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METHYLTHIOMETHYL NITRONES DERIVED FROM BENZOPHENONE

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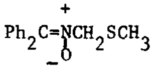
Reaction between cholesterol (and i- chlolesterol) and dimethylsulphoxide and acetic anhydride is thought to proceed by way of an alkoxy dimethylsulphonium ion that is in equilibrium with the cholesteryl carbonium ion and DMSO (1). An analogous situation with a sulphonium ion derived from an oxime might result in a Beckmann rearrangement. This possibility has been tested for benzophenone oxime. DMSO/Ac_2O conditions afforded the oxime acetate, but reaction with DMSO/dicyclohexylcarbodiimide/H^+ (Moffat conditions) (2), afforded, in about 75% yield, the methylthiomethyl nitrone (I).* The spectroscopic evidence excluded the alternatives (II) and (III, from a Beckmann rearrangement), and mild acid hydrolysis gave a mixture of benzophenone and its oxime.

Reaction of nitrone (I) with aqueous ethanolic alkali under reflux gave a mixture of benzophenone, its oxime, and an acidic compound, and the smell of methane thiol was evident. Analytical and spectroscopic evidence suggested this new compound to be N-diphenylmethylformohydroxamic acid (IV)* and this was confirmed by the formation of an acetate (V),* and a methyl derivative (VI)* with diazomethane. Reaction with methanol/sulphuric acid converted the hydroxamic acid (IV) into N-diphenylmethyl hydroxylamine (VII), which could be formylated with ethyl formate and sodium ethoxide in ethanol to regenerate the hydroxamic acid.

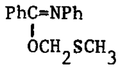


$Ph_2C{=}\underset{-O}{\overset{+}{N}}CH_2SCH_3$

(I)

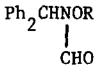
$Ph_2C{=}NOCH_2SCH_3$

(II)



$Ph\underset{OCH_2SCH_3}{C}{=}NPh$

(III)



$Ph_2CH\underset{CHO}{N}OR$

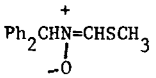
(IV) $R{=}H$

(V) $R{=}COCH_3$

(VI) $R{=}CH_3$

$Ph_2CHNHOH$

(VII)



$Ph_2CH\underset{-O}{\overset{+}{N}}{=}CHSCH_3$

(VIII)

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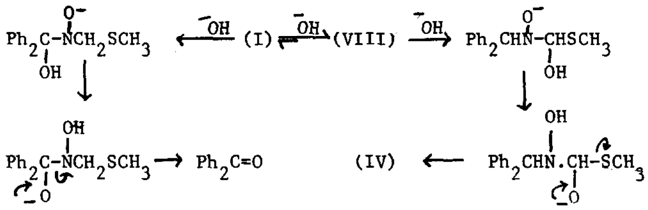
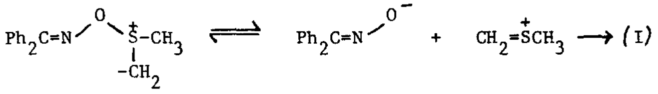
*New compounds; satisfactory analyses, i.r., u.v. and n.m.r. spectra.

The mechanism of formation of hydroxamic acid (IV) became apparent when the alkaline hydrolysis of nitrone (I) was attempted at room temperature. A new compound crystallised out from the solution, which analysis and spectra showed to be the tautomeric nitrone (VIII)*. Tautomerism of arylmethyl nitrones has been reported before (3). The reaction of these tautomers with a large excess of alkali was followed by u.v. spectroscopy, when the nitrone (I) ($\lambda_{max.}$ 302 mμ) reacted at a rate 2.5 times that of its tautomer (VIII) ($\lambda_{max.}$ 277 mμ), both cases giving good first order plots for about the first third of reaction, after which the products of hydrolysis began to complicate the u.v. curves. Nitrone (I) was converted mainly into nitrone (VIII) whereas the reverse reaction could not be detected by u.v. Consistent with this, hydrolysis of nitrone (VIII) under preparative conditions gave mainly the hydroxamic acid (IV) and very little benzophenone and its oxime. The formation of this hydroxamic acid and benzophenone is probably as outlined:



Benzophenone oxime may well arise from S_N2 reaction at the $-CH_2-$ of nitrone (I).

A tempting speculation on the formation of nitrone (I) is that the oxime oxygen is the nucleophilic centre to attack the DMSO- diimide intermediate to give, perhaps, (IX) (2,4) which then dissociates in the way suggested by Johnson and Phillips (5) for some alkoxydialkylsulphonium ions, to be followed by reaction of the oxime anion with nitrogen as nucleophilic centre (3).



(IX)

Further reactions of these and similar nitrones are currently being studied.

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