-1}); NMR [44(18-H,s) 58(19-H,s) 129(methyl ketone,s) 220(17-H,t) cps]} and III [amorphous, IR (1700 cm^{-1}, 2110 cm^{-1}, 3300 cm^{-1})] in 45-70% yields.



II



III R = CH_3
IIIa R = H



IV R = CH_3
IVa R = H

Compound IIIa was recently reported (mp 74-78°) to be isolated from a thermal treatment of the tosylhydrazone of the corresponding epoxy keto steroid.[1a] We had extended the diaziridine synthesis to models like the oxides of isophorone [bp 78 (0.5 mm)]; 3-methyl cyclohexenone (mp 88-90°); and $\Delta^{1,9}$-10-methyl-2-octalone (amorphous, dec at 135°) for conversion to the fragmentation products but utility of the reported procedure[1] is much simpler in operation.

Further extension of these novel terminal acetylene derivatives in the Li-NH_3 cyclization procedure described by Stork[6] were investigated. When compound III was reduced with the Li-NH_3-THF-NH_4Cl conditions, the inter-

mediate exomethylene hydroxy analog (mp 149-150°; C: 76.92%, H: 10.45%, $C_{20}H_{32}O_2$, 0.5 CH_3OH; IR: 3060 cm^{-1}, 1655 cm^{-1}, and 890 cm^{-1}) was isolated in 35% yield as well as the A-nor derivative IV (18%) [mp 130-132°; C: 83.07%, H: 11.09%, $C_{20}H_{32}O$; IR: no exocyclic methylene bands; λ_{max}: 205 mμ (ϵ 7,900); NMR: 53(18-H,s) 55(19-H,s) 73(17-H,s) 95(3'-H,s) cps].

When keto compound IIIa was similarly reduced, the corresponding (IVa) A-nor steroid (mp 121-123°; C: 83.06%, H: 10.98%, $C_{19}H_{30}O$, IR: 1640 cm^{-1} no exocyclic methylene bands) [λ_{max} 205 mμ, (ϵ 8,500), NMR: 45(18-H,s) 54(19-H,s) 94(3'-H,s) 218(17-H,t) cps] was obtained in 32% overall yield.

Biological studies of these novel steroids are in progress.

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3. B. Camerino, B. Patelli, and A. Vercellone, J. Am. Chem. Soc., 78, 3540 (1956). Experimental details were not provided in the reference. Our procedure involved dissolving the epoxide (1 mmole) in 15 ml acetic acid and adding to it at 0° and with stirring a solution of 10 mmole of sodium iodide and 1 mmole of sodium acetate in 2 ml of water and 15 ml of acetic acid. The reaction was worked up after 24 hours at 0°.
4. The diazirine function is stable and recoverable under these conditions.
5. See 1b and Novo, Neth. Appl. 6,607,160, Derwent 24079 (11/28/66), Chem. Abs. 67, 310.
6. G. Stork, S. Malhotra, H. Thompson, and M. Uchibayashi, J. Am. Chem. Soc. 87, 1148 (1965).