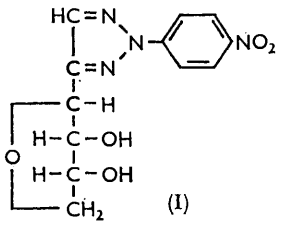
432. *The Scope and Mechanism of Carbohydrate Osotriazole Formation. Part XII.* Anhydro- and Other Triazole Derivatives.*

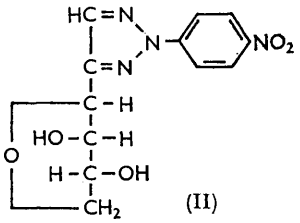
By H. El Khadem, M. H. Meshreki, and (in part) G. H. Labib.

Nitration of glucose and galactose phenylosotriazoles results in the formation of the corresponding 3,6-anhydro-*p*-nitrophenylosotriazoles. Glucose *p*-hydroxyaminophenylosotriazole is described, as well as a number of halogeno-2-phenyl-1,2,3-triazole-4-carboxylic acid esters and amides for screening as insecticides.

Nitration and hydrolysis of monosaccharide phenylosotriazole tetra-acetates yields the *p*-nitrophenylosotriazoles.[1-3] The unacetylated glucose and galactose phenylosotriazoles have now been nitrated with nitric and sulphuric acids, to give the 3,6-anhydro-*p*-nitrophenylosotriazoles (I) and (II). The structure of the glucose derivative was determined by oxidation with potassium permanganate to the known 2-*p*-nitrophenyl-1,2,3-triazole-4-carboxylic acid (III).[4] The anhydroglucose *p*-nitrophenylosotriazole yielded a diacetate and an isopropylidene derivative which on hydrolysis were converted back into the starting material, denoting the presence of two adjacent hydroxyl groups (positions 4



(I)



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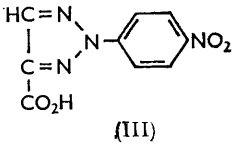

(III)

and 5). Periodate oxidation resulted in the consumption of one mole of periodate with the formation of an aldehyde and no formaldehyde. The stability of the anhydro-osotriazole towards acids and alkalis eliminated the possibility of an ethylene oxide ring, and its failure to react with trityl chloride suggested the absence of a primary hydroxyl group. The configuration at C-3 still remained uncertain since the possibility existed of a Walden inversion similar to that produced during the treatment of glucose phenylosazone and osotriazole with methanolic sulphuric acid, to give the anhydro-osazone described by Diels and Meyer, and its osotriazole, which were shown to be mainly formed of the 3,6-anhydro-D-*ribo*-hexose isomers.[5] We nitrated the 3,6-anhydrophenylosotriazole obtained from Diels and Meyer's anhydroglucose phenylosazone and isolated a 3,6-anhydro-*p*-nitrophenylosotriazole with a lower melting point. We therefore concluded that the anhydro-ring formed during nitration of glucose phenylosotriazole was not accompanied by Walden inversion, and that the isomer we obtained was 3,6-anhydro-*arabino*-hexose *p*-nitrophenylosotriazole (I). Nitration of galactose phenylosotriazole yielded 3,6-anhydro-*lyxo*-hexose *p*-nitrophenylosotriazole (II) identical with that obtained on nitration of Diels and Meyer's anhydrogalactose phenylosotriazole. Since the latter is known to be formed without Walden inversion,[6] the structure was established without difficulty. Another anhydrophenylosotriazole, obtained by hydrolysis of the 6-tosylate of glucose phenylosotriazole, is being investigated.

* Part XI, Bishey, El Khadem, and El-Shafei, *J.*, 1963, 4980.

[1] El Khadem and Meshreki, *Nature*, 1962, **194**, 373.
[2] Bishay, El Khadem, El-Shafei, and Meshreki, *J.*, 1962, 3154.
[3] El Khadem, Labib, and Meshreki, *J.*, 1963, 3528.
[4] Bischop, *Science*, 1953, **117**, 715.
[5] Hardegger and Schreier, *Helv. Chim. Acta*, 1952, **35**, 243; El Khadem, Schreier, Stöhr, and Hardegger, *ibid.*, p. 993.
[6] Bayne, *J.*, 1952, 4993.

An insoluble compound, occasionally obtained during the hydrogenation of glucose *p*-nitrophenylosotriazole tetra-acetate to the amino-derivative, is shown to be glucose *p*-hydroxyaminophenylosotriazole tetra-acetate, formed by the incomplete reduction of the nitro-compound especially when a relatively small amount of catalyst is used. It shows infrared bands at 3560 (OH), 3225 (NH), and 1750 cm.$^{-1}$ (OAc). On hydrolysis it gave glucose *p*-hydroxyaminophenylosotriazole, and on reduction it yielded glucose *p*-aminophenylosotriazole tetra-acetate.[2]

Halogeno-2-phenyl-1,2,3-triazole-4-carboxyamides and methyl and ethyl carboxylates, as well as the halogenophenyl-1,2,3-triazoles, were prepared for screening as insecticides.[7] The methyl esters were prepared from the acids by treatment with diazomethane, and the ethyl esters from the silver salts by treatment with ethyl iodide. The ethyl esters were converted into the amides by treatment with ethanolic ammonia, and the silver salts decarboxylated to the 2-halogenophenyl-1,2,3-triazoles.

The ultraviolet spectra of the esters, amides, and triazoles are characterised by a single peak between 265 and 310 mμ, and, as with the osotriazoles studied earlier,[7] there is a gradual shift towards longer wavelength for the *para*-monosubstituted derivatives as we go from the fluoro- through the chloro- to the bromo-derivatives.

Experimental

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

3,6-*Anhydroglucose* p-*Nitrophenylosotriazole*.—To a stirred, cooled solution of glucose phenylosotriazole (7 g.) in glacial acetic acid (40 ml.) and sulphuric acid (*d* 1·84) (40 ml.), nitric acid (*d* 1·52) (12 ml.) was added dropwise during 1 hr., the temperature being kept below 15°. After a further hour's stirring, the mixture was poured on ice and extracted with chloroform, and the chloroform layer was washed, dried, and evaporated. The residue was hydrolysed (in case of partial acetylation during nitration) by ethanolic ammonia (100 ml.) at room temperature for 24 hr. The 3,6-*anhydro*-p-*nitrophenylosotriazole*, which separated, crystallised from dilute ethanol in needles, m. p. 155°; it was soluble in hot ethanol and methanol, and insoluble in water (Found: C, 48·8; H, 4·5; N, 18·7. $C_{12}H_{12}N_4O_5$ requires C, 49·3; H, 4·1; N, 19·2%), $\lambda_{max.}$ 310 mμ (log ε 4·25), $\lambda_{min.}$ 260 mμ (log ε 3·23), $[\alpha]_D$ −85° (*c* 0·5 in EtOH).

A solution of the 3,6-anhydro-*p*-nitrophenylosotriazole (1 g.) in dry pyridine (15 ml.) was treated with acetic anhydride (15 ml.), left for 24 hr., poured on ice, and the whole extracted with ether. The ether layer was washed, dried, and evaporated. The *diacetate* crystallised from dilute ethanol in needles, m. p. 138°; it was soluble in ethanol, methanol, and ether, and insoluble in water (Found: C, 50·9; H, 4·5; N, 15·0. $C_{16}H_{16}N_4O_7$ requires C, 51·1; H, 4·3; N, 14·9%).

The 3,6-anhydro-*p*-nitrophenylosotriazole (0·2 g.) was dissolved in a solution of hydrogen chloride in acetone (15 ml.). The mixture was shaken with anhydrous sodium sulphate (1 g.) for 24 hr., filtered, neutralised with silver carbonate, and the filtrate evaporated to dryness. The *isopropylidene derivative* crystallised from ethanol in needles, m. p. 192° (solubility as for the diacetate) (Found: N, 17·2. $C_{15}H_{16}N_4O_5$ requires N, 16·9%).

The 3,6-anhydro-*p*-nitrophenylosotriazole (292 mg.) was suspended in a solution of sodium metaperiodate (755 mg.) in water (10 ml.), and the mixture shaken for 24 hr. The aldehyde obtained (200 mg.) crystallised from dilute ethanol in needles, m. p. 125°. The filtrate was diluted to 1 l., treated with excess of arsenite, and back-titrated against standard iodine solution; periodate consumption was 1·2 moles.

2-p-*Nitrophenyl*-1,2,3-*triazole*-4-*carboxylic Acid*.—A boiling suspension of the 3,6-anhydro-*p*-nitrophenylosotriazole (0·3 g.) in water (100 ml.) was heated with potassium permanganate (4 g.) for 1 hr. The hot mixture was filtered, decolourised by sulphur dioxide, and acidified. The triazolecarboxylic acid which separated had m. p. and mixed m. p.[4] 237° (from dilute ethanol).

Nitration of Diels and Meyer's Anhydroglucose Phenylosotriazole Diacetate.—The anhydroglucose phenylosotriazole diacetate (5 g.), nitrated and hydrolysed as described above, yielded

[7] El Khadem, Kolkaila, and Meshreki, *J.*, 1963, 3531.

a 3,6-*anhydro*-p-*nitrophenylosotriazole*, m. p. 145°, $[\alpha]_D$ −50° (*c* 0·2 in EtOH) (Found: C, 49·2; H, 4·4; N, 19·0. $C_{12}H_{12}N_4O_5$ requires C, 49·3; H, 4·1; N, 19·2%), $\lambda_{max.}$ 310 mμ (log ε 3·20), $\lambda_{min.}$ 260 mμ (log ε 2·20).

3,6-*Anhydrogalactose* p-*Nitrophenylosotriazole*.—To a stirred, cooled solution of galactose phenylosotriazole (5 g.) in glacial acetic acid (35 ml.) and sulphuric acid (*d* 1·84) (35 ml.), nitric acid (*d* 1·52) (10 ml.) was added dropwise during 1 hr.; treatment was as for the glucose derivative. The *osotriazole* which separated crystallised from dilute ethanol in needles, m. p. 178—180°, $[\alpha]_D$ −41·5° (*c* 0·2 in EtOH) (Found: C, 49·9; H, 4·5; N, 18·9. $C_{12}H_{12}N_4O_5$ requires C, 49·3; H, 4·1; N, 19·2%), $\lambda_{max.}$ 310 mμ (log ε 4·45), $\lambda_{min.}$ 260 mμ (log ε 3·42). In another preparation, Diels and Meyer's anhydrogalactose phenylosotriazole diacetate (4 g.), nitrated and hydrolysed as before, yielded the osotriazole, m. p. and mixed m. p. 178—180° (Found: N, 18·8%).

A solution of the *p*-nitrophenylosotriazole (1 g.) in dry pyridine (10 ml.) was treated with toluene-*p*-sulphonyl chloride (1·2 g.); the mixture was left for 24 hr., poured on ice, and extracted with ether. The ether layer was washed, dried, and evaporated. The *monotosylate* crystallised from ethanol in needles, m. p. 116°, soluble in hot ethanol, methanol, and ether, and insoluble in water (Found: C, 50·7; H, 3·7. $C_{19}H_{18}N_4O_7S$ requires C, 51·1; H, 4·0%).

A solution of the *p*-nitrophenylosotriazole (1 g.) in dry pyridine (10 ml.) was treated with toluene-*p*-sulphonyl chloride (4 g.), and treated as for the mono-derivative. The *ditosylate* crystallised from ethanol in needles, m. p. 224° (solubility as for the mono-derivative) (Found: C, 52·3; H, 3·9; N, 9·6. $C_{26}H_{24}N_4O_9S_2$ requires C, 52·0; H, 4·0; N, 9·3%).

The *p*-nitrophenylosotriazole, when treated exactly as for the glucose derivative, consumed 0·85 mole of periodate.

Glucose Arylosotriazole 6-*Tosylates*.—A solution of the osotriazole (1 g.) in dry pyridine (5 ml.) was treated with toluene-*p*-sulphonyl chloride (1·2 g.), left for 24 hr., poured on ice, and extracted with ether. The ether layer was washed, dried, and evaporated. The products (Table 1) crystallised from ethanol, and were soluble in ethanol, methanol, and ether, and insoluble in water.

TABLE 1.

Glucose arylosotriazole 6-tosylates.

			Found (%)				Required (%)		
Subst. in Ph	M. p.	Yield (%)	C	H	N	Formula	C	H	N
Ph	140°	20	54·4	4·9	—	$C_{19}H_{21}SN_3O_6$	54·4	5·1	—
p-Me [8]	117	18	55·8	5·5	—	$C_{20}H_{23}SN_3O_6$	55·4	5·3	—
p-Br [9]	153	15	—	—	8·1	$C_{19}H_{20}BrSN_3O_6$	—	—	8·4

Glucose p-*Hydroxyaminophenylosotriazole Tetra-acetate*.—Glucose *p*-nitrophenylosotriazole tetra-acetate [2] (11·5 g.) in methanol (300 ml.) was hydrogenated at 1 atm. over palladium–barium sulphate (1 g.). After 3 hr., the yellow *product* was filtered off, and repeatedly crystallised from hot acetic acid, to give needles, m. p. 208°; it was soluble in hot acetic acid, sparingly soluble in hot ethanol and in methanol, and insoluble in water (Found: C, 51·8; H, 4·7; N, 12·4; Ac, 41·1. $C_{20}H_{24}N_4O_9$ requires C, 51·7; H, 5·1; N, 12·1; Ac, 38·0%).

Glucose p-*Hydroxyaminophenylosotriazole*.—Glucose *p*-hydroxyaminophenylosotriazole tetra-acetate (5 g.) was hydrolysed by boiling in 5% ethanolic sodium hydroxide (100 ml.) for 30 min. On cooling, the *product* was filtered off, washed several times with water, and dried. It crystallised from hot acetic acid in needles, m. p. 232° (solubility less than for the acetate) (Found: C, 48·4; H, 5·2. $C_{12}H_{16}N_4O_5$ requires C, 48·6; H, 5·4%).

Glucose p-*Aminophenylosotriazole Tetra-acetate*.—Glucose *p*-hydroxyaminophenylosotriazole tetra-acetate (1 g.) in methanol (50 ml.) was hydrogenated at 1 atm. over palladium–barium sulphate (4 g.) within 4 hr.; 200 ml. of hydrogen were absorbed. The mixture was filtered and concentrated; the tetra-acetate product separated, m. p. and mixed m. p.[2] 120°.

Methyl 2-*Aryl*-1,2,3-*triazole*-4-*carboxylates*.—The 2-aryl-1,2,3-triazole-4-carboxylic acid (0·5 g.), dissolved in ether (100 ml.), was treated with 5% diazomethane in ether (200 ml.), and the

[8] Hardegger and El Khadem, *Helv. Chim. Acta*, 1947, **30**, 1478.
[9] Hardegger, El Khadem, and Schreier, *Helv. Chim. Acta*, 1951, **34**, 253.

ether was left to evaporate slowly at room temperature. After 24 hr., the ester that separated was filtered off and recrystallised from ethanol (see Table 2). The esters were soluble in ethanol or methanol, and insoluble in water.

Glucose p-*Carboxyphenylosotriazole Methyl Ester.*—Glucose *p*-carboxyphenylosotriazole [10] (0·3 g.), suspended in ether (75 ml.), was treated as above. The *ester* (0·4 g.) crystallised from ethanol in prismatic needles, m. p. 255° (solubility as above) (Found: N, 13·1. $C_{14}H_{17}N_3O_6$ requires N, 13·0%).

To a suspension of the 2-aryl-1,2,3-triazole-4-carboxylic acid (0·5 g.) in ammoniacal silver nitrate (50 ml.), a mixture of equal volumes of acetone–methanol (150 ml.) was added. The clear solution was concentrated on a water-bath, and the silver salt separated. The salts were used without purification for the preparation of the ethyl esters and triazoles.

Ethyl 2-Aryl-1,2,3-triazole-4-carboxylates.—A suspension of the silver salt of the acid (0·5 g.) in ethyl iodide (60 ml.) was refluxed on a water-bath for 3 hr., and filtered. Ethanol (50 ml.) was added to the filtrate, and the solution concentrated. The *esters* (Table 2) that separated crystallised from ethanol and were soluble in hot ethanol or methanol, and insoluble in water.

2-*Aryl*-1,2,3-*triazole*-4-*carboxyamides.*—A saturated solution of ethanolic ammonia (100 ml.) was added to ethyl 2-aryl-1,2,3-triazole-4-carboxylate (0·4 g.) and the mixture left overnight at room temperature. The solution was concentrated on a water-bath and the *amide* that separated was recrystallised from ethanol; the amides were soluble in boiling ethanol or methanol, and insoluble in water (Table 2).

2-*Aryl*-1,2,3-*triazoles.*—The silver salts of 2-aryl-1,2,3-triazole-4-carboxylic acids (0·7 g.) were decarboxylated by heating at 170—180°, and the sublimates obtained were recrystallised from ethanol. The *triazoles* were soluble in ethanol, methanol, acetone, and chloroform, and insoluble in light petroleum (Table 2).

TABLE 2.

Subst. in Ph	M. p.	Yield (%)	Found N (%)	Formula	Required N (%)	$\lambda_{max.}$ (mμ)	log ε	$\lambda_{min.}$ (mμ)	log ε
Methyl 2-aryl-1,2,3-triazole-4-carboxylates.									
p-Cl	120°	95	18·1	$C_{10}H_8ClN_3O_2$	17·7	275	4·41	230	3·32
p-Br	152	95	15·1	$C_{10}H_8BrN_3O_2$	14·8	276	4·37	230	3·31
p-NO_2	218	90	23·0	$C_{10}H_8N_4O_4$	22·6	300	4·47	252	3·51
Ethyl 2-aryl-1,2,3-triazole-4-carboxylates.									
Ph	59—60° [11]	65	19·5	$C_{11}H_{11}N_3O_2$	19·4	270	4·29	230	3·39
m-F	64	60	17·6	$C_{11}H_{10}FN_3O_2$	17·9	—	—	—	—
p-F	79	64	17·8	$C_{11}H_{10}FN_3O_2$	17·9	—	—	—	—
m-Cl	57—58	68	16·5	$C_{11}H_{10}ClN_3O_2$	16·7	—	—	—	—
p-Cl	86—87	70	16·5	$C_{11}H_{10}ClN_3O_2$	16·7	275	4·25	230	3·16
p-Br	89—90	72	13·7	$C_{11}H_{10}BrN_3O_2$	14·2	278	4·35	232	3·17
p-NO_2	123	75	21·9	$C_{11}H_{10}N_4O_4$	21·4	305	4·28	255	3·45
2-Aryl-1,2,3-triazole-4-carboxyamides.									
p-F	201°	85	27·1	$C_9H_7FN_4O$	27·2	275	4·25	230	3·52
p-Cl	212	85	25·0	$C_9H_7ClN_4O$	25·2	—	—	—	—
p-Br	226	78	21·0	$C_9H_7BrN_4O$	21·0	280	4·35	235	3·37
p-NO_2	256	83	30·4	$C_9H_7N_5O_3$	30·4	310	4·34	255	3·52
2-Aryl-1,2,3-triazoles.									
m-Cl	40°	40	23·1	$C_8H_6ClN_3$	23·4	265	4·24	228	3·35
p-Cl	102	45	23·0	$C_8H_6ClN_3$	23·4	266	4·26	222	3·82
p-Br *	114 [10]	50	19·3	$C_8H_6BrN_3$	18·7	—	—	—	—

* Crystallised from chloroform–light petroleum.

FACULTY OF SCIENCE, ALEXANDRIA UNIVERSITY,
ALEXANDRIA, U.A.R.

[*Received, August 9th,* 1963.]

[10] El Khadem, El-Shafei, and Mohammed, *J.*, 1960, 3993.
[11] Jonas and von Pechmann, *Annalen*, 1891, **262**, 287.