327. *The Scope and Mechanism of Carbohydrate Osotriazole Formation. Part III.*[1] *The Action of Oxidising Agents on* ortho- *and* meta-*Substituted Osazones and Osotriazoles.*

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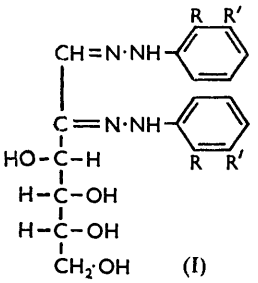
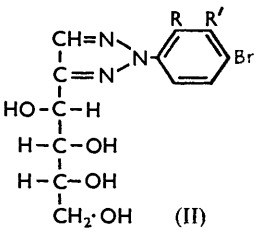
Bromine water oxidises *o*- and *m*-tolyl- and *m*-bromophenyl-osazones to osotriazoles and brominates them in the 4-position. Potassium permanganate oxidises the sugar residue and the methyl group in the 3- but not in the 2-position.

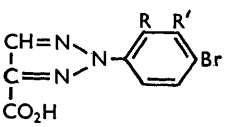
It has been shown[1] that bromine water converts carbohydrate phenylosazones into osotriazoles and brominates them in the 4-position. In the present work, the study was extended to *o*- and *m*-tolyl- and *m*-bromophenyl-osazones and -osotriazoles. Glucose *o*-tolyl-osazone (Ia) and -osotriazole yielded the 4-bromo-2-methylphenylosotriazole (IIa), and the *meta*-isomers yielded the 4-bromo-3-methylphenylosotriazole (IIb). Glucose *m*-bromophenyl-osazone and -osotriazole were likewise brominated in the 4-position, yielding glucose 3 : 4-dibromophenylosotriazole. On similar treatment, glucose *o*-bromophenylosazone gave an osotriazole, m. p. 156°, which is being investigated.



(I)



(II)



(III)

(a) R = Me, R′ = H
(b) R = H, R′ = Me

To identify the osotriazoles produced, disubstituted osazones were prepared and refluxed with aqueous copper sulphate. The disubstituted osotriazoles were readily obtained except from glucose 2 : 4-dibromophenylosazone which lost one bromine atom and yielded glucose *p*-bromophenylosotriazole.

The action of potassium permanganate on carbohydrate osotriazoles was also studied. This reagent is known[1] to oxidise the sugar residue and methyl group, if present, to carboxylic groups. Thus, glucose *m*-bromophenylosotriazole yielded 2-*m*-bromophenyl-1 : 2 : 3-triazole-4-carboxylic acid, and glucose *m*-tolylosotriazole yielded 2-*m*-carboxyphenyl-1 : 2 : 3-triazole-4-carboxylic acid. In the case of osotriazoles having the methyl group in the *ortho*-position to the triazole ring, potassium permanganate oxidised only the sugar residue: glucose *o*-tolylosotriazole yielded 2-*o*-tolyl-1 : 2 : 3-triazole-4-carboxylic acid, and glucose 4-bromo-2-methylphenylosotriazole (IIa) yielded 2-(4-bromo-2-methylphenyl)-1 : 2 : 3-triazole-4-carboxylic acid (IIIa). This is probably due to the steric

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effect of the osotriazole ring. 2-(4-Bromo-2-methylphenyl)-1 : 2 : 3-triazole-4-carboxylic acid (IIIa) was also obtained by the action of bromine water on 2-*o*-tolyl-1 : 2 : 3-triazole-4-carboxylic acid whereas 2-*m*-carboxyphenyl-1 : 2 : 3-triazole-4-carboxylic acid was unaffected by bromine water.

It seems from the above experiments that the controlling factor is the $-I$ effect of the osotriazole ring, initiated from the positive charge on the 2-nitrogen atom. Thus bromination takes place in the 4-position, the least affected by the $-I$ effect, and debromination, as in 2 : 4-dibromophenylosazone, takes place in the 2-position which is the most affected.

The ultraviolet absorption spectra of the above compounds are characterised by a peak between 258 and 276 mμ.

Experimental

Absorption spectra were determined for ethanolic solutions with a Unicam S.P. 500 spectrophotometer. Microanalyses were by A. Bernhardt, Mülheim, W. Germany.

Glucose o-*Bromophenylosazone.*—Glucose (10 g.) in water (50 ml.) was treated successively with *o*-bromophenylhydrazine hydrochloride (35·5 g.) in water (150 ml.), sodium acetate (35·5 g.) in water (50 ml.), and few drops of acetic acid and heated on the water-bath for 2 hr. The crystalline *osazone* which separated (15 g.) recrystallised from ethanol in needles, m. p. 203—204°, moderately soluble in boiling ethanol and methanol and insoluble in ether and water (Found: C, 41·8, 41·8; H, 3·9, 3·9; N, 10·7, 10·7; Br, 31·0, 31·3. $C_{18}H_{20}O_4N_4Br$ requires C, 41·9; H, 3·9; N, 10·9; Br, 31·0%).

Glucose m-*Bromophenylosazone.*—Glucose (1 g.) in water (50 ml.) was heated with *m*-bromophenylhydrazine (3 g.) and acetic acid (4 ml.) on the water-bath for 40 min. The *osazone* separated (0·8 g.); it recrystallised from ethanol–water in needles, m. p. 204—205° (solubility as above) (Found: C, 42·1; H, 4·0; N, 10·7; Br, 31·4%).

Glucose 4-*Bromo-2-methylphenylosazone.*—Glucose (10 g.) was treated with 4-bromo-2-methylphenylhydrazine hydrochloride (35 g.) and sodium acetate as before. The *osazone* (15 g.) recrystallised from ethanol in needles, m. p. 184—185° (solubility as above) (Found: C, 44·0; H, 4·7; N, 10·1; Br, 29·3. $C_{20}H_{24}O_4N_4Br_2$ requires C, 44·1; H, 4·4; N, 10·3; Br, 29·4%).

Glucose 4-*Bromo-3-methylphenylosazone.*—Glucose (10 g.) was treated with 4-bromo-3-methylphenylhydrazine hydrochloride and sodium acetate as before, giving a reddish-brown amorphous precipitate which could not be obtained crystalline. It was filtered off, washed with water, and used as such for the preparation of the osotriazole.

Glucose 2 : 4-*Dibromophenylosazone.*—Glucose (4 g.) was treated with 2 : 4-dibromophenylhydrazine hydrochloride (19 g.) and sodium acetate as before. The *osazone* (4·5 g.) crystallised from dilute ethanol in needles, m. p. 243—244° (solubility as above) (Found: C, 32·2; H, 2·5; N, 8·3; Br, 47·3. $C_{18}H_{18}O_4N_4Br_4$ requires C, 32·0; H, 2·6; N, 8·3; Br, 47·5%).

Glucose 3 : 4-*dibromophenylosazone*, similarly prepared, has m. p. 205—206° (Found: C, 31·9; H, 2·9; N, 8·1; Br, 47·0%).

Glucose o-*Tolylosotriazole.*—Glucose *o*-tolylosazone (1·4 g.), suspended in 1% aqueous copper sulphate (100 ml.) and dioxan (20 ml.), was refluxed for 30 min. and filtered. The solution was freed from copper sulphate by passing in hydrogen sulphide and neutralising the mixture with barium carbonate. The filtrate was evaporated to dryness under reduced pressure, and the brown *osotriazole* (0·4 g.) sublimed at 230°/10 mm.; it then crystallised from ethanol in plates, m. p. 126—127°, moderately soluble in hot ethanol and methanol and insoluble in water (Found: C, 55·9; H, 6·3; N, 15·1. $C_{13}H_{17}O_4N_3$ requires C, 55·9; H, 6·1; N, 15·1%).

Glucose m-*tolylosotriazole* crystallised from ethanol in needles, m. p. 194—195°, soluble in hot ethanol and methanol and insoluble in ether and water (Found: C, 55·8; H, 6·1; N, 15·1%).

Glucose m-*Bromophenylosotriazole.*—A solution of glucose *m*-bromophenylosazone (1 g.) in dioxan (20 ml.) was added to a boiling solution of copper sulphate (1 g.) in water (50 ml.) and refluxed for 30 min., then filtered. On concentration, the *osotriazole* separated (0·5 g.) and recrystallised from ethanol in needles, m. p. 209—210° (solubility as above) (Found: C, 41·7; H, 4·2; N, 12·2; Br, 23·2. $C_{12}H_{14}O_4N_3Br$ requires C, 41·9; H, 4·1; N, 12·2; Br, 23·3%).

Glucose p-*Bromophenylosotriazole*.—Glucose 2 : 4-dibromophenylosazone (2 g.), suspended in a solution of copper sulphate (2 g.) in water (100 ml.) and dioxan (100 ml.), was refluxed for 4 hr. and filtered. To remove dioxan, water (100 ml.) was added, and the solvent distilled off until 200 ml. were collected. The residue was concentrated on the water-bath and the crystals that separated were filtered off (0·5 g.) and recrystallised from ethanol in needles, m. p. 228° alone or mixed with glucose *p*-bromophenylosotriazole (Found: C, 41·6; H, 4·1; N, 12·0; Br, 23·3%).

Glucose 4-*Bromo*-2-*methylphenylosotriazole*.—(*a*) Glucose *o*-tolylosazone (1·6 g.) was treated in the cold with bromine (2 ml.), and the mixture kept overnight. The reddish-brown mass obtained was filtered off (1 g.) and washed with water and ethanol. *Glucose* 4-*bromo*-2-*methylphenylosotriazole* recrystallised from water–ethanol in needles, m. p. 175° (solubility as above) (Found: C, 43·5; H, 4·5; N, 11·4; Br, 22·7. $C_{13}H_{16}O_4N_3Br$ requires C, 43·6; H, 4·5; N, 11·7; Br, 22·3%).

(*b*) Glucose *o*-tolylosotriazole (1·5 g.), similarly treated, gave the same product (1·5 g.), m. p. and mixed m. p. 175° (Found: C, 43·1; H, 4·6; N, 11·4; Br, 22·7%).

(*c*) A suspension of glucose 4-bromo-2-methylphenylosazone (5 g.) in dioxan (70 ml.) and 5% aqueous copper sulphate (100 ml.) was refluxed for 1·5 hr. and filtered hot. Dioxan was removed as before, and the solution concentrated on the water-bath. The osotriazole that separated was filtered off (2 g.) and recrystallised from water–ethanol in needles, m. p. and mixed m. p. 175° (Found: C, 43·4; H, 4·7; N, 11·5; Br, 22·6%).

Glucose 4-*Bromo*-3-*methylphenylosotriazole*.—(*a*) Glucose *m*-tolylosazone (2 g.), suspended in water (100 ml.), was treated in the cold with bromine (3 ml.), and the mixture kept overnight. The mass formed was filtered off and washed with water and ethanol (1 g.). The *osotriazole* recrystallised from ethanol in needles, m. p. 221—222°, soluble in boiling ethanol and methanol and insoluble in acetone and water (Found: C, 43·1; H, 4·4; N, 11·3; Br, 22·0%).

(*b*) Glucose *m*-tolylosotriazole (0·8 g.), treated as in (*a*), gave the same product (0·6 g.), m. p. and mixed m. p. 221—222° (Found: C, 43·1; H, 4·6; N, 11·4; Br, 22·5%).

(*c*) A hot solution of glucose 4-bromo-3-methylphenylosazone (10 g.), in dioxan (100 ml.) was added to a boiling solution of copper sulphate (8 g.) in water (200 ml.), then refluxed for 2 hr. and filtered hot. Dioxan was removed as before, and the solution concentrated on the water-bath. The osotriazole which separated was filtered off (2 g.) and recrystallised from ethanol in needles, m. p. and mixed m. p. 221—222° (Found: C, 43·5; H, 4·7; N, 11·7; Br, 22·5%).

Glucose 3 : 4-*Dibromophenylosotriazole*.—(*a*) Glucose *m*-bromophenylosazone (2 g.), suspended in water (75 ml.), was treated in the cold with bromine (3 ml.) as before. The *osotriazole* was filtered off, washed (1 g.), and recrystallised from ethanol in needles, m. p. 209—210° (solubility as for the preceding compound) (Found: C, 34·1, 34·0; H, 3·1, 3·2; N, 9·8; Br, 38·1. $C_{12}H_{13}O_4N_3Br_2$ requires C, 34·0; H, 3·1; N, 9·9; Br, 37·8%).

(*b*) Glucose *m*-bromophenylosotriazole (2 g.), similarly treated as in (*a*), gave the same product (1·9 g.), m. p. and mixed m. p. 209—210°.

(*c*) Glucose 3 : 4-dibromophenylosazone (2 g.) was treated with copper sulphate as above. The product separated (0·6 g.) and crystallised from ethanol in needles, m. p. and mixed m. p. 209—210° (Found: C, 33·8; H, 3·2; N, 10·0; Br, 37·9%).

2-o-*Tolyl*-1 : 2 : 3-*triazole*-4-*carboxylic Acid*.—A boiling suspension of glucose *o*-tolylosotriazole (0·9 g.) in water (100 ml.) was heated with potassium permanganate (4 g.) for 1·5 hr. The mixture was filtered, treated with sodium hydrogen sulphite, and acidified. The crystals (0·35 g.) recrystallised from water–ethanol in needles, m. p. 146°. 2-o-*Tolyl*-1 : 2 : 3-*triazole*-4-*carboxylic acid* is freely soluble in ethanol and methanol and insoluble in water (Found: C, 59·3; H, 4·4; N, 20·4. $C_{10}H_9O_2N_3$ requires C, 59·1; H, 4·4; N, 20·7%).

2-m-*Carboxyphenyl*-1 : 2 : 3-*triazole*-4-*carboxylic Acid*.—To a boiling suspension of glucose *m*-tolylosotriazole (0·6 g.) in water (100 ml.), potassium permanganate (4 g.) was added, and the mixture treated as above. 2-m-*Carboxyphenyl*-1 : 2 : 3-*triazole*-4-*carboxylic acid* (0·15 g.) crystallised from water–ethanol in needles, m. p. 312° (solubility as for the other acid) (Found: C, 52·0; H, 3·3; N, 18·1. $C_{10}H_7O_4N_3$ requires C, 51·5; H, 3·0; N, 18·0%).

A cold suspension of this acid (0·2 g.) in water (50 ml.) was treated with bromine as before, giving unchanged acid (0·2 g.), m. p. and mixed m. p. 312° (Found: C, 51·7; H, 3·3; N, 18·2%).

2-(4-*Bromo*-2-*methylphenyl*)-1 : 2 : 3-*triazole*-4-*carboxylic Acid*.—(*a*) To a boiling suspension of glucose 4-bromo-2-methylphenylosotriazole (0·9 g.) in water (60 ml.), potassium permanganate (4 g.) was added, and the mixture treated as above. The crystals (0·3 g.) recrystallised from water–ethanol in needles, m. p. 198°. 2-(4-*Bromo*-2-*methylphenyl*)-1 : 2 : 3-*triazole*-4-*carboxylic*

acid is soluble in methanol, ethanol, and chloroform and insoluble in water (Found: C, 42·4; H, 3·0; N, 14·5; Br, 28·5. $C_{10}H_8O_2N_3Br$ requires C, 42·6; H, 2·8; N, 14·9; Br, 28·4%).

(*b*) A cold suspension of 2-*o*-tolyl-1 : 2 : 3-triazole-4-carboxylic acid (0·15 g.) in water (30 ml.) was treated with bromine (1 ml.) and left overnight. The light brown mass obtained was filtered off, washed with water (0·19 g.), and recrystallised from water–ethanol in needles, m. p. and mixed m. p. 198°.

2-m-*Bromophenyl*-1 : 2 : 3-*triazole*-4-*carboxylic Acid.*—Glucose *m*-bromophenylosotriazole (1 g.) in water (150 ml.) was treated with solid potassium permanganate (4 g.) as before. 2-m-*Bromophenyl*-1 : 2 : 3-*triazole*-4-*carboxylic acid* (0·4 g.) recrystallised from water–ethanol in needles, m. p. 197—198° (solubility as in the last case) (Found: C, 40·7; H, 2·6; N, 15·3; Br, 29·6. $C_9H_6O_2N_3Br$ requires C, 40·3; H, 2·2; N, 15·7; Br, 29·9%).

Spectra.—See Table.

Osotriazole (II)					Triazole (cf. III)				
R	R′	*p*-Subst.	$\lambda_{max.}$ (mμ)	log ε	R	R′	*p*-Subst.	$\lambda_{max.}$ (mμ)	log ε
H	Me	H	268	4·07	H	CO_2H	H	272	4·42
H	Br	H	270	4·25	Me	H	Br	258—262	4·06
Me	H	Br	260	4·30	H	Br	H	270	4·19
H	Me	Br	274—276	4·49					
H	Br	Br	274—276	4·54					

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