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A PUMMERER TYPE REARRANGEMENT DURING ATTEMPTED OXIDATION WITH DIMETHYL SULFOXIDE AND DICYCLOHEXYL CARBODIIMIDE

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We wish to report the formation of the methylthiomethoxy derivative IV during attempted oxidation of 3β-hydroxyandrost-5-en-17-one(I) with dimethylsulfoxide (DMSO) and dicyclohexylcarbodiimide (DCC). Compound IV presumably arises by rearrangement of the intermediate sulfoniumoxy salt III. (Dimethylsulfoniumoxy salts of this type have been postulated as intermediates in oxidations involving DMSO (1,2).)

This rearrangement, where C to O migration is accompanied by rupture of the $\overset{+}{S}-O$ bond, resembles the Pummerer reaction (3) in which sulfoxides react with acetic anhydride to give α-acetoxysulfides. However, as the latter reaction has been shown to proceed by a double S_N2 displacement mechanism (4), the present example appears to be more closely analogous to the Stevens rearrangement (5), in which C to C migration occurs with $C-\overset{+}{N}$ or $C-\overset{+}{S}$ cleavage. (A referee has pointed out that the carbonium ion mechanism proposed for the Pummerer reaction by Parham and co-workers (10) is also consistent with the experimental data of Oae et al. (4). Accordingly, any distinction between the mechanistic pathways of the Pummerer and Stevens rearrangements may well be a very fine one.)

The rearrangement was observed during a survey carried out to determine the optimum conditions for the Moffatt-Pfitzner (6) oxidation of the alcohol I to the corresponding 3-ketone II with DMSO, DCC and pyridinium trifluoracetate. When one mole of DCC was used instead of the usual excess (6), only a 5% yield of the expected ketone II was obtained together with an equal amount of a compound, m.p. 172°, which analysed for $C_{21}H_{32}O_2S$ (348.55). (Found: C, 72.03; H, 9.31; S, 9.39%. Calculated: C, 72.34; H, 9.26; S, 9.20%.) On the basis of the infrared spectrum, which showed no hydroxyl absorption and which contained bands at 1735 (five membered ring carbonyl) and 1045 cm^{-1} (ether C - O), and from the n.m.r. spectrum (see Figure 1), the material was assigned structure IV.

The mass spectrum of IV showed only a small molecular ion peak at m/e 348. However, the spectrum contained a large peak at m/e 271 corresponding to the steroid ion arising from

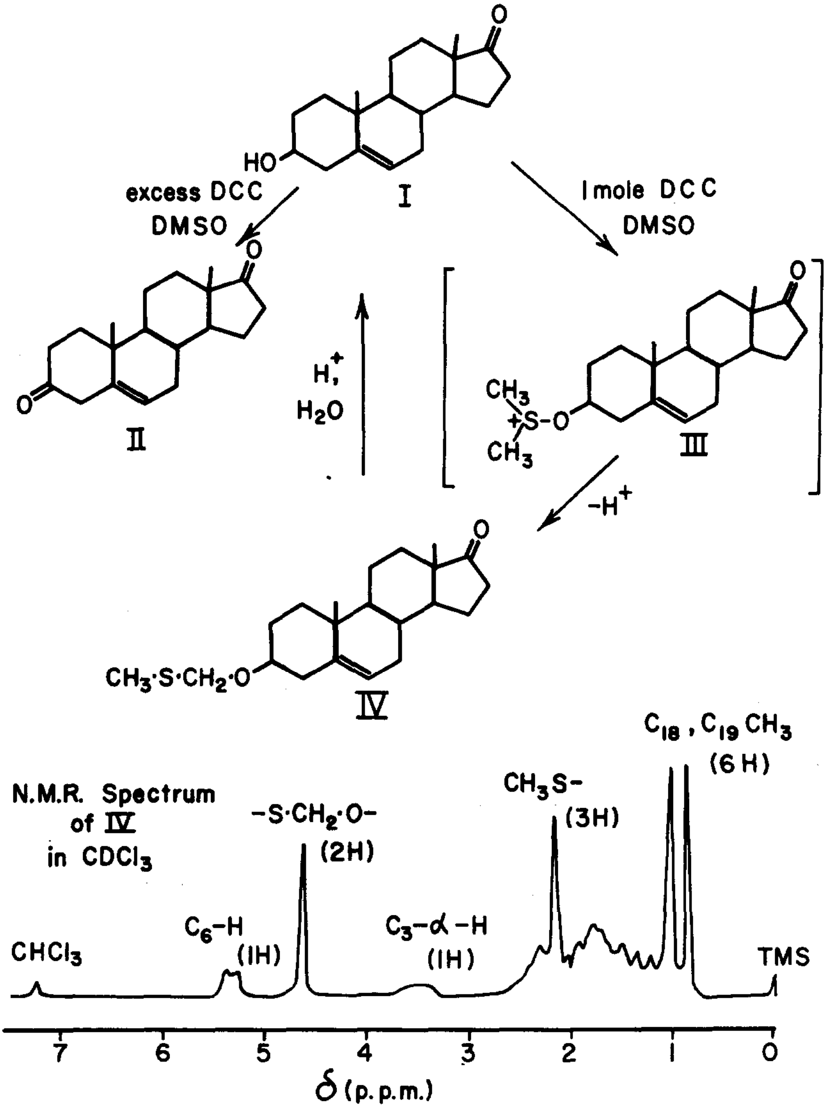

HO
I
excess DCC
DMSO
I mole DCC
DMSO
O
II
H+,
H2O
CH3
+S-O
CH3
III
-H+
CH3·S·CH2·O
IV
N.M.R. Spectrum
of IV
in CDCl3
CHCl3
C6-H
(1H)
-S·CH2·O-
(2H)
C3-α-H
(1H)
CH3S-
(3H)
C18, C19 CH3
(6 H)
TMS
7
6
5
4
3
2
1
0
δ (p.p.m.)

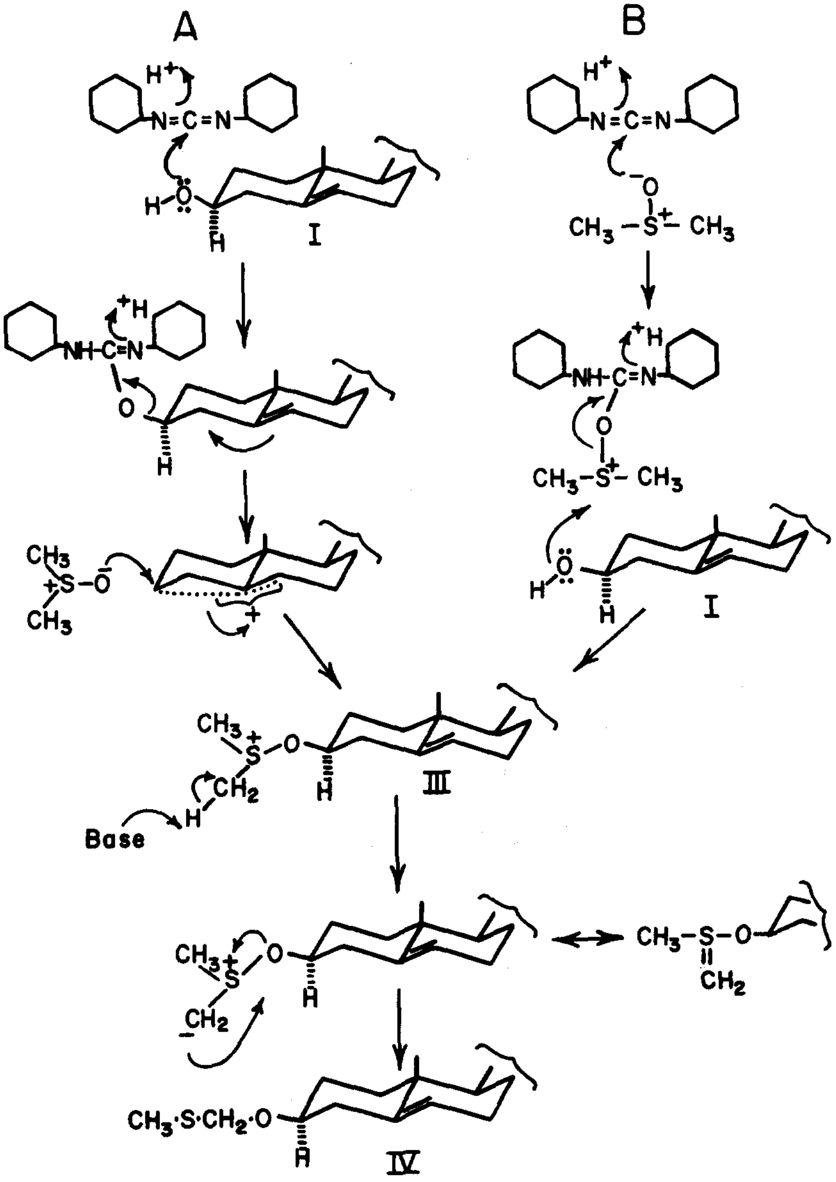
FIG. 1

loss of the $CH_3.S.CH_2.O$ side chain, and also a very intense peak at m/e 61 which is ascribed to the ion $CH_3.S.CH_2^+$. (An intense peak due to this ion has been reported in the mass spectra of alkyl sulfides (7).)

The methylthiomethoxy group of IV is assigned the β-equatorial configuration on the basis of its n.m.r. spectrum, the broad multiplet C_3 - H peak being characteristic of an axial proton adjacent to an electron withdrawing group (8). The configuration at C_3 was confirmed by acid hydrolysis of IV to give a quantitative yield of the starting alcohol I.

A mechanism accounting for the observed stereochemistry at C_3 of the product IV is proposed on the following page.

The intermediate III may arise by activation of the 3β-hydroxyl group of I by DCC, followed by elimination with participation of the Δ^5 double bond (9) and equatorial nucleophilic attack of the resulting carbonium ion by DMSO as shown in A. Alternatively, III may be produced via path B in which initial attack of DCC by DMSO is suggested. The latter route resembles the initial steps of the mechanism established for the Pummerer reaction (4,10). The present data does not allow a choice to be made between the two pathways.


A
B
H+
N=C=N
H
O
I
+H
NH-C=N
O
H
CH3
S-O
CH3
O
CH3-S+-CH3
NH-C=N
O
CH3-S+-CH3
I
CH3
S
O
CH2
H
Base
III
CH3
S
O
CH2
H
CH3-S-O
CH2
CH3·S·CH2·O
H
IV

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