787. *The Scope and Mechanism of Carbohydrate Osotriazole Formation. Part IV.*[1] *Debromination and Oxidation of Substituted Osazones and Osotriazoles.*

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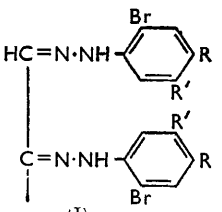
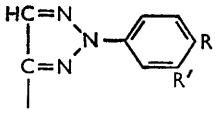
Copper precipitated during conversion of osazones into osotriazoles with copper sulphate causes *ortho*-debromination similar to that of *o*-bromocarboxylic acids. The action of copper sulphate, bromine water, and potassium permanganate on *p*-methoxyphenyl- and carboxyphenyl-osazones is investigated.

It was shown [1] that glucose 2,4-dibromophenylosazone, when refluxed with aqueous copper sulphate, did not yield the expected 2,4-dibromophenylosotriazole, but instead lost its 2-bromine atom and gave the *p*-bromophenylosotriazole. Similar debrominations were found when osazones having bromine atoms in the 2-position were converted into osotriazoles. Thus, glucose *o*-bromophenylosazone (I; R = R′ = H) afforded glucose phenylosotriazole (II; R = R′ = H); glucose 2-bromo-4-methyl- (I; R = Me, R′ = H) and 2,5-dibromo-phenylosazone (I; R = H, R′ = Br) yielded glucose *p*-tolyl- (II; R = Me, R′ = H) and *m*-bromophenyl-osotriazole (II; R = H, R′ = Br) respectively.



(I)



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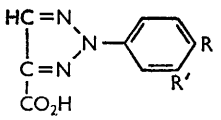
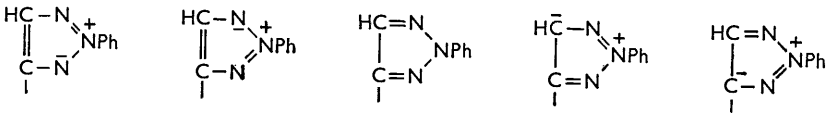


(III)

Electron-attracting groups such as the nitro-group are known to increase the reactivity of the *o*- and *p*-halogen atoms; similarly a bromine atom *ortho* to a carboxylic group is very reactive. Thus, *o*-bromobenzoic acid was shown by Hurtley [2] to be debrominated by a refluxing aqueous suspension of copper powder, yielding benzoic acid, though the *meta*- and *para*-acids were unaffected. In the present work, 2-(4-bromo-3-carboxyphenyl)-1,2,3-triazole-4-carboxylic acid (III; R = Br, R′ = CO_2H) was likewise debrominated by copper powder to the 2-*m*-carboxyphenyl-acid (III; R = H, R′ = CO_2H). It is unlikely that the latter debromination is due to the presence of the bromine *para* to the triazole

[1] Part III, *J.*, 1959, 1655.
[2] Hurtley, *J.*, 1929, 1870.

ring since glucose *p*-bromophenylosazone was not debrominated by copper sulphate,[3] or 2-*p*-bromophenyl-1,2,3-triazole-4-carboxylic acid (III; R = Br, R′ = H) by copper powder. It was also found that copper sulphate alone failed to debrominate *o*-bromobenzoic acid in the absence of copper powder. Therefore, by analogy, it is suggested that the copper precipitated during the conversion of osazones into osotriazoles is responsible for removal of the *o*-bromine atom. The 2-phenyltriazole system can exist in the annexed

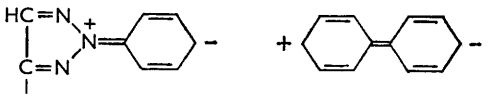


five resonating structures. The presence of a positive charge on the 2-nitrogen atom will probably cause it to behave as an electron-attracting group [4] and thus account for the similarity between the debromination of *o*-bromotriazoles and *o*-bromo-carboxylic acids.

o-Methoxyphenyl- and *o*-carboxyphenyl-osotriazoles were difficult to prepare, like the tolyl- and bromophenyl-derivatives,[1,5] though the *meta*- and *para*-triazoles were readily obtained from the osazone and copper sulphate. It seems (see Table) that triazole formation is inhibited by electron-attracting *para*-groups and facilitated by electron-donating ones, in harmony with the view that triazole formation occurs by oxidation of osazones [5] (which of course involves loss of electrons).

Glucosazone refluxed with aq. $CuSO_4$	Approx. time (hr.) for triazole formation	Yield (%)
p-Methoxyphenylosazone	¼	71
Phenylosazone	2	59
p-Carboxyphenylosazone	4	29
p-Nitrophenylosazone	No reaction	—

Glucose *m*-methoxyphenyl-osazone and -osotriazole, when treated with bromine water, afforded a dibromophenylosotriazole, presumably glucose 4,5-dibromo-3-methoxyphenyl-osotriazole. Unlike the *m*-tolyl- and *m*-bromophenyl derivatives, where mono-substitution takes place in the 4-position, the methoxy-group here seems to facilitate the introduction of a second bromine atom. Bromination in the 4- and the 5-position is most likely since in previous experience it was impossible to introduce a bromine atom *ortho* to the triazole ring (probably because of a steric effect by the latter). On the other hand, no bromination took place when *p*-methoxy- or *p*-carboxy-phenyl-osazones or -osotriazoles were treated with bromine water. The triazole ring, thus, appears to be mainly *para*-directing and if this position is occupied no bromination takes place. This behaviour can be attributed to the electromeric effect of the approaching bromine cation which would temporarily lead to the formation of a negative centre in the *para*-position, as in the case of biphenyl.



Treatment of glucose *o*-, *m*-, and *p*-methoxyphenylosotriazoles with potassium permanganate yielded the corresponding 2-(methoxyphenyl)-1,2,3-triazole-4-carboxylic acids. Similarly, glucose *m*- and *p*-carboxyphenylosotriazoles were converted into 2-(carboxyphenyl)-1,2,3-triazole-4-carboxylic acids.[1,5] Since the *m*-acid resisted bromination, probably because of $-I$ and $-T$ effects of the carboxylic group, 2-(4-bromo-3-carboxyphenyl)-1,2,3-triazole-4-carboxylic acid was prepared from glucose 4-bromo-3-methylphenylosotriazole by oxidation with potassium permanganate.

For glyoxal bisarylhydrazones and aryltriazoles there was the same pattern of reactions as with the sugar derivatives. Thus, glyoxal bisphenylhydrazone was converted

[3] Hardegger, El Khadem, and Schreier, *Helv. Chim. Acta*, 1951, **34**, 253.
[4] Benson and Savell, *Chem. Rev.*, 1950, **46**, 1.
[5] El Khadem and El-Shafei, *J.*, 1958, 3117.

into 2-bromophenyl-1,2,3-triazole by bromine water, and the *p*-tolyl derivative was obtained from the corresponding bisarylhydrazone either by copper sulphate or by bromine water; here too no bromination took place since the 4-position was occupied. Finally, potassium permanganate readily oxidised the methyl group and afforded 2-*p*-carboxyphenyl-1,2,3-triazole.

The ultraviolet absorption spectra of *m*- and *p*-methoxy- and -carboxy-phenyltriazoles are characterised by a peak between 268 and 284 mμ. As with the tolyl and bromophenyl derivatives,[1,5] the peaks of the *para*-isomers are higher and shifted towards longer wavelength. Similarly, the peaks for triazole-4-carboxylic acids (III) are shifted more than for the corresponding glucose osotriazoles (II).

Experimental

Absorption spectra were determined for ethanolic solutions with a Unicam S.P. 500 spectrophotometer.

Glucose Phenylosotriazole.—Glucose *o*-bromophenylosazone [1] (16 g.), suspended in a solution of copper sulphate (15 g.) in water (250 ml.) and dioxan (70 ml.), was refluxed for 2·5 hr. and then filtered. The solution was freed from copper sulphate by passing in hydrogen sulphide and neutralising the mixture with barium carbonate. On concentration, the osotriazole separated (2·5 g.); it recrystallised from dilute ethanol in needles, m. p. 196° alone or mixed with glucose phenylosotriazole [6] (Found: C, 54·2; H, 5·8; N, 16·1. Calc. for $C_{12}H_{15}O_4N_3$: C, 54·3; H, 5·7; N, 15·8%).

Glucose 2-Bromo-4-methylphenylosazone.—Glucose (10 g.), in water (50 ml.), was treated successively with 2-bromo-4-methylphenylhydrazine hydrochloride (35 g.) in water (150 ml.), sodium acetate (35 g.) in water (50 ml.), and a few drops of acetic acid, and then heated on the water-bath for 3 hr. The *osazone* which separated (12 g.) recrystallised from ethanol in needles, m. p. 219—220° (decomp.), difficultly soluble in boiling ethanol and methanol and insoluble in ether and water (Found: C, 44·1; H, 4·3; N, 10·5; 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 p-*Tolylosotriazole.*—A suspension of glucose 2-bromo-4-methylphenylosazone (5 g.) in dioxan (50 ml.) was refluxed with copper sulphate (5 g.) in water (120 ml.) for 1 hr., then filtered. To remove dioxan, water (50 ml.) was added and the solvent distilled off until 100 ml. were collected. On cooling, the osotriazole separated (2 g.); it recrystallised from dilute ethanol in needles, m. p. 204°, alone or mixed with glucose *p*-tolylosotriazole [7] (Found: C, 55·7; H, 5·9; N, 15·0. Calc. for $C_{13}H_{17}O_4N_3$: C, 55·9; H, 6·1; N, 15·1%).

Glucose 2,5-Dibromophenylosazone.—Glucose (6 g.) was treated with 2,5-dibromophenylhydrazine (26 g.) as above, giving an amorphous precipitate. This was washed with water and used for the preparation of the osotriazole.

Glucose m-*Bromophenylosotriazole.*—Glucose 2,5-dibromophenylosazone (2 g.) was treated with copper sulphate (2 g.) as above. The product that separated (0·2 g.) sublimed at 180°/0·5 mm.; it then crystallised from ethanol in needles, m. p. 209°, alone or mixed with glucose *m*-bromophenylosotriazole.[1]

Glucose o-*Methoxyphenylosotriazole.*—Glucose *o*-methoxyphenylosazone (9 g.) was refluxed in aqueous copper sulphate (9 g. in 300 ml.) for 1 hr., then filtered and freed from copper sulphate. The filtrate was evaporated to dryness under reduced pressure; the brown *osotriazole* (5 g.) crystallised from water–ethanol in needles, m. p. 151°, soluble in ethanol and methanol and insoluble in water (Found: C, 52·7; H, 5·8; N, 14·2. $C_{13}H_{17}O_5N_3$ requires C, 52·9; H, 5·8; N, 14·2%).

2-o-*Methoxyphenyl-1,2,3-triazole-4-carboxylic Acid.*—A suspension of glucose *o*-methoxyphenylosotriazole (2 g.) was boiled with potassium permanganate (5 g.) in water (150 ml.) for 20 min., filtered hot, treated with sodium hydrogen sulphite, and acidified. The crystals (1 g.) recrystallised from water–ethanol in needles, m. p. 136°. 2-o-*Methoxyphenyl-1,2,3-triazole-4-carboxylic acid* is soluble in ethanol and methanol and insoluble in acetone and water (Found: C, 54·9; H, 4·4; N, 19·2. $C_{10}H_9O_3N_3$ requires C, 54·8; H, 4·1; N, 19·2%).

Glucose m-*Methoxyphenylosazone.*—This osazone, prepared as above, separated (2 g. from 5 g. of the hydrazine) from dilute ethanol in needles, m. p. 182° (decomp.).

[6] Hann and Hudson, *J. Amer. Chem. Soc.*, 1944, **66**, 735.
[7] Hardegger and El Khadem, *Helv. Chim. Acta*, 1947, **30**, 1478.

Glucose m-*Methoxyphenylosotriazole*.—Glucose *m*-methoxyphenylosazone (3 g.) was treated with copper sulphate (3 g.) as for the *o*-isomer. On concentration, the *osotriazole* separated (1 g.) and recrystallised from dilute ethanol in needles, m. p. 177° (solubility as for the *ortho*-isomer) (Found: C, 52·6; H, 5·8; N, 14·0%).

Action of Bromine.—(*a*) Glucose *m*-methoxyphenylosazone (5 g.) in cold water (200 ml.) was treated with bromine (5 ml.), giving a *dibromophenylosotriazole* (1 g.), needles, m. p. 178° (from dilute ethanol), soluble in ethanol and methanol and insoluble in water (Found: C, 34·1; H, 3·5; N, 9·4; Br, 35·3. $C_{13}H_{15}O_5N_3Br_2$ requires C, 34·4; H, 3·2; N, 9·4; Br, 35·3%).

(*b*) Glucose *m*-methoxyphenylosotriazole with bromine water yielded the same product, m. p. and mixed m. p. 178°.

2-m-*Methoxyphenyl*-1,2,3-*triazole*-4-*carboxylic Acid*.—To a boiling suspension of glucose *m*-methoxyphenylosotriazole (2 g.) in water (150 ml.), potassium permanganate (5 g.) was added and the mixture treated as for the *o*-isomer. 2-m-*Methoxyphenyl*-1,2,3-*triazole*-4-*carboxylic acid* (1 g.) crystallised from water–ethanol in needles, m. p. 166° (solubility as for the other acid) (Found: C, 54·3; H, 4·2; N, 19·0%).

Glucose p-*Methoxyphenylosazone*.—Glucose (3 g.), in water (150 ml.), was heated with *p*-methoxyphenylhydrazine (7 g.) and acetic acid (4 ml.) on the water-bath for 3 hr. The crystalline *osazone* which separated (2·8 g.) recrystallised from dilute ethanol in needles, m. p. 210° (decomp.), soluble in ethanol and methanol and insoluble in ether and water (Found: C, 57·6; H, 6·4; N, 13·5. $C_{20}H_{26}O_6N_4$ requires C, 57·4; H, 6·2; N, 13·4%).

Glucose p-*Methoxyphenylosotriazole*.—(*a*) A suspension of the preceding osazone (3 g.) in aqueous copper sulphate (3 g. in 150 ml.) was refluxed for 15 min., then filtered. On cooling, the *osotriazole* separated (1·5 g.) and recrystallised from dilute ethanol in needles, m. p. 199° (solubility as for the *meta*-isomer) (Found: C, 52·5; H, 5·6; N, 14·0%).

(*b*) Glucose *p*-methoxyphenylosazone (1 g.), suspended in water (100 ml.), when treated with bromine (2 ml.), afforded the preceding osotriazole, m. p. and mixed m. p. 199°.

2-p-*Methoxyphenyl*-1,2,3-*triazole*-4-*carboxylic Acid*.—Glucose *p*-methoxyphenylosotriazole (2 g.) in water (150 ml.) was treated with solid potassium permanganate (5 g.) as described above. The *acid* (1 g.) recrystallised from water–ethanol in needles, m. p. 203° (solubility as for the *ortho*-acid) (Found: C, 55·0; H, 4·0; N, 19·2%).

Glucose m-*Carboxyphenylosazone*.—Glucose (16 g.) was treated with *m*-carboxyphenylhydrazine (50 g.) as above. The osazone which separated (20 g.) crystallised from dilute ethanol in needles, m. p. 240° (decomp.).

Glucose m-*Carboxyphenylosotriazole*.—Glucose *m*-carboxyphenylosazone (5 g.) in dioxan (100 ml.) was refluxed in aqueous copper sulphate (5 g. in 100 ml.) for 2 hr., then filtered. Dioxan was removed as described above and the solution concentrated. The *osotriazole* (1 g.) separated and recrystallised from water–ethanol in needles, m. p. 209—210° (solubility as for the other osotriazoles) (Found: C, 50·5; H, 4·6; N, 13·4. $C_{13}H_{15}O_6N_3$ requires C, 50·5; H, 4·9; N, 13·6%).

Glucose p-*Carboxyphenylosazone*.—Glucose (13 g.) was treated with *p*-carboxyphenylhydrazine hydrochloride (38 g.) as above. The osazone (16 g.) crystallised from dilute ethanol in needles, m. p. 211° (decomp.).

Glucose p-*Carboxyphenylosotriazole*.—(*a*) Glucose *p*-carboxyphenylosazone when treated with copper sulphate in the same way as the *meta*-isomer, yielded the osotriazole, m. p. 268° (Found: C, 50·7; H, 4·7; N, 13·7%). If no dioxan was used, the reaction required 4 hr. for completion.

(*b*) A cold suspension of glucose *p*-carboxyphenylosazone (5 g.) in water (200 ml.) was treated with bromine (5 ml.) and left overnight. The osotriazole was then filtered off, washed with water (1 g.), and recrystallised from dilute ethanol as needles, m. p. and mixed m. p. 268° (Found: C, 50·3; H, 4·8; N, 13·1%).

Glucose p-*Carboxyphenylosotriazole Tetra-acetate* [Prepared by M. H. Meshreki].—A solution of the osotriazole in dry pyridine was treated with acetic anhydride; the *tetra-acetate* crystallised from ethanol in needles, m. p. 165° (Found: C, 53·0; H, 4·9; N, 8·6. $C_{21}H_{23}O_{10}N_3$ requires C, 53·0; H, 4·8; N, 8·8%).

2-p-*Carboxyphenyl*-1,2,3-*triazole*-4-*carboxylic Acid*.—Glucose *p*-carboxyphenylosotriazole (1 g.), suspended in water (120 ml.), when treated with potassium permanganate (3 g.) yielded 2-*p*-carboxyphenyl-1,2,3-triazole-4-carboxylic acid,[5] m. p. and mixed m. p. 344° (decomp.).

2-(4-*Bromo*-3-*carboxyphenyl*)-1,2,3-*triazole*-4-*carboxylic Acid*.—To a boiling suspension of

glucose 4-bromo-3-methylphenylosotriazole [1] (1 g.), in water (200 ml.), potassium permanganate (5 g.) was added and the mixture refluxed for 1·5 hr. and treated as above. 2-(4-*Bromo*-3-*carboxyphenyl*)-1,2,3-*triazole*-4-*carboxylic acid* (0·7 g.) crystallised from water–ethanol in needles, m. p. 265° (solubility as for the other acids) (Found: C, 38·3; H, 2·1; N, 13·1; Br, 25·4. $C_{10}H_6O_4N_3Br$ requires C, 38·5; H, 1·9; N, 13·5; Br, 25·6%).

2-m-*Carboxyphenyl*-1,2,3-*triazole*-4-*carboxylic Acid*.—(*a*) 2-(4-Bromo-3-carboxyphenyl)-1,2,3-triazole-4-carboxylic acid (2·5 g.), suspended in water–ethanol mixture (2 : 1; 150 ml.), was refluxed with copper powder (5 g.) for 2 hr. The mixture was filtered and the filtrate concentrated to about 50 ml. and left to cool. The crystals that separated (1·5 g.) recrystallised from water–ethanol in needles, m. p. 312°, alone or mixed with 2-*m*-carboxyphenyl-1,2,3-triazole-4-carboxylic acid.[1]

(*b*) Glucose *m*-carboxyphenylosotriazole (1 g.), suspended in water (100 ml.), when treated with potassium permanganate (4 g.), afforded the same acid, m. p. and mixed m. p. 312°.

2-(3,4-*Dibromophenyl*)-1,2,3-*triazole*-4-*carboxylic Acid*.—(*a*) A boiling suspension of glucose 3,4-dibromophenylosotriazole [1] (1·5 g.), in water (100 ml.), was treated with potassium permanganate (3·5 g.) as above. 2-(3,4-*Dibromophenyl*)-1,2,3-*triazole*-4-*carboxylic acid* (0·8 g.) crystallised from water–ethanol in needles, m. p. 205° (solubility as for the other acids) (Found: C, 31·1; H, 1·5; N, 12·3; Br, 46·2. $C_9H_5O_2N_3Br_2$ requires C, 31·1; H, 1·4; N, 12·1; Br, 46·1%).

(*b*) A cold suspension of 2-*m*-bromophenyl-1,2,3-triazole-4-carboxylic acid [1] (0·8 g.) in water (75 ml.) was treated with bromine (1 ml.) and left overnight. The light brown mass obtained was filtered off, washed with water (0·6 g.), and recrystallised from water–ethanol in needles, m. p. and mixed m. p. 205°.

Glyoxal Bis-p-*tolylhydrazone*.—A solution of *p*-tolylhydrazine (26 g.) in 60% acetic acid (500 ml.) was heated to 70° and added to 40% aqueous formaldehyde (15 ml.) in 60% acetic acid (500 ml.). The mixture was kept overnight at room temperature and the *bishydrazone* that separated (8 g.) recrystallised from ethanol in plates, m. p. 225° (decomp.), soluble in boiling ethanol and methanol and insoluble in ether and water (Found: C, 71·9; H, 6·9; N, 20·6. $C_{16}H_{18}N_4$ requires C, 72·2; H, 6·8; N, 21·0%).

2-p-*Tolyl*-1,2,3-*triazole*.—(*a*) Glyoxal bis-*p*-tolylhydrazone (4 g.) was refluxed in a solution of copper sulphate (5 g.) in 20% aqueous dioxan (125 ml.) for 1·5 hr. The solution was then steam-distilled and the distillate (200 ml.) extracted with ether. The ethereal layer was washed with dilute hydrochloric acid and dried (Na_2SO_4). The *triazole* (1·5 g.) remaining after removal of the ether was repeatedly sublimed at 120°/2 mm., yielding plates, m. p. 55°, soluble in ethanol and methanol and insoluble in water (Found: C, 67·8; H, 5·4; N, 26·6. $C_9H_9N_3$ requires C, 67·9; H, 5·7; N, 26·4%).

(*b*) Glyoxal bis-*p*-tolylhydrazone (2 g.), suspended in water (100 ml.), was treated in the cold with bromine (1 ml.), and kept overnight. The mass formed was filtered off, steam-distilled, and purified as in (*a*), giving the same product, m. p. and mixed m. p. 55°.

2-p-*Carboxyphenyl*-1,2,3-*triazole*.—To a boiling suspension of 2-*p*-tolyl-1,2,3-triazole (1·5 g.) in water (250 ml.), potassium permanganate (4 g.) was added and the mixture treated as above. The acid which separated (0·9 g.) recrystallised from water–ethanol in needles, m. p. above 280° (Found: C, 57·2; H, 3·8; N, 22·2. Calc. for $C_9H_7O_2N_3$: C, 57·1; H, 3·7; N, 22·2%).

2-p-*Bromophenyl*-1,2,3-*triazole*.—Glyoxal bisphenylhydrazone (2 g.), suspended in water (100 ml.), was treated in the cold with bromine (1·5 ml.) and kept overnight. The mass formed was filtered off, steam-distilled, and purified as for the *p*-tolyltriazole. The sublimed *triazole* (0·7 g.) recrystallised from chloroform–light petroleum (b. p. 40—60°) in elongated prisms, m. p. 113—114°, soluble in ethanol, methanol, acetone, and chloroform, and insoluble in light petroleum (Found: C, 43·0; H, 2·9; N, 18·4. $C_8H_6N_3Br$ requires C, 42·9; H, 2·7; N, 18·7%).

Spectra.—See Table.

Osotriazole (cf. II)				Triazole (cf. III)			
R	R′	$\lambda_{max.}$ (mμ)	log ε	R	R′	$\lambda_{max.}$ (mμ)	log ε
H	OMe	268	4·21	H	OMe	272	4·18
OMe	H	278	4·25	OMe	H	284	4·52
H	CO_2H	268	4·25				
CO_2H	H	280	4·37				

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