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REACTIONS OF BICYCLOBUTANES WITH HEXAFLUOROACETONE

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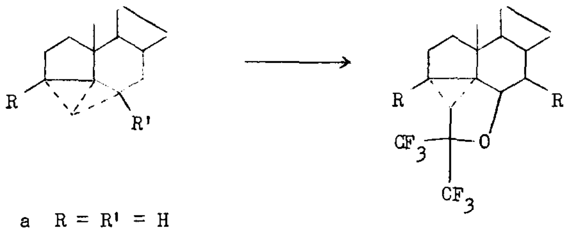
Bicyclobutanes have been shown to exhibit strong nucleophilic character towards suitable electrophilic reagents such as protons, aldehydes and ketones (1 - 4). We wish to report some novel electrophilic reactions of steroidal bicyclobutanes I a-c which were obtained from the photolyses of the appropriately substituted cholesta-3,5-diene in anhydrous pentane in a helium atmosphere (4)[+], with hexafluoroacetone.

Hexafluoroacetone reacted with bicyclobutane Ib to give a 1:1 adduct in 54% yield (m.p. 109 - 110°) which was assigned the structure IIb based on the following evidence: The adduct showed a low field triplet at 4.55 p.p.m. in the NMR spectrum, peaks at 3030, 1250-1050 cm^{-1} in the IR spectrum indicating cyclopropyl and ether groups. The absence of peaks in the region 1800 - 1650 cm^{-1} was indicative that the carbonyl group was not present. The low resolution fluorine



IIb

I a R = R' = H

b R = CH_3, R' = H

c R = H, R' = CH_3

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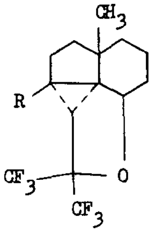
[+] Solutions (100 ml.) containing 0.3% diene in pentane were irradiated for 12 hours in a Rayonet Photolysis chamber with 2537 Å low pressure mercury lamps.

magnetic resonance spectrum of IIb showed two quartets with coupling constant J = 10 Hz indicative of the $CF_3 - C - CF_3$ group. The signal corresponding to the C-3 methyl group was obscured by methylene absorptions of the steroid skeleton, and in order to observe the appearance of this signal the analogous adduct IIIa was prepared from the reaction of the bicyclobutane derived from 3,10-dimethyl-3,5-hexalin with hexafluoroacetone.

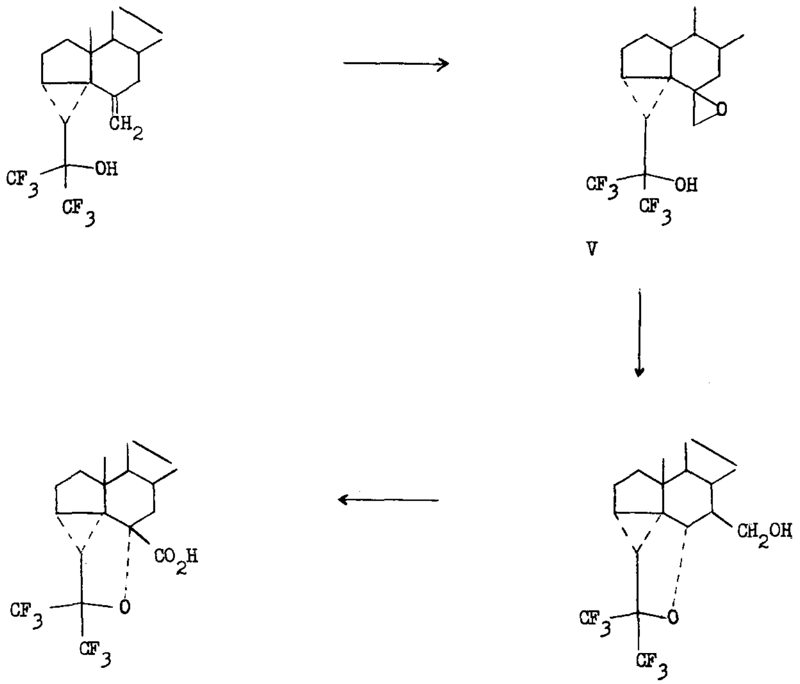


III a $R = CH_3$

b $R = CD_3$

The proton NMR spectrum of IIIa showed a singlet at 0.90 p.p.m. corresponding to the C-10 methyl group and a quartet at 1.30 p.p.m. (J = 2 Hz) that could be attributed to the C-3 methyl group. In order to prove that the quartet corresponded to the C-3 methyl group, the adduct IIIb was prepared from photolysis of 10-methyl-3-trideutero methyl-3,5-hexalin and addition of hexafluoroacetone. The proton NMR spectrum of IIIb was identical with that of IIIa except the quartet at 1.30 p.p.m. was absent. The appearance of this quartet in the NMR spectrum of IIIa indicated that the C-3 methyl group was coupled to one of the trifluoromethyl groups. To ascertain this, the high resolution fluorine magnetic resonance spectrum of IIIa and IIb showed that one of the quartets was further split into a quartet of quartets (J = 2 Hz). Such long range H - F coupling has been observed in several cases (5 - 7).

Reaction of bicyclobutane Ic with hexafluoroacetone gave IV as an oil. Its structure was based on spectral and analytical data along with the following chemical evidence: Ozonolysis of IV in chloroform gave a 3:1 mixture of epoxide V and alcohol VI. The identical epoxide V was prepared by peracetic acid oxidation of IV in chloroform. The epoxide V was converted to VI upon acid catalyzed hydrolysis. Jones oxidation of epoxide VI gave the carboxylic acid VII as an oil in quantitative yield.

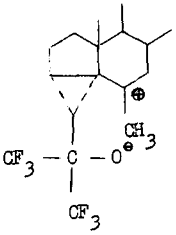


IV

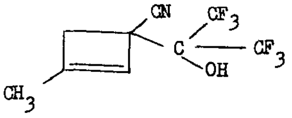
V

VII

VI



VIII



IX

Evidence that IV is a primary product and not a product derived from an intermediate IIc was found by T L C monitoring of the reaction mixture during addition of hexafluoroacetone. It seems unlikely that IIc spontaneously rearranges to IV when IIa is stable under extreme acidic conditions. The formation of IV can be rationalized by postulating a zwitterion VIII which can undergo the "ene" reaction quite readily due to the proximity of the oxide anion to the C-6 methyl group suggested by models.

Reaction of bicyclobutane Ia with hexafluoroacetone yielded the adduct IIa as a minor constituent. The major component was an oxidation product ($C_{30}H_{44}O_2F_6$) which was not further characterized. This may have resulted from oxidation during work-up of the reaction mixture.

It has been reported (8) that 3-methylbicyclobutane carbonitrile reacts with hexafluoro acetone to give the "ene" product IX. The absence of 1,3- additions of steroidal bicyclobutanes suggests that the transition states involving 1,3 cleavage reactions in these derivatives are highly improbable as is evident from Dreyding models.

Acknowledgements

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