# 1,2- and 1,4-Additions to Methyl 2- and 3-Phenylazo-glycopyrano-2-enosides

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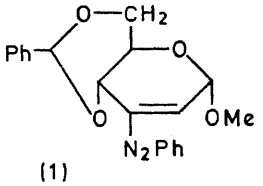
*Summary* Syntheses of methyl 4,6-*O*-benzylidene-2,3-dideoxy-3-phenylazo-α-D-*erythro*-hexopyrano-2-enoside (**1**) and the corresponding 2-phenylazo-compound (**2**) are described: they differ in their behaviour (i) towards nucleophiles—whereas for compound (**1**) there is 1,4-addition across the structural component –N=N–C=C–, for compound (**2**) a rearrangement of the unsaturated system ensues, and (ii) towards dimethylsulphoxonium methylide which adds a methylene group at the olefinic bond in compound (**2**), but with which 1,4-addition occurs with compound (**1**).

METHYL 4,6-*O*-benzylidene-2,3-dideoxy-3-phenylazo-α-D-*erythro*-hexopyrano-2-enoside (**1**)† [orange crystals with m.p. 172—173°; $[\alpha]_D$ + 964°; τ 4·78(q, $J_{1,2}$ 3·0, $J_{1,4}$ 1·0 Hz, 1-H), 3·62(q, $J_{2,4}$ 2·0 Hz, 2-H)] was formed in 95% yield by methoxide-induced 1,4-elimination of benzoic acid from the phenylhydrazone of methyl 2-*O*-benzoyl-4,6-*O*-benzylidene-α-D-*ribo*-hexopyranosid-3-ulose, itself obtainable in high yield by standard methods.[1] The 2-phenylazo-2-enoside (**2**) [orange crystals with m.p. 142—143°; $[\alpha]_D^{24}$ – 1004°; τ 2·98(d, $J_{3,4}$ 2·0 Hz, 3-H), 4·57 (s, 1-H)] was obtained in like manner[2] in 70% yield.



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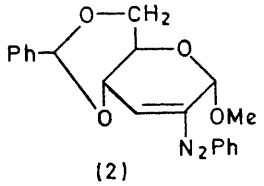

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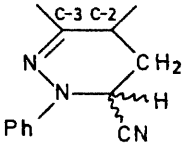

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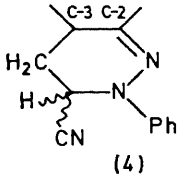

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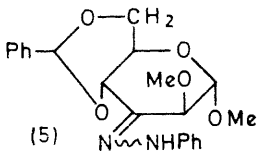
Compounds (**1**) and (**2**) undergo smooth reaction with a range of dienophiles in a Diels–Alder reaction. For example, with acrylonitrile compound (**1**) gives the isomeric tetrahydropyridazines (**3**) which could be separated by fractional crystallisation. The azoalkene (**2**) affords the isomeric mixture (**4**).‡

In contrast to this similarity of reaction of compounds (**1**) and (**2**), these substances differ in their behaviour with nucleophilic reagents. The 3-phenylazoalkene (**1**) with sodium methoxide in methanol undergoes a 1,4-addition of methanol to afford the phenylhydrazone of methyl 4,6-*O*-benzylidene-2-*O*-methyl-α-D-*arabino*-hexopyranosid-3-ulose (**5**) [85% yield; m.p. 136—138°; $[\alpha]_D^{20}$ + 50·4°; $\nu_{max}$ 3400(NH); 1620 and 1520 $cm^{-1}$ (>C=N–NHPh); τ 5·16 (s, $J_{1,2}$ < 1 Hz, 1-H), 6·15(s, 2-H), 6·56(s, 3-MeO)], identical with material prepared by treating the parent 3-ulose with phenylhydrazine. This reaction has wide scope since it has been extended to a range of nucleophiles of various types, *e.g.* azide, 2-methoxyethoxide, nitromethane, methylmagnesium iodide, and acetic acid in acetic anhydride: all have been found to give 1,4-addition products. On the other hand, when the 2-phenylazoalkene (**2**) was treated in the same way, it underwent rearrangement to give the αβ-unsaturated phenylhydrazone (**6**) [71% yield; m.p. 119—122°; τ 4·06 (d, $J_{3,5}$ 2·0 Hz, 3-H), 5·33 (o, $J_{5,3}$ 2·0, $J_{5,6}$ 6·0, $J_{5,6'}$ 10·0 Hz, 5-H), *ca.* 2·5(NH)].



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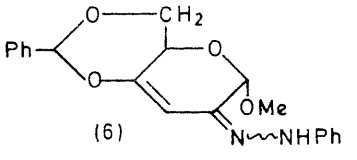

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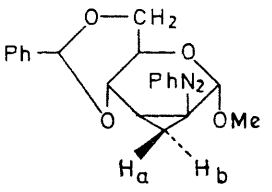

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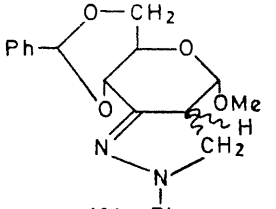

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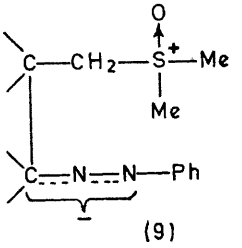

(9)

These compounds (**1**) and (**2**) also exhibit differences in reaction with dimethylsulphoxonium methylide. The 2-phenylazo-isomer (**2**) afforded the cyclopropyl derivative (**7**) [60% yield; yellow crystals with m.p. 170—171°, $[\alpha]_D^{20}$ + 101°; τ 5·92 (q, $J_{4,3}$ 4·5, $J_{4,5}$ 9·0 Hz, 4-H), 7·53 (o, $J_{3,H_b}$ 6·3, $J_{3,H_a}$ 9·0, $J_{3,4}$ 4·5 Hz, 3-H), 7·9 (t, $J_{H_b,3}$ 6·3, $J_{H_b,H_a}$ 5·5 Hz), 8·31 (q, $J_{H_a,3}$ 9·0, $J_{H_a,H_b}$ 5·5 Hz), ($H_a$,$H_b$); *cf.* $J_{3,4}$ with 2,3-epoxides[3] and the cyclopropyl derivative reported by Horton *et al.*[4]] presumably formed in a manner analogous to the way this reagent reacts with αβ-unsaturated ketones to give cyclopropyl ketones.[5] Treatment of the 3-phenylazoalkene (**1**) with this ylide yielded, however, a mixture of isomers with the tricyclic structure (**8**) which was separated into two compounds, each of which gave a positive Knorr test[6] for 1-phenyl-2-pyrazolines and both of which had $\nu_{max}$ 1610 and 1510 $cm^{-1}$ (>C=N–N–Ph). One compound

† All compounds gave satisfactory elemental analyses; n.m.r. spectra were consistent with assigned structures. N.m.r. spectra were measured on solutions in $CDCl_3$ and $[\alpha]_D$ in $CHCl_3$. $\nu_{max}$ relate to KBr discs.

‡ The assignment of structures to these isomers will be described elsewhere.

had m.p. 221—223°; $[\alpha]_D^{20}$ + 224°; $\tau$ 5·09 (d, $J_{1,2}$ 4·0 Hz, 1-H), 6·50 (o, 2-H), 6·2—6·4 (m, ring methylene protons), and the other had m.p. 148—149°; $[\alpha]_D^{20}$ − 277°; $\tau$ 5·33 (d, $J_{1,2}$ 5·5 Hz, 1-H), 6·6 (m, 2-H), 5·45—6·50 (hidden ring methylene protons). The latter compound was dehydrogenated with lead tetra-acetate[7] to give a pyrazole derivative which was oxidized with potassium permanganate to afford the known 1-phenylpyrazole-3,4-dicarboxylic acid.[8]

As each phenylazoalkene reacts with the ylide *via* an intermediate of the type (**9**), the divergence in reaction must occur at the next stage. With the intermediate from compound (**1**) the terminal nitrogen displaces dimethyl sulphoxide to give the five-membered ring in (**8**), whereas with that from compound (**2**), attack occurs by C-2 of the pyranoid ring to afford the cyclopropyl derivative (**7**). Consideration of the intermediates formed in the two cases shows that, when the intermediate originates from compound (**2**), the negative charge is more localised on C-2, owing to the electron-withdrawing groups on C-1, than it would be on C-3 in the intermediate, formed from compound (**1**). On this basis, attack from C-2 would be more likely with compound (**2**) than would attack from C-3 with compound (**1**). This could be responsible for the different products obtained, but further work is necessary to establish this point.

These reactions with the phenylazoalkenes (**1**) and (**2**) lead to new types of carbohydrate derivatives and, in a wider context, raise interesting problems in the chemistry of phenylazoalkenes. Compounds (**1**) and (**2**) provide useful model substances for studies of reaction mechanisms and afford a particularly interesting application of carbohydrate molecules.

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