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Acid-catalysed decomposition of (20 R) and (20 S)-20-azido-5α-pregnane : *bis* steroid Schiff base formation *via* imine coupling.

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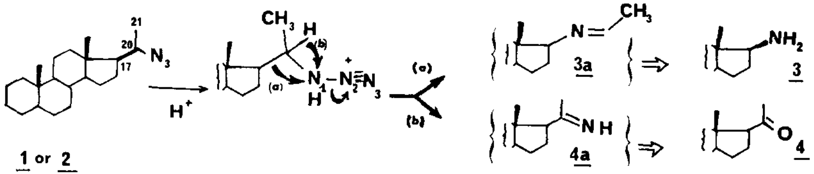
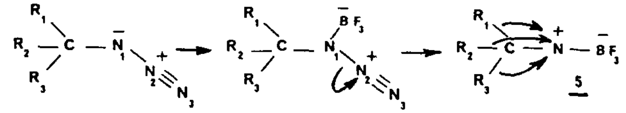
Summary : BF_3-OEt_2 decomposition of azides 1 or 2 leads to the coupling product Schiff base 6 *via* imine intermediates.

Sulfuric acid decomposition of steroid azides[1] involves the protonation of N_1 followed by the migration of the substituent antiparallel to the N_1-N_2 bond, a concerted process with loss of nitrogen. Treatment of the title compounds 1 or 2 with H_2SO_4 gave 17β-amino-5α-pregnane 3 and 20-oxo-5α-pregnane 4 (3:4 = 1:1). Methyl migration was not observed. Protonic acid decomposition of azides did not involve the nitrenium intermediate[2,3]. In the decomposition of alkyl azides with aluminium chloride "nitrenium ions have been trapped for the first time" by Kreher and Jäger[4]. Thus, it was reasonable to consider that the use of BF_3-OEt_2, for the decomposition of alkyl azides, could lead to the nitrene-complexed 5 (Scheme 2), in which the axial symmetry allowed the migration of all substituents R_1, R_2, R_3.

Scheme 1

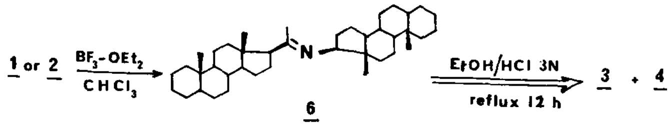


Scheme 2

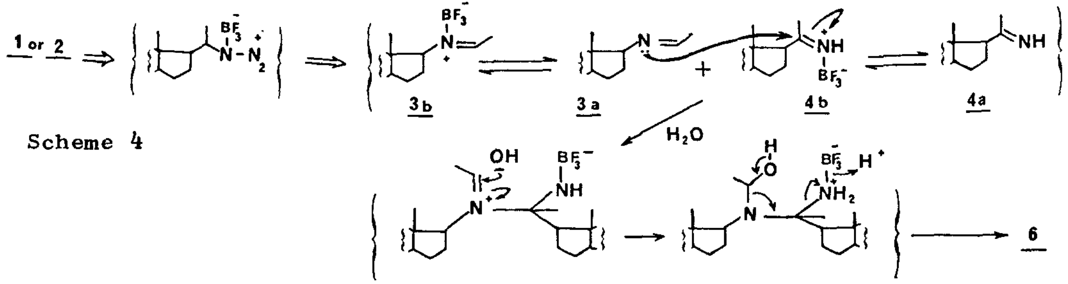


However, treatment of azide 1 or 2 with BF_3-OEt_2 in $CHCl_3$, did not give the imine corresponding to the methyl migration but led instead to the crystalline compound 6, (74%) mp. 286°C ; IR(nujol) 1650 cm^{-1} ; $M^{+\cdot}$ = 559, m/e 328 (base peak) ; analysis for $C_{40}H_{65}N$: found : C 85.45, H 11.9, N 2.61, calcd. : C 85.79, H 11.70, N 2.50, identical in all aspects to the bis-steroid Schiff-base obtained by the photolysis of the azide 1 or 2[6]. Acid hydrolysis of 6 (EtOH/HCl 3N, reflux, 3h) led to the amine 3 and the ketone 4 (Scheme 3).

Scheme 3



The mechanism proposed for the formation of 6 involved nucleophilic attack of the imine 3a on the iminium complex 4b (Scheme 4).



Scheme 4

This phenomenon is analogous with a *trans*-imination[7]. Basic extractive conditions[8] allowed the formation of the Schiff base 6. To our knowledge, coupling products were not previously described in protonic or Lewis acid catalysed decomposition of azides[9]. Different results from H_2SO_4 and BF_3-OEt_2 catalysed decomposition of azides is due to the anhydrous medium with BF_3-OEt_2 which inhibits hydrolysis of the imines 3a and 4a and favoured the coupling reaction between these imines.

The use of BF_3-OEt_2 in this reaction did not provide evidence for a nitrene-complexed intermediate. The mechanism of the formation of the imine intermediates 3a and 4a from azides could involve a concerted process with loss of nitrogen, irrespective of whether protonic acid or BF_3-OEt_2 is employed.

References :

[1] A. Pancrazi and Q. Khuong-Huu, Tetrahedron, 31, 2049 (1975).

[2] J.H. Boyer, F.C. Canter, J. Hamer and R.K. Putney, J. Amer. Chem. Soc., 78, 325 (1956).

[3] T. Curtius and A. Darapsky, J. Prakt. Chem., 2 63, 428 (1901) ; Ber., 35, 3229 (1902) ; K.W. Sherk, A.G. Houpt and A.W. Brown, J. Amer. Chem. Soc., 62, 329 (1940).

[4] R. Kreher and J. Jäger, Angew. Chem. Int. Ed. Engl., 4, 952 (1965).

[5] A solution of azide 1 or 2 (1.6 mmol, 520 mg) in $CHCl_3$ (5 ml) was stirred 24 h with BF_3-OEt_2 (40 mmol), then made basic with aqueous 10% NaOH and extracted with $CHCl_3$ to give 320 mg of 6 (74%).

[6] A. Pancrazi and Q. Khuong-Huu, Tetrahedron, 31, 2041 (1975).

[7] K. Koehler, W. Sandström and E.H. Cordes, J. Amer. Chem. Soc., 86, 2413 (1964).

[8] Treatment of azide 1 or 2 with BF_3-OEt_2, without addition of aqueous NaOH at the end of the reaction, afforded neither Schiff base 6 nor the complex obtained by treatment of 6 with BF_3-OEt_2. Basic hydrolysis was the final step in the formation of 6.

[9] Abramovitch has observed some coupling product in thermolysis of azide. R.A. Abramovitch in Organic Reactive Intermediates, S.P. McManus Editor, Academic Press, New York and London, p. 139 (1973).

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