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Preliminary communication

One-step spin-labeling of unprotected D-glucose and 2-deoxy-D-*arabino*-hexose

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The products of reactions between various amines and sugars, and in some cases their *N*-nitrosated derivatives, have been synthesized, characterized, and tested for their biological activity[1–8]. Glycosylamines and their derived Amadori compounds, found in many food items, are formed during the early stages of nonenzymic browning (Maillard reaction)[4–6]. Furthermore, a substantial amount of information is available on the techniques of spin labeling of protected disaccharides, and, in particular, of polysaccharides[9]. However, only sparse information is available on the synthesis of selectively spin-labeled, but otherwise unsubstituted, water-soluble monosaccharides[9–11]. We now report convenient one-step spin-labeling of unblocked sugars.

Briefly, the methodology is as follows. To a solution of either 4-amino-2,2,6,6-tetramethylpiperidin-1-oxyl (**1**) or 3-amino-2,2,5,5-tetramethylpyrrolidin-1-oxyl (**2**) in dry ethanol is added either powdered D-glucose or 2-deoxy-D-*arabino*-hexose, and the mixture is heated for 1–2 h at 60–70°, allowed to cool to 25°, and evaporated in a rotary evaporator at 30°/2.66 kPa. The products were repeatedly recrystallized from ethanol and ether to give pure spin-labeled compounds[3–6]. T.l.c. analysis [Silica Gel $60F_{254}$, precoated sheets, EM reagents, 4:1 (v/v) chloroform–methanol] indicated one spot.

The microanalyses for C, H, and N in these compounds were in satisfactory agreement (±0.3%) with the calculated values, and the mass spectra were consistent with the structures proposed. The spin-labeled D-glucose derivatives **3–6** are water-soluble, and exhibit a three-line e.s.r. spectrum with a_N = 16.0 G (water).

Thus were prepared 4-(α,β-D-glucopyranosylamino)-2,2,6,6-tetramethylpiperidin-1-oxyl [**3**, 74% yield, m.p. 76–77° (dec.)], 4-(2-deoxy-α,β-D-*arabino*-hexopyranosylamino)-2,2,6,6-tetramethylpiperidin-1-oxyl [**4**, 66% yield, m.p. 74–75° (dec.)], 3-(α,β-D-glucopyranosylamino)-2,2,5,5-tetramethylpyrrolidin-1-oxyl [**5**, 64% yield, m.p. 84–86° (dec.)], and 3-(2-deoxy-α,β-D-*arabino*-hexopyranosylamino)-2,2,5,5-tetramethylpyrrolidin-1-oxyl [**6**, 56% yield, m.p. 83–84° (dec.)]. Compound **3** was also synthesized by two different routes, *i.e.*, treating

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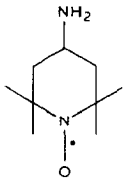

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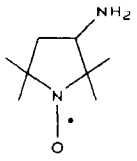

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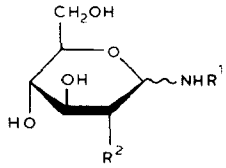

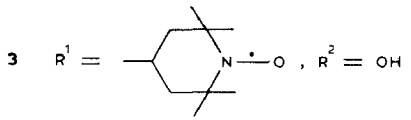

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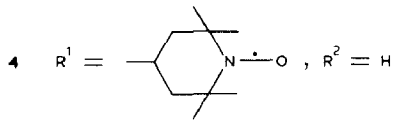

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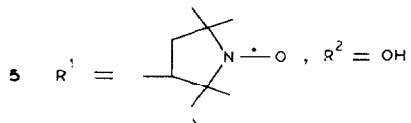

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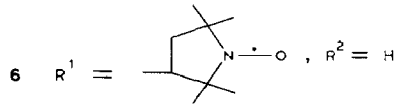

6 $R^1 =$, $R^2 = H$

either 2,3,4,6-tetra-*O*-acetyl-α-D-glucosyl bromide or 2,3,4,6-tetra-*O*-acetyl-1-thio-D-glucose with **1**, followed by *O*-deacetylation with saturated methanolic ammonia solution[10]. The yields were 26 and 20%, respectively.

Compounds **3–6** are hygroscopic, and darken on exposure to air and moisture, presumably, by undergoing transformation to Maillard products. Nonetheless, these spin-labeled, water-soluble compounds may be employed as contrast-enhancing agents for magnetic resonance imaging (m.r.i.) studies, and as spin probes for biochemical research.

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