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NATURE OF THE STRUCTURAL CHANGE DURING THE MUTAROTATION OF SUGAR OSAZONES.

L. Mester, E. Moczar, G. Vass and A. Schimpl,
Institut de Chimie des Substances Naturelles, Gif-sur-Yvette,
Centre National de la Recherche Scientifique, Paris, France.

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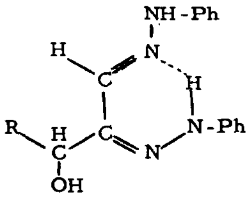
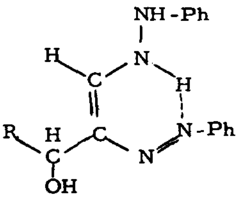
The interpretation of the mutarotation of sugar osazones was for long controversial (1-5). Discarding all earlier views, in 1957, Mester and Major (6) considered mutarotation to be a consequence of a reversible isomerisation between the initial chelate structure (I) and the N-chelated structure (II) (6) or the O-chelated structure (III) (7) through the action of basic solvents.



I



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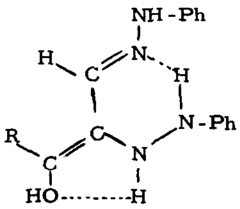
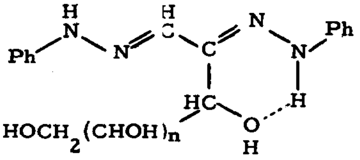
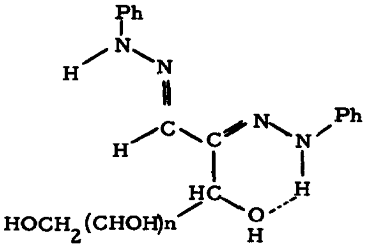


III

Based essentially on u.v. spectrophotometric investigations, Henseke and Köhler (8) suggested the opening of the O-chelated structure (IV) and the formation of Fischer's open-chain osazone structure.



IV



V

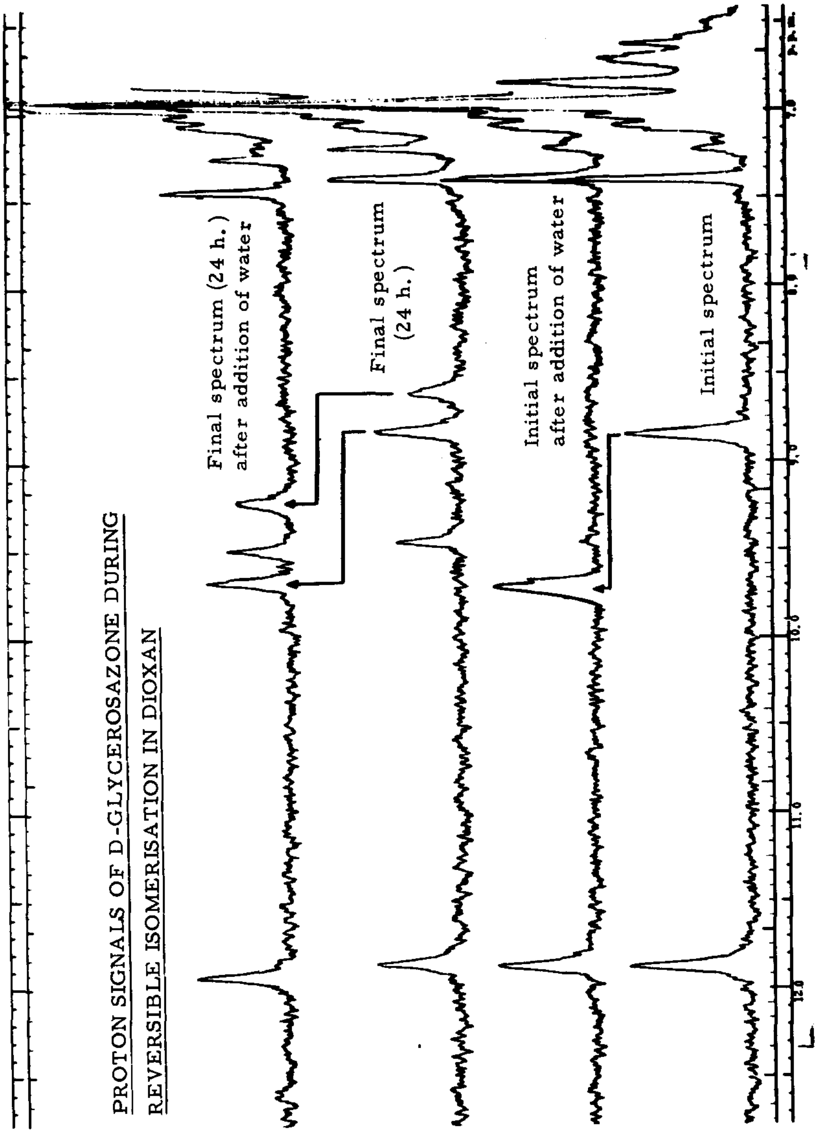
Based on the changes of the proton signals in the n. m. r. spectra of the osazone during mutarotation, Chapman and coworkers (12, 14) accepted the chelate structure (I) (9-13) as the initial structure, but they advanced for the final form of the osazones in mutarotation structure (IV).

To find the exact nature of the reversible isomerisation during mutarotation, we re-examined the changes observed in the most characteristic properties of the osazones :

1) - N. m. r. spectra.

Proton signals of the osazones during mutarotation in deuteropyridine and dioxan are set out in table I. The initial form of the osazones 1-5, and the final form of 6 show a strongly chelated and a solvent-bonded N-H proton. In the initial form of 6 and the final form of osazones 1-5 two N-H signals appear in the solvent-bonded region.

Addition of water to the dioxan solution manifests itself in a downfield shift of the non-chelated N-H proton signals by about one p. p. m., due certainly to solvation by water of the N-H group. N- or O-chelated imino protons do not show this phenomenon. This method established the presence of a chelated imino-group besides a non-chelated one in the final form of sugar osazones in mutarotation (fig. 1), and the presence of two non-chelated imino protons in the initial form of n-propyl-glyoxalosazone. The position of N-chelated N-H proton signals being shifted much further downfield, the chelated imino proton in the final form of sugar osazones must be O- rather than N-chelated.



PROTON SIGNALS OF D-GLYCEROSAZONE DURING REVERSIBLE ISOMERISATION IN DIOXAN

FIG. 1

2) - U.v. spectra.

The absence of N-chelation in the final form of sugar osazones in mutarotation was confirmed also by u.v. spectroscopy.

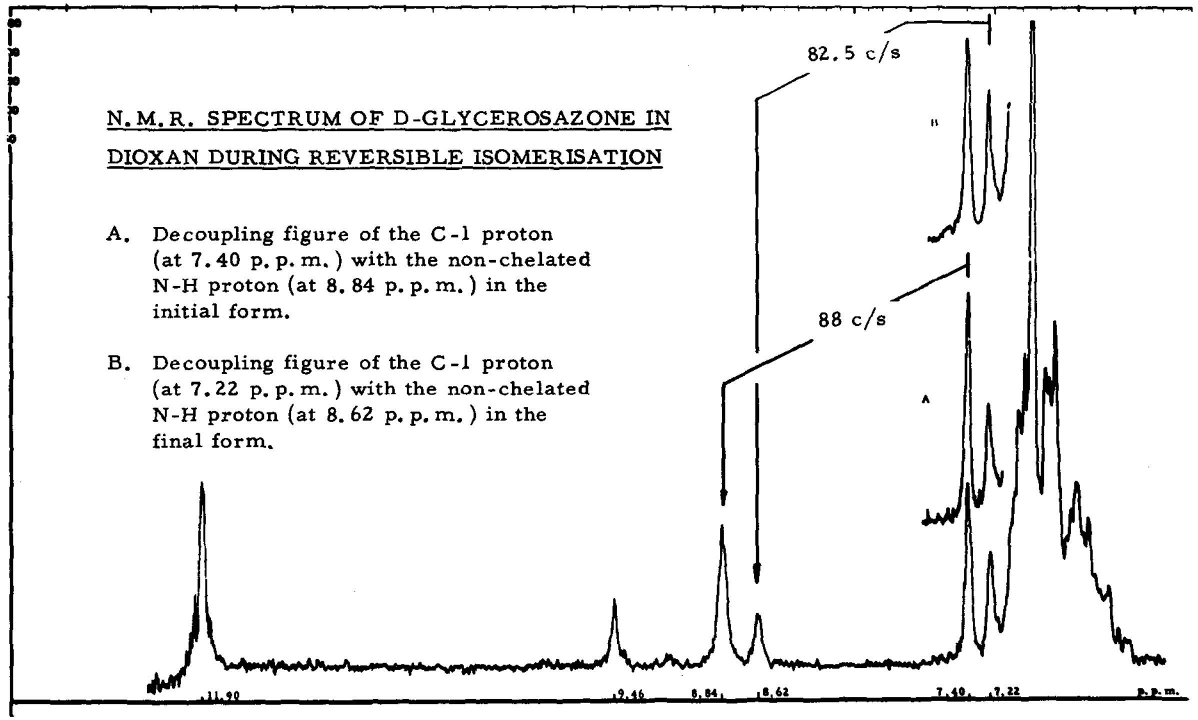
The initial and final forms of the osazones being in progressing equilibrium during mutarotation, the simultaneously registered shift of the u.v. maximum is the result of the superposition of the u.v. spectra of the two forms in equilibrium.

By recording the u.v. spectra of sugar osazones in mutarotation against a freshly prepared solution containing the same amount of the non-isomerized osazone (the amount was established by n.m.r. spectroscopy), we obtained by subtraction the spectra of the final forms of sugar osazones in mutarotation. The new maxima (372mμ for D-glycerosazone and 368mμ for D-xylosazone in dioxan) in the u.v. spectra of the final forms of sugar osazones correspond with the maxima at 366mμ measured for the non-chelated n-propyl-glyoxylosazone. Thus, u.v. spectral evidence supports also the rupture of the N-H...N chelation and the formation of a bisphenylhydrazone or similar structure during mutarotation.

3) - Long-range spin-spin coupling.

A long-range spin-spin coupling was reported by Mester, Moczar and Parello (10, 11) between the C-1 proton and the non-chelated N-H proton in the n.m.r. spectra of the initial form of sugar osazones. A similar long-range coupling, characteristic of the syn (i.e. cis C_1-H and NH-Ph) geometric isomers of aldehydo-phenylhydrazones (15), has now been observed in the n.m.r. spectra of the final form of D-glycerosazone and D-glucosazone in mutarotation (fig. 2) .

This evidence indicates that the geometry of the final form of sugar osazones in mutarotation is very similar to that of the initial form (I) and, along with arguments previously adduced, has led us to consider structure (V). This structure is a restricted-rotation isomer of structure (IV) about



N.M.R. SPECTRUM OF D-GLYCEROSAZONE IN DIOXAN DURING REVERSIBLE ISOMERISATION

A. Decoupling figure of the C-1 proton (at 7.40 p.p.m.) with the non-chelated N-H proton (at 8.84 p.p.m.) in the initial form.

B. Decoupling figure of the C-1 proton (at 7.22 p.p.m.) with the non-chelated N-H proton (at 8.62 p.p.m.) in the final form.

FIG. 2

the C(1)-C(2) bound, the phenylimino group of the C(1)-phenylhydrazone in (IV) being hindered by the sugar chain.

4) - Formazan formation.

The formation of structure (V) during mutarotation has been confirmed by measuring the yield in radioactive formazan obtained through reaction of diazotized ^{14}C-aniline with samples taken from the solution of D-glucosazone, D-galactosazone and D-glycerosazone in mutarotation :

TABLE II

Formation of osazone-formazans through reaction of diazotized ^{14}C-aniline with osazones in mutarotation.

	Yields in osazone-formazan ^{14}C	
Obtained from :	before mutarotation	after mutarotation
D-glucosazone	31,0 %	25,0 %
D-galactosazone	26,5 %	23,0 %
D-glycerosazone	48,5 %	54,5 %

Data presented in the table show a decrease in formazan formation from D-glucosazone and D-galactosazone. In contrast, D-glycerosazone shows a distinct increase in ability to form formazan during progressing isomerisation. The transition of the initial structure (I) to the structure (V) can give a satisfactory explanation of these data;

In form (V) of sugar osazones the formazan formation is rendered more difficult, because attack of the diazonium cation on the C-1 proton is hindered by the sugar chain, and this shows itself in diminished formazan formation. The same difficulty is not found with D-glycerosazone because of absence of the sugar chain, and the yield of formazan during progressing isomerisation increased, as expected.

Thus, formazan formation, n.m.r. and u.v. spectral data support the restricted rotation isomer (V) of the syn (i.e. cis C_1-H, NH-Ph) isomerized, N-H...O chelated, bisphenylhydrazone structure as the final form of sugar osazones in mutarotation.

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TABLE I

Nuclear Magnetic Resonance Spectral Data (p.p.m.) of Osazones during Reversible Isomerisation

	In deuteropyridine						In dioxan					
	Initial form			Final form			Initial form			Final form		
	N-H	N-H	C_1-H	N-H	N-H	C_1-H	N-H	N-H	C_1-H	N-H	N-H	C_1-H
1. D-glycer-osazone	12.71	11.36	8.22	11.36	10.97	7.99	11.88	8.84	7.40	9.46	8.62	7.21
							+ H_2O: 11.94	9.69	7.46	9.50	9.23	7.28
2. D-xylosazone							11.89	8.90	7.40	9.95	8.53	*
							+ H_2O: 11.97	9.68	7.40	9.98	9.15	*
3. L-rhamn-osazone	12.74	11.18	8.69	11.44	10.73	8.04						
4. D-gluc-osazone	12.53	11.40	8.36	11.40	10.57	7.77						
5. i-propyl-glyoxal-osazone	12.50	11.17	7.70	unchanged			11.65	8.64	7.13	unchanged		
							+ H_2O: 11.65	9.45	7.26			
6. n-propyl-glyoxal-osazone							8.45	7.95	7.09	11.52	8.55	*
							+ H_2O: 9.03	8.36	7.14	11.52	9.38	*

* : Signal included with benzene peaks.