943. *New Anhydrophenylosazones.*

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Dianhydrophenylosazone acetates have been obtained by refluxing monosaccharide phenylosazones with acetic anhydride. The hexose and methylpentose dianhydrophenylosazones have only one asymmetric carbon atom, and pentoses yield an optically inactive compound. Glucose phenylosazone yielded also a new triacetylmonoanhydrophenylosazone.

Anhydrophenylosazones have been prepared by dehydrating osazones with methanolic sulphuric acid to monoanhydrophenylosazones[1] or by hydrolysis of the osazone acetates to yield dianhydrophenylosazones.[2] We have prepared new types of anhydrophenylosazones by refluxing phenylosazones with acetic anhydride. Thus, D-glucose phenylosazone yielded a colourless triacetyldianhydrophenylosazone (I; R = Ac); the same compound was also obtained from D-galactose phenylosazone, and its enantiomorph from L-sorbose phenylosazone. This triacetyldianhydrophenylosazone, when hydrolysed by Kunz and Hudson's method,[3] revealed the presence of two hydrolysable *O*-acetyl groups and of one *N*-acetyl group which resisted hydrolysis. The presence of both *O*- and *N*-acetyl groups was apparent in the infrared spectrum which showed the ester band at 1725 and the amide band at 1670 cm.$^{-1}$.

D-Glucose *N*-acetyldianhydrophenylosazone (I; R = H) and the L-isomer were obtained by hydrolysis of the corresponding triacetyl compounds with ethanolic ammonia. The former showed the amide band at 1640 and the hydroxyl band at 3350 cm.$^{-1}$ and on acetylation gave the starting triacetyl compounds. With acetone it gave an isopropylidene derivative, denoting the presence of two adjacent hydroxyl groups. It consumed one mol. of sodium periodate, yielding a pyrazolealdehyde (V) and formaldehyde, suggesting that the primary 6-hydroxyl group was free and that the isopropylidene was linked in positions 5 and 6. Oxidation with potassium permanganate yielded 1-phenylpyrazole-3,5-dicarboxylic

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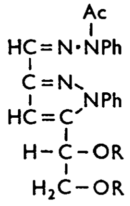
[1] Diels and Meyer, *Annalen*, 1935, **519**, 157; Percival, *Adv. Carbohydrate Chem.*, 1948, **3**, 31; El Khadem, Schreier, Stohr, and Hardegger, *Helv. Chim. Acta*, 1952, **35**, 994; Bayne, *J.*, 1952, 4993.

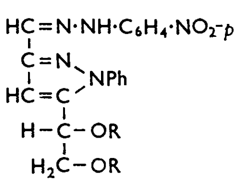
[2] Percival, *J.*, 1936, 1770; Percival and Percival, *J.*, 1937, 1320.

[3] Kunz and Hudson, *J. Amer. Chem. Soc.*, 1926, **48**, 1982.

acid (VI), identical with a specimen prepared from 3-methyl-1-phenylpyrazole-5-carboxylic acid.[4]



(I)



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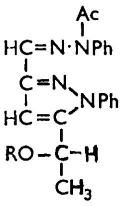

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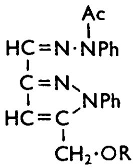

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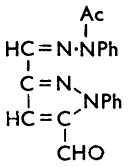

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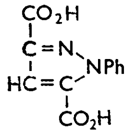

(VI)

The formation of this acid (VI) suggests that closure of the pyrazole ring took place by removal of water from the 3- and 4-hydroxyl groups and the hydrogen atoms from C-4 and the NH group of the phenylhydrazone residue on C-2 of the osazone. Since both the triacetyldianhydrophenylosazone and the *N*-acetyldianhydrophenylosazone gave Knorr's pyrazoline reaction,[5] it was concluded that the pyrazole ring was formed during the reaction with acetic anhydride and not as a result of oxidation with permanganate.

The *N*-acetylphenylhydrazone residue on C-1 was replaced on treatment with *p*-nitrophenylhydrazine by a process of trans-hydrazone-formation. The product (II; R = H) no longer possessed the amide band at 1640 cm.$^{-1}$ and on acetylation gave a di-*O*-acetate (II; R = Ac) which showed only the ester band at 1735 cm.$^{-1}$. It was therefore concluded that the triacetyldianhydrophenylosazone obtained was the *N'*-acetylphenylhydrazone of 5-(D-1,2-diacetoxyethyl)-3-formyl-1-phenylpyrazole.

Another anhydrophenylosazone was obtained by refluxing glucose phenylosazone with acetic anhydride in the presence of zinc dust (to prevent the formation of the triacetyldianhydrophenylosazone). It was also prepared in small amounts from the mother-liquor when the latter compound was prepared without use of zinc dust. The formula of this compound agrees with that of a glucose triacetylmonoanhydrophenylosazone. Hydrolysis by Kunz and Hudson's method showed the presence of two hydrolysable *O*-acetyl groups and one *N*-acetyl group (ester band at 1725, amide band at 1675 cm.$^{-1}$). The structure of this compound is under investigation.

Methylpentose phenylosazones reacted with acetic anhydride to give diacetyldianhydrophenylosazone which existed in two forms. The L-derivative (III; R = Ac) was obtained from L-rhamnose, and its enantiomorph from D-fucose phenylosazone. Hydrolysis with ethanolic ammonia removed one *O*-acetyl group, and *p*-nitrophenylhydrazine replaced the *N*-acetylphenylhydrazone residue.

The presence of only two isomeric hexose or methylpentose dianhydrophenylosazones, one D and one L, affords a means of recognising the configuration of the 5-hydroxyl group.

Pentose phenylosazones yielded an optically inactive diacetyldianhydrophenylosazone (IV; R = Ac) which was obtained from both D-xylose and L-arabinose phenylosazone. It was likewise hydrolysed with ethanolic ammonia to the compound (IV; R = H) and then treated with *p*-nitrophenylhydrazine.

EXPERIMENTAL

Infrared absorption spectra were measured on Zeiss U.R. 10 and Perkin-Elmer infracord spectrophotometers, and ultraviolet absorption spectra on a Unicam S.P. 500 spectrophotometer. *O*-Acetyl groups were determined by Kunz and Hudson's method,[3] and total acetyl according to Kuhn and Roth's directions.[6]

D-Hexose N-*Acetyldianhydrophenylosazone Diacetate*.—(*A*) *From* D-*glucose phenylosazone*. The osazone (20 g.) was refluxed in acetic anhydride (100 ml.) for 30 min., the osazone dissolving in

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[4] Claisen and Roosen, *Annalen*, 1894, **278**, 269, 272, 286.

[5] Knorr, *Ber.*, 1893, **26**, 100.

[6] Kuhn and Roth, *Ber.*, 1933, **66**, 1274.

5 min. The mixture was poured on ice (500 g.) and left overnight. The aqueous solution was decanted and the residual oil washed repeatedly with water; after several days it solidified, The N-*Acetyldianhydrophenylosazone diacetate* crystallised from dilute ethanol in needles, m. p. 131°, $[\alpha]_D$ +68° (*c* 1 in $CHCl_3$), soluble in ethanol, chloroform, and ether and insoluble in water (Found: C, 64·5; H, 5·3; N, 13·1; OAc, 18·0; Total Ac, 24·2. $C_{24}H_{24}N_4O_5$ requires C, 64·3; H, 5·4; N, 12·5; OAc, 19·2; Total Ac, 27·7%), $\lambda_{max.}$ 282 mμ (log ε 4·6), $\lambda_{min.}$ 240 mμ (log 4·0).

(*B*) *From* D-*galactose phenylosazone.* D-Galactose phenylosazone, on similar treatment, yielded the same dianhydrophenylosazone, m. p. and mixed m. p. 131°, $[\alpha]_D$ +68° (*c* 1 in $CHCl_3$) (Found: C, 64·4; H, 5·6; N, 13·0%).

(*C*) *From the* N-*monoacetyldianhydrophenylosazone.* The *N*-monoacetyldianhydrophenylosazone was treated with acetic anhydride and pyridine overnight and the mixture poured on ice. The precipitate, when washed with water and crystallised from dilute ethanol, had m. p. and mixed m. p. 131°.

L-*Hexose* N-*Acetyldianhydrophenylosazone Diacetate.*—L-Sorbose phenylosazone, on treatment as above, yielded the enantiomorphic N-*Acetyldianhydrophenylosazone diacetate*, m. p. and mixed m. p. 131°, $[\alpha]_D$ −68° (*c* 1 in $CHCl_3$) (Found: C, 65·0; H, 5·5; N, 12·8%).

DL-*Hexose* N-*Acetyldianhydrophenylosazone Diacetate.*—A solution of either triacetyl-D- or triacetyl-L-dianhydrophenylosazone (0·1 g.) in hot ethanol (10 ml.) was treated with warm water (5 ml.). The triacetyl-DL-dianhydrophenylosazone triacetate crystallised in needles, m. p. 131, $[\alpha]_D$ 0°.

D-*Hexose* N-*Monoacetyldianhydrophenylosazone.*—The triacetyl-D-hexose dianhydrophenylosazone (0·2 g.) was hydrolysed with 20% ethanolic ammonia (20 ml.) overnight at room temperature. The solution was concentrated on the water-bath; the N-*monoacetyldianhydrophenylosazone* separated on addition of water. It was also conveniently prepared by carrying out the hydrolysis on the crude oily residue obtained by refluxing D-glucose or D-galactose phenylosazone with acetic anhydride. The product crystallised from dilute ethanol in needles, m. p. 175°, as a *hemihydrate* (Found: C, 64·1; H, 6·0; N, 15·0. $C_{20}H_{20}N_4O_3,\frac{1}{2}H_2O$ requires C, 64·3; H, 5·6; N, 15·0%), which on prolonged dehydration under reduced pressure lost the water (Found: C, 66·4; H, 6·1; N, 14·9; O, 12·8; Ac, 8·2. $C_{20}H_{20}N_4O_3$ requires C, 65·9; H, 5·5; N, 15·4; O, 13·2; Ac, 11·2%); it had $[\alpha]_D$ +13° (*c* 1 in EtOH), $\lambda_{max.}$ 284 mμ (log ε 4·5), $\lambda_{min.}$ 244 mμ (log ε 3·9).

L-*Hexose* N-*Monoacetyldianhydrophenylosazone.*—This was similarly prepared from triacetyl-L-dianhydrophenylosazone and had m. p. and mixed m. p. 175°, $[\alpha]_D$ −13° (*c* 1 in EtOH).

DL-*Hexose* N-*Monoacetyldianhydrophenylosazone.*—A solution of either the D- or L-*N*-monoacetyldianhydrophenylosazone (0·1 g.) in hot ethanol (10 ml.) was treated with warm water (10 ml.). The DL-*N*-monoacetyldianhydrophenylosazone crystallised in needles, m. p. 175°, $[\alpha]_D$ 0°.

Periodate Oxidation.—The D-*N*-monoacetyldianhydrophenylosazone (364 mg.) was suspended in a solution of sodium periodate (750 mg.) in water (10 ml.) and shaken for 24 hr. The *aldehyde* (V) (0·3 g.) crystallised from dilute ethanol in needles, m. p. 149—150° (Found: N, 16·8. $C_{19}H_{16}N_4O_2$ requires N, 16·6%). The filtrate was diluted to 1 l., treated with an excess of arsenite, and back-titrated against iodine solution (periodate consumption = 0·93 mol.). Another sample (1 g.) was treated with sodium periodate (0·6 g.) in water (5 ml.) for 24 hr. and the filtrate treated with 1% dimedone solution; formaldehyde dimedone separated, having m. p. and mixed m. p. 187°.

Isopropylidene Derivative.—The D-*N*-monoacetyldianhydrophenylosazone (0·2 g.) was dissolved in a solution of hydrogen chloride in acetone (20 ml.), and shaken with anhydrous sodium sulphate (1 g.) for 24 hr. The mixture was then filtered, neutralised with silver carbonate, filtered, and evaporated to dryness. The *isopropylidene derivative* crystallised from dilute ethanol in needles, m. p. 162° (Found: C, 68·7; H, 6·1; N, 13·7. $C_{23}H_{24}N_4O_3$ requires C, 68·3; H, 5·9; N, 13·9%).

Oxidation with Potassium Permanganate.—The D-*N*-monoacetyldianhydrophenylosazone (0·6 g.) in water (50 ml.) was refluxed with an excess of potassium permanganate for 30 min. The mixture was filtered, decolorised with sulphur dioxide, acidified, and extracted with ether. The residue left after evaporation of ether was sublimed at 250°/0·1 mm., yielding 1-phenylpyrazole-3,5-dicarboxylic acid, m. p. 270°, not depressed on admixture with an authentic specimen which gave an identical infrared spectrum (Found: N, 12·1%; Equiv., 117. Calc. for $C_{11}H_8N_2O_4$: N, 12·1%; Equiv., 116).

Authentic 1-*Phenylpyrazole*-3,5-*dicarboxylic Acid.*—3-Methyl-1-phenylpyrazole-5-carboxylic acid (1 g.) was refluxed for 3 hr. with potassium permanganate solution, filtered, decolorised with sulphur dioxide, and extracted with ether. The residue left after evaporation of ether was sublimed as above, then having 270°.

Reaction with p-*Nitrophenylhydrazine.*—The D-*N*-monoacetyldianhydrophenylosazone (0·5 g.) in ethanol (10 ml.) was treated with a solution of *p*-nitrophenylhydrazine (0·2 g.) in hot ethanol (10 ml.), followed by acetic acid (1 ml.). The mixture was refluxed for 1 hr. On cooling, the p-*nitrophenylhydrazone derivative* (II; R = H) separated and crystallised from ethanol in orange needles, m. p. 236° (Found: C, 59·0; H, 4·8; N, 19·5. $C_{18}H_{17}N_5O_4$ requires C, 58·9; H, 4·6; N, 19·1%). This product on acetylation with acetic anhydride and pyridine for 24 hr. yielded the *di*-O-*acetate* (II; R = Ac), which crystallised from dilute ethanol in yellow needles, m. p. 165—166° (Found: C, 59·0; H, 4·9; N, 15·6. $C_{22}H_{21}N_5O_6$ requires C, 58·5; H, 4·7; N, 15·5%).

D-*Glucose* N-*Acetylmonoanhydrophenylosazone Diacetate.*—A mixture of glucose phenylosazone (20 g.) and zinc powder (10 g.) was refluxed with acetic anhydride (100 ml.) for 30 min. then poured on ice (500 g.). After several days the oily residue solidified and it was washed with ethanol and crystallised from hot ethanol in yellow needles, m. p. 172—173° (Found: C, 61·3; H, 5·9; N, 12·2; O, 20·7; OAc, 17·9; Total Ac, 26·5. $C_{24}H_{26}N_4O_3$ requires C, 61·8; H, 5·6; N, 12·0; O, 20·6; OAc, 18·4; Total Ac, 27·5%), $\lambda_{max.}$ 270 mμ (log ε 4·4), $\lambda_{min.}$ 310 mμ (log ε 3·6).

L-*Methylpentose Dianhydrophenylosazone Diacetate.*—L-Rhamnose phenylosazone (5 g.) was refluxed with acetic anhydride (25 ml.) for 30 min. and then poured on ice (100 g.). After 1 hr., the crystals that separated (5 g.) were collected and crystallised from dilute ethanol; this *diacetate* (III; R = Ac), m. p. 175°, $[\alpha]_D$ −64° (*c* 0·5 in $CHCl_3$) (Found: C, 67·3; H, 5·5; N, 14·7. $C_{22}H_{22}N_4O_3$ requires C, 67·7; H, 5·6; N, 14·4%).

D-*Methylpentose Dianhydrophenylosazone Diacetate.*—D-Fucose phenylosazone (0·3 g.), on treatment as above, yielded the enantiomorphic diacetate, m. p. and mixed m. p. 175°, $[\alpha]_D$ +64° (*c* 0·5 in $CHCl_3$) (Found: C, 67·7; H, 6·0; N, 14·1%).

Reaction with p-*Nitrophenylhydrazine.*—L-Methylpentose dianhydrophenylosazone diacetate (0·5 g.) was hydrolysed with 20% ethanolic ammonia (50 ml.) overnight at room temperature. The solution was concentrated on the water-bath. The product separated as a gelatinous precipitate. It was treated with *p*-nitrophenylhydrazine (0·2 g.) in hot ethanol (25 ml.), followed by acetic acid (1 ml.), then refluxed for 1 hr. The p-*nitrophenyl derivative* crystallised from ethanol in orange needles, m. p. 211° (Found: N, 20·1. $C_{18}H_{17}N_5O_3$ requires N, 19·9%).

Pentose N-*Acetyldianhydrophenylosazone Acetate* (IV; R = Ac).—D-Xylose or L-arabinose phenylosazone (5 g.) was refluxed with acetic anhydride (25 ml.) for 30 min. and then poured on ice. After 1 hr., the crystals that separated (5 g.) were collected and crystallised from ethanol; this *product* had m. p. 196° (Found: C, 66·8; H, 5·7; N, 15·6. $C_{21}H_{20}N_4O_3$ requires C, 67·0; H, 5·3; N, 14·9%).

Pentose N-*Acetyldianhydrophenylosazone* (IV; R = H). The diacetyl compound (0·5 g.) was hydrolysed with 20% ethanolic ammonia (50 ml.) overnight at room temperature. On concentration, the *product* crystallised in needles, m. p. 155° (Found: C, 68·1; H, 5·6; N, 16·9. $C_{19}H_{18}N_4O_2$ requires C, 68·3; H, 5·4; N, 16·7%).

Reaction with p-*Nitrophenylhydrazine.*—Pentose *N*-acetyldianhydrophenylosazone (0·5 g.) in ethanol (10 ml.) was treated with a solution of *p*-nitrophenylhydrazine (0·2 g.) in hot ethanol (10 ml.), followed by acetic acid (1 ml.). The mixture was refluxed for 1 hr., yielding, on cooling, orange needles of p-*nitrophenyl derivative*, m. p. 190° (Found: N, 21·0. $C_{17}H_{15}N_5O_3$ requires N, 20·8%). This, on acetylation, yielded the monoacetate, m. p. 179° (Found: N, 19·6. $C_{19}H_{17}N_5O_4$ requires N, 19·5%).

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