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Note

The synthesis of *N*-glycosyl-1,2-dialkoxycarbonylhydrazines

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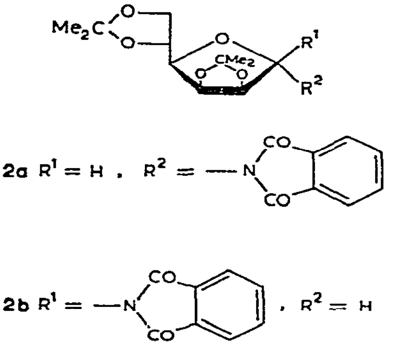
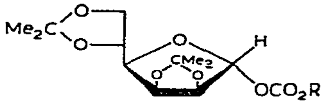
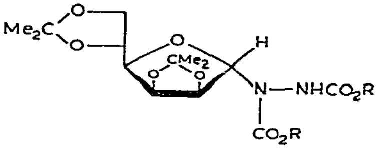
We have recently reported the synthesis of *N*-glycosylphthalimides from monosaccharide derivatives by means of triphenylphosphine, dialkyl azodicarboxylate, and phthalimide[1]. When 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose (**1**) was treated with these reagents, the anomeric *N*-(2,3:5,6-di-*O*-isopropylidene-D-mannofuranosyl)phthalimides (**2a**, **2b**) were formed together with minute proportions of two hitherto unknown derivatives of D-mannose. These compounds were identified as 1-*O*-ethoxycarbonyl-2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose (**3**) and *N*-(2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranosyl)-1,2-diethoxycarbonylhydrazine(**4**).





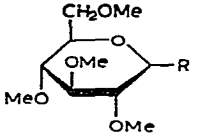
3 R = Et
11 R = Bu



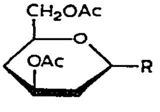
4 R = Et
10 R = Bu

Therefore, the Ph_3P–dialkyl azodicarboxylate system *without phthalimide* should be capable of reacting with anomeric hydroxyl groups. Thus, 2,3:5,6-di-*O*-isopropylidene-D-mannofuranose (**1**), 2,3,4,6-tetra-*O*-methyl-D-glucose (**5**), 3,6-di-*O*-acetyl-2,4-dideoxy-DL-*threo*-hexopyranose (**6**), 3,6-di-*O*-acetyl-2,4-dideoxy-DL-*erythro*-hexopyranose (**7**), 2,3,6-trideoxy-5-*C*-methyl-DL-hex-2-enopyranos-4-ulose (**8**), and 6-acetoxymethyl-2-hydroxy-5,6-dihydro-2*H*-pyran (**9**) separately in tetrahydrofuran at room temperature reacted smoothly with the stoichiometric amount of triphenylphosphine and a slight excess of diethyl or dibutyl azodicarboxylate to give *N*-glycosyl-1,2-dialkoxycarbonylhydrazines (**4**, **10**–**19**) in yields of 40–80%. The products were isolated by column chromatography. Single anomers resulted from compounds **1** and **5**–**8**, and both possible isomeric 1,2-dialkoxycarbonylhydrazines were obtained from **9**. The anomeric configuration assignment was based on p.m.r. data. The p.m.r. spectra of each product showed clearly, besides signals attributable to the carbohydrate moiety, the presence of two butoxy (6H, t, δ 0.95; 8H, m, δ 1.1–1.9; 4H, t, δ 4.15) or two ethoxy (6H, t, δ 1.25 and 4H, q, δ 4.15) residues. Hydrazino derivatives of **1** and **5** were accompanied by 10–18% of the corresponding carbonates[2].

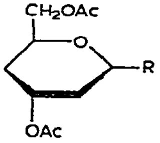
N-Glycosyl-1,2-dialkoxycarbonylhydrazines constitute a new class of *N*-glycosides. They are distillable oils, and are stable in moderately acidic (80% acetic acid) and basic (dry pyridine) solutions. Their chemical properties are under investigation.



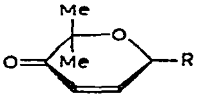
5 R = OH
12 R = β-N(CO$_2$Bu)NHCO$_2$Bu
13 R = α-OCO$_2$Bu



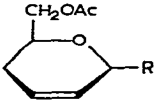
6 R = OH
14 R = β-N(CO$_2$Bu)NHCO$_2$Bu



7 R = OH
15 R = β-N(CO$_2$Bu)NHCO$_2$Bu



8 R = OH
16 R = N(CO$_2$Et)NHCO$_2$Et
17 R = N(CO$_2$Bu)NHCO$_2$Bu



9 R = OH
18 R = β-N(CO$_2$Bu)NHCO$_2$Bu
19 R = α-N(CO$_2$Bu)NHCO$_2$Bu

EXPERIMENTAL

Boiling points refer to bath temperatures and are not corrected. P.m.r. spectra were recorded on Jeol JMN-4H-100 (100 MHz) and Varian HA-60/IL (60 MHz) spectrometers for solutions in deuteriochloroform with tetramethylsilane as internal standard. I.r. spectra were recorded on Unicam SP-200 and UR-10 spectrophotometers. Optical rotations were measured at 18 ±2° on solutions in ethanol (*c* 1) with a Perkin–Elmer 141 automatic polarimeter. Mass spectra were obtained with a LKB 9000 spectrometer at 70 eV, using a direct-inlet system. T.l.c. was performed on Silica Gel G Merck, and Machery-Nagel silica gel was used for column chromatography.

N-*Glycosyl-1,2-dialkoxycarbonylhydrazines*. — Solutions of sugar derivative (**1** or **5**–**9**, 1 mmol) and triphenylphosphine (262 mg, 1 mmol) in 10 ml of dry tetrahydrofuran were treated with diethyl azodicarboxylate (0.2 ml, ~1.25 mmol) or dibutyl azodicarboxylate (0.3 ml, ~1.25 mmol) for ~1 h at room temperature and then concentrated under reduced pressure. Each residue was eluted from silica gel with benzene–ether (95:5–4:1) or light petroleum–ethyl acetate (9:1–4:1).

Thus, **1**, with diethyl azodicarboxylate, gave *N*-(2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranosyl)-1,2-diethoxycarbonylhydrazine (**4**, 77%), b.p. 160°/10^{-4} torr, $[\alpha]_D$ +46°, ν_{max}^{liquid} 3370 (NH) and 1720 cm^{-1} (ester C=O). P.m.r. data: δ 7.08 (s, broad, 1H, NH), 5.77 (s, broad, 1H, H-1). The mass spectrum contained the following more-important peaks: *m/e* 418 (M^+, 1%), 403 (14), 345 (15), 243 (6), 205 (11), 185 (57), 176 (25), 141 (21), 127 (30), 104 (29), 101 (64), 85 (31), 59 (77), and 43 (100).

Anal. Calc. for $C_{18}H_{30}N_2O_9$: C, 51.7; H, 7.2; N, 6.7. Found: C, 51.8; H, 7.2; N, 6.7.

Also formed was 1-*O*-ethoxycarbonyl-2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose[3] (**3**, 10%).

The reaction of dibutyl azodicarboxylate with **1** gave *N*-(2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranosyl)-1,2-dibutoxycarbonylhydrazine (**10**, 79%), b.p. 170°/10^{-4} torr, $[\alpha]_D$ +42.5°, ν_{max}^{liquid} 3300 (NH) and 1720 cm^{-1} (ester C=O). P.m.r. data: δ 7.21 (s, broad, 1H, NH), 5.75 (broad s, 1H, H-1). Mass spectrum: *m/e* 474 (M^+, 1%), 459 (13), 401 (8), 261 (18), 185 (100), 161 (18), 145 (20), 141 (36), 127 (40), 101 (87), 99 (33), 98 (35), 84 (36), 59 (40), 57 (56), and 43 (96).

Anal. Calc. for $C_{22}H_{38}N_2O_9$: C, 55.7; H, 8.1; N, 5.9. Found: C, 55.8; H, 8.1; N, 5.7.

1-*O*-Butoxycarbonyl-2,3:5,6-di-*O*-isopropylidene-α-D-mannofuranose (**11**, 12%) was also formed.

N-(2,3,4,6-Tetra-*O*-methyl-β-D-glucopyranosyl)-1,2-dibutoxycarbonylhydrazine (**12**, 55%) obtained from **5** had b.p. 180°/10^{-4} torr, $[\alpha]_D$ +26°, ν_{max}^{liquid} 3290 (NH) and 1740 cm^{-1} (ester C=O). P.m.r. data: δ 7.00 (broad s, 1H NH), 5.05 (broad s, 1H, H-1).

Anal. Calc. for $C_{20}H_{38}N_2O_9$: C, 53.3; H, 8.5; N, 6.2. Found: C, 53.2; H, 8.7; N, 6.0.

Also formed was 1-*O*-butoxycarbonyl-2,3,4,6-tetra-*O*-methyl-α-D-glucopyranose (**13**, 18%).

N-(3,6-Di-*O*-acetyl-2,4-dideoxy-β-DL-*threo*-hexopyranosyl)-1,2-dibutoxycarbonylhydrazine (**14**) was obtained (45%) from **6**[4] and had b.p. 180°/10^{-3} torr, ν_{max}^{liquid} 3300 (NH) and 1745 cm^{-1} (ester C=O). P.m.r. data: δ 6.93 (broad s, 1H, NH), 5.38 (poorly resolved dd, $J_{1,2a}$ ~10, $J_{1,2e}$ ~2 Hz, H-1).

Anal. Calc. for $C_{20}H_{34}N_2O_9$: C, 53.8; H, 7.7; N, 6.3. Found: C, 53.9; H, 7.9; N, 6.1.

N-(3,6-Di-*O*-acetyl-2,4-dideoxy-β-DL-*erythro*-hexopyranosyl)-1,2-dibutoxycarbonylhydrazine (**15**) obtained (42%) from **7**[4] had b.p. 180°/10^{-3} torr, ν_{max}^{liquid} 3300 (NH) and 1745 cm^{-1} (ester C=O). P.m.r. data: δ 6.70 (broad s, 1H, NH), 5.67 (dd, $J_{1,2a}$ 10, $J_{1,2e}$ 2.5 Hz, H-1).

Anal. Calc. for $C_{20}H_{34}N_2O_9$: C, 53.8; H, 7.7; N, 6.3. Found: C, 54.1; H, 7.6; N, 5.9.

Reaction of **8**[5] with diethyl azodicarboxylate gave *N*-(2,3,6-trideoxy-5-*C*-methyl-DL-hex-2-enopyranosyl-4-ulose)-1,2-diethoxycarbonylhydrazine (**16**, 44%), b.p. 170°/10^{-4} torr; ν_{max}^{liquid} 3300 (NH), 1720 (ester C=O), and 1700 cm^{-1} (shoulder, ketone C=O). P.m.r. data: δ 6.90 (s, 1H, NH), 6.37 (broad s, 1H, W/2 9 Hz, H-1).

Anal. Calc. for $C_{13}H_{20}N_2O_6$: C, 52.0; H, 6.7; N, 9.3. Found: C, 52.0; H, 6.7; N, 8.6.

The reaction of **8** with dibutyl azodicarboxylate gave *N*-(2,3,6-trideoxy-5-*C*-methyl-DL-hex-2-enopyranosyl-4-ulose)-1,2-dibutoxycarbonylhydrazine (**17**, 47%), b.p. 180°/10^{-4} torr, ν_{max}^{liquid} 3300 (NH), 1730 (ester C=O), and 1695 cm^{-1} (ketone C=O). P.m.r. data: δ 6.67 (broad s, 1H, NH), 6.35 (broad s, W/2 9 Hz, H-1).

Anal. Calc. for $C_{17}H_{28}N_2O_6$: C, 57.3; H, 7.9; N, 7.9. Found: C, 57.4; H, 8.1; N, 7.7.

The reaction of 6-acetoxymethyl-2-hydroxy-5,6-dihydro-2*H*-pyran[6] (**9**) with dibutyl azodicarboxylate afforded two compounds to which the *cis* and *trans* configurations were assigned on the basis of chemical-shift differences for the anomeric protons observed in the p.m.r. spectra of the hydrogenated compounds[7]. *cis*-*N*-(6-Acetoxymethyl-5,6-dihydro-2*H*-pyran-2-yl)-1,2-dibutoxycarbonylhydrazine (**18**, 65%) had b.p. 160°/10^{-3} torr, ν_{max}^{liquid} 3300 (NH) and 1745 cm^{-1} (ester C=O). N.m.r. data: δ 6.70 (s, 1H, NH), 6.07 (broad s, 1H, H-1); for dihydro derivative: δ 5.32 (broad s, 1H, W/2 13 Hz, H-1).

Anal. Calc. for $C_{18}H_{30}N_2O_7$: C, 55.9; H, 7.8; N, 7.3. Found: C, 55.7; H, 7.9; N, 7.3.

trans-*N*-(6-Acetoxymethyl-5,6-dihydro-2*H*-pyran-2-yl)-1,2-dibutoxycarbonylhydrazine (**19**, 16%) had b.p. 160°/10^{-3} torr, ν_{max}^{liquid} 3300 (NH) and 1745 cm^{-1} (ester C=O). P.m.r. data: δ 6.85 (s, 1H, NH), 6.01 (s, 1H, H-1); for dihydro derivative: δ 5.62 (broad s, 1H, W/2 9 Hz, H-1).

Hydrogenation was carried out over a platinum catalyst in ethanol solutions at 1 atm. of hydrogen.

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