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A REAPPRAISAL OF THE REACTION OF QUINONES WITH HYDRAZOIC ACID

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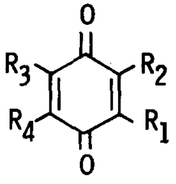
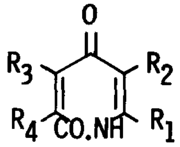
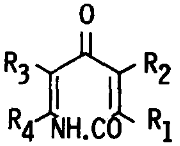
The Schmidt reaction, using concentrated sulphuric acid and hydrazoic acid at 0°, as applied to alkyl substituted quinones has been the subject of recent studies(1), Folkers et al. come to the conclusion that in the case of quinones such as Ia and Ib the products are exclusively of type IIa and IIb.



I



II

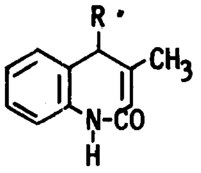


III

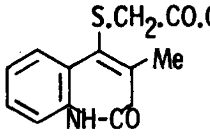
	R1	R2	R3	R4
a	H	CH_3	Benzo	
b	H	$CH(CH_3)_2$	H	CH_3

Their deductions are based solely on the observation that in the products the NH-proton is directly coupled to a = CH proton in the n.m.r. spectra. Therefore, they assign to the products structures of type IIa and IIb, in which these two groups are adjacent. Consequently they deduce that in the Schmidt reaction of quinones, the least substituted group (at the least hindered end of the quinone), in preference, always migrates.

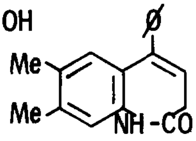
This reaction of quinones thus presented a direct method of obtaining the previously rare 2,5$\underline{H}$-2,5 azepindiones, which encouraged us to study their chemistry. During this investigation, the major azepindione from 2-methyl-1,4-naphthoquinone (Ia) was reduced with sodium borohydride, and the resulting secondary alcohol (IV) was converted using thionyl chloride into the corresponding chloro derivative (V), whose nucleophilic substitution reactions were investigated. Treatment of V with thioglycollic acid yielded a compound whose spectroscopic properties could best be accomodated by structure VI.



(IV) R=OH; (V) R=Cl



VI

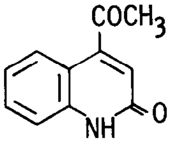


VII

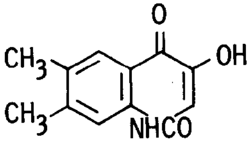
The n.m.r. spectrum of a deuterium oxide/sodium carbonate solution of VI was characterized by a singlet (2H) at τ 6.95 (-S.$\underline{CH_2}$.CO.O$^-$) and an AB pattern (2H) centered at τ 7.3 (CO.$\underline{CH_2}$.C=). The aromatic region of the spectrum showed two multiplets, one centered at τ 2.1 (IH) and the other at τ 2.75 (3H). The mass spectrum of VI showed an initial loss of 42 mass units

(m^*185.7) followed by a loss of 59 mass units (m^*118.8). Accurate mass measurement showed these to be losses of $CH_2 = CO$ and $-CH_2.CO.OH$ respectively. A comparison of the mass spectrum of VII, which was prepared (2) by ring closing the acid side chain onto the aromatic amine, with that of VI revealed their essential similarity, both spectra being characterized by the loss of $CH_2 = CO$.

Acid hydrolysis of the major azepindione derived from Ia, resulted in the isolation in good yield of 4-acetylcarbostyril (VIII) which was characterized by spectroscopic results and whose identity was confirmed by comparison with an authentic synthetic sample (3). A similar rearrangement under alkaline conditions has been reported by Rees (4) for IX. Having thus established the structure for this rearrangement product we can now say that the major azepindione derived from 2-methyl-1,4-naphthoquinone Ia must be 4-methyl-1*H*,2*H*,5*H*-benz[f]azepine-2,5-dione IIIa and not IIa.



VIII



IX

The mass spectra of IIa and its unsaturated derivatives were of no assistance in ascertaining where the NH group had been inserted. The main fragmentation path consisted of the loss of two molecules of carbon monoxide, giving rise to substituted indoles whose spectra, from here down, were found to agree with the published spectra(5). Accordingly we were led to reinvestigate the spin decoupling evidence on which Folkers' proposal was based. The azepindione IIIa exhibited a broad singlet (half-band width ~4c/s) at 3.21 (=C$\underline{H}$) and a doublet J = 1.4 c/s at τ 7.79 (-C$\underline{H}_3$). The multiplicity of the signal due to the olefinic proton was reduced by either decoupling or deuterium substitution of the NH proton.

The major azepindione (m.p. 168°) derived from thymoquinone (Ib) presented a particularly favourable case for investigating the long range coupling effects. The n.m.r. spectrum showed signals at τ 3.49 and τ 4.20 (=C$\underline{H}$). These signals were a doublet of doublets (J=2.0, 0.6 c/s)(proton adjacent to isopropyl group) and a doublet of quartets (J=1.8, 0.7 c/s) (proton adjacent to methyl group). A broad signal at τ -0.3 was assigned to the NH proton. Double irradiation of this signal collapsed the one olefinic signal to a doublet (J=0.6 c/s) and the other to a quartet (J=0.7 c/s). A similar result was obtained if the NH proton was replaced by deuterium. This evidence is best interpreted in terms of structure IIIb, the NH coupling being of allylic type to the one olefinic proton and of amidic type to the other olefinic proton.

Similar results have been obtained independantly by workers at Manchester University (6) for the unsymmetrical azepindiones described by Folkers and will be reported separately. A paper describing some chemical studies in the benzazepindione series is in preparation.

References

(1) D. Misiti, H.W. Moore and K. Folkers, Tetrahedron Lett. No. 16, 1071 (1965).

(2) We should like to thank Dr. R.F. Maisey (these laboratories) for kindly providing a sample of VII.

(3) E. Ochiai, M. Takahashi, Y. Tamai and H. Kataoka, Chem. Pharm. Bull. (Tokyo) 11, 137, (1963).

(4) A.H. Rees, J. Chem. Soc. 3111 (1959).

(5) H. Budzikiewicz, C. Djerassi and D.H. Williams, Interpretation of Mass Spectra of Organic Compounds, Holden-Day (1964) and references cited therein.

(6) R.W. Rickards and R. Smith, Tetrahedron Lett. this issue.