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THE STRUCTURE OF SUGAR OSAZONES *

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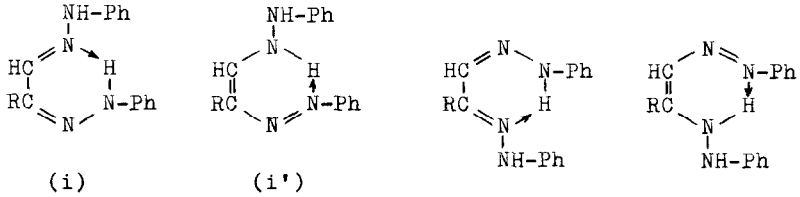
The structure of sugar osazones and related compounds was long time controversial. Fieser and Fieser (1) on theoretical grounds proposed two alternate chelate structures i and j , these being stabilized by their ability to exist in the resonance forms i' and j'.



(i) (i') (j) (j')

The first chemical evidence supporting the open-chain chelate structure was advanced by Mester (2), who also favored (2,3,4) the formula i. Additional support came from X-ray data presented by Bjamer, Dahm, Furberg and Petersen (5).

The recently published work of Wolfrom, Fraenkel, Lineback and Komitsky (6), on the basis of the n.m.r. spectra of acetylated sugar osazones, supports the chelate structure j. The i formula however is now known to be the correct one according to the evidence presented in this paper.

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The evidence for the chemical shift of the C(1) proton and the protons bonded to nitrogen in sugar osazones, dehydro-osazones and a number of related compounds in dimethylsulfoxide and deuteropyridine is given in Table I.

In each of the compounds 1 to 5 a signal corresponding to a chelated N-H proton is present between 12 to 13 p.p.m., but it is absent in 6, the aldehydo phenylhydrazone structure of which compound has been proved (7,8), and also in the symmetric bisphenylhydrazone 7.

The non-chelated imino proton signal of 6 at 11 p.p.m. in deuteropyridine (at 10.12 p.p.m. in dimethylsulfoxide) is also present in the compounds 1 to 5. A strong signal in the same region corresponding by integration to two protons was found in 7. Further more a signal in the 7 to 8 p.p.m. region, corresponding to the C(1) proton is present in the spectra of the compounds 3 to 7, but it is absent in the cyclic compounds 1 and 2.

The identity of the signals corresponding to the NH protons in dehydro-D-glucosazone with signals in the spectra of sugar osazones suggests a great similarity in the chelate structure of the two types of compounds.

Since the axial position of the C(3) hydroxyl has been proved in dehydro-D-glucosazone (9), the chelation can not be located between the C(2) phenylhydrazine residue and the C(3) hydroxyl as was proposed by Henseke (10) for the sugar osazones. The possibility of such a chelation in sugar osazones was excluded also by X-ray spectroscopy (11). Thus the chelation must be located between the two phenylhydrazine residues in the dehydro-osazones as well in the sugar osazones according to the chelated structures proposed by Fieser and Fieser.

A more exact deliniation of these chelate structures has been made possible by exchange of the hydrogens bonded to nitrogen with deuterium oxide in deuterochloroform.

In deuterochloroform (Table II) the signal of the free imino proton is located between 7 to 8 p.p.m. and disappears easily on shaking with deuterium oxide. The signal at 12 to

13 p.p.m., corresponding to the proton involved in the chelation disappears somewhat less easily on deuteration, because shaking and heating are needed. The signal of the C(1) proton is located at 7.56 p.p.m. in compounds 4 and 9, while in the spectra of compounds 5 and 8 it is encumbered with the signals of the aromatic rings. In compound 2 there is no C(1) proton.

The fact that the substitution of the α-imino hydrogen of the C(1) phenylhydrazine residue with a methyl group in compound 8 is without noteworthy influence on the position of the signal corresponding to the chelated NH group, while the signal of the non-chelated NH group disappears, proves that the position of the non-chelated imino group in the sugar osazones is the same as the position of the methyl group in the 1-methylphenyl 2-phenylosazones (fig. 1.), which is a chemically well-defined position (2,12). This fact supports structures i and i' rather then structures j and j'.

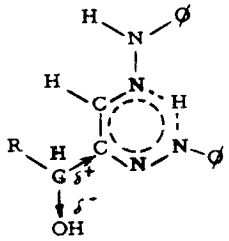
Moreover, a long range spin-spin coupling between the C(1) proton and the non-chelated NH proton was observed, which is a decisive proof in favor of the structures i and i'. The weak splitting ($J \sim 1$ c.p.s.) of the C(1) proton at p.p.m. 7.56 in compounds 4 and 9 disappears during exchange of the non-chelated NH proton by deuterium oxide, giving place to a singular but more accentuated peak (fig. 1.).

High resolution n.m.r. spectroscopy (100 Mc) using the double resonance method (fig. 2.) also confirmed that the C(1) proton is coupled with the non-chelated NH proton at 8.0 p.p.m. and not with the chelated NH proton at 12.34 p.p.m.

A similar long range spin-spin coupling between the C(1) proton and the α-imino proton was reported in the "syn" isomers of aldehyde 2,4-dinitro-phenylhydrazones (13). The position of the C(1) proton and the α-imino proton in these compounds and in the i and i' forms of the sugar osazones is very similar. A similar coupling between the C(1) proton and the distant free NH proton in the j and j' forms of the sugar osazones is highly inprobable. Thus, evidences presented

in this communication favor for sugar osazones as well for dehydro sugar osazones the structures i and i' of the chelated structures proposed by Fieser and Fieser.

However on account of the behaviors of the sugar osazones, and considering their UV, IR, N.M.R. and X-ray data, it seems to be probable that the sugar osazones are stabilized neither in the i nor in the i' form, but that they are present in a quasi-aromatical structure between the resonance limit forms i and i', as represented by the following formula:



This structure besides may explain the sharp difference between the C(1) and C(2) phenylhydrazone groups in almost all their reactions such as methylation (14), osotriazole formation (15) etc., as well as the privileged position (16, 17,18) of the C(3) hydroxyl in the sugar osazones. This is due to the electron attractive effect of the quasi-aromatic chelate system.

TABLE I

NUCLEAR MAGNETIC RESONANCE SPECTRAL DATA (p.p.m.)

	in Dimethylsulphoxide			in Deuteropyridine		
	N-H (chelated)	N-H	C(1)-H	N-H (chelated)	N-H	C(1)-H
1. Dehydro-D-glucose phenylosazone	12.45	9.35	-	12.95	9.61	-
2. Dehydro-D-glucose phenylosazone acetate	12.48	9.55	-	12.90	10.05	-
3. D-Glucose phenylosazone	12.20	10.66	7.89	12.65	11.20	8.68
4. D-Galactose phenylosazone acetate	12.20	10.80	7.73	12.86	11.49	8.05
5. D-Glycerosazone	12.05	10.70	7.79	12.63	11.27	8.23
6. D-Galactose phenylhydrazone acetate	-	10.12	*	-	11.00	7.58
7. Glyoxal bisphenylhydrazone	-	10.33	7.69	-	11.10	8.12

* - Signal included in the benzene peaks.

TABLE II

NUCLEAR MAGNETIC RESONANCE DATA (p.p.m.)

IN DEUTEROCHLOROFORM

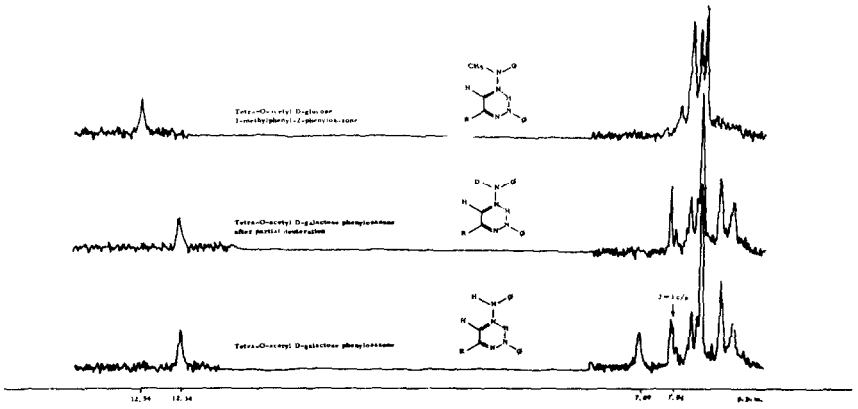
	N-H (chelated)	N-H	C(1)-H
2. Dehydro-D-glucose phenylosazone acetate	12.50	7.97	-
4. D-Galactose phenylosazone acetate	12.34	7.89	7.54
5. D-Glycerosazone	12.16	7.78	*
8. D-Glucose 1-methyl-phenyl-2-phenylosazone acetate	12.54	-	*
9. D-Arabinose phenylosazone acetate	12.42	7.88	7.56

* - Signal included in the benzene peaks.

N.M.R. Spectra

The n.m.r. spectra of the compounds reported in this communication were determined at 60 Mc with tetramethylsilane as an internal reference on a A-60 Varian Associates spectrometer, Palo Alto, California.

High resolution n.m.r. spectrum at HR 100 Mc of tetra-O-acetyl D-galactos phenylosazone and decoupling with the double resonance method (fig. 2) was det mined by Dr. A. Melera, Service Center of the Varian A.G., Zürich,



NUCLEAR MAGNETIC RESONANCE SPECTRA (60 Mc, $CDCl_3$)

Fig. 1

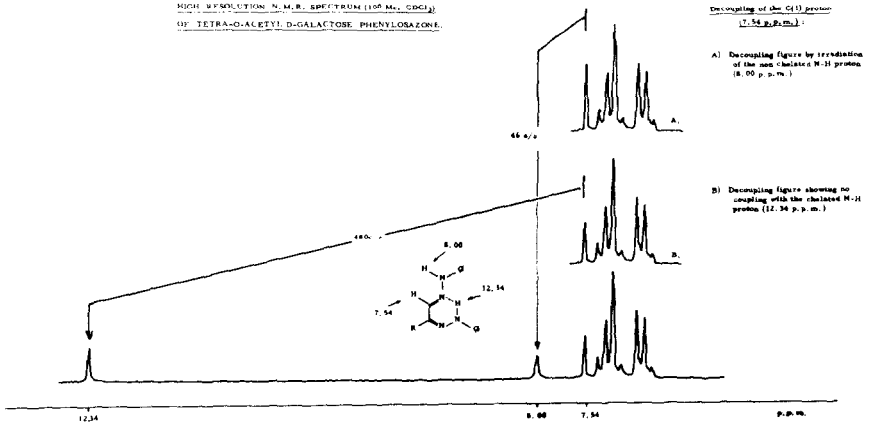


Fig. 2

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