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Note

Synthesis of 5-(4-carboxy-D-*galacto*-tetritol-1-yl)tetrazole and some of its derivatives

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Oxidation of galactose with nitric acid to afford galactaric acid was first described[1] in 1876. A variation of this reaction has now been applied to 5-(D-*galacto*-pentitol-1-yl)tetrazole[2], giving 5-(4-carboxy-D-*galacto*-tetritol-1-yl)tetrazole (**1**) in 70% yield.

The esterification of **1** with methyl and with ethyl alcohol gave the corresponding esters, and treatment of the methyl ester with amines gave the corresponding amides.

This opens a synthetic pathway to a group of substances in which, in addition to the possible pharmacological activity of the heterocyclic moiety, the steric distribution of the hydroxyl groups on the side chain, and the presence of a carboxyl or carboxamide group on C-4 of this chain, may prove advantageous.

EXPERIMENTAL

*5-(4-Carboxy-*D-galacto-*tetritol-1-yl)tetrazole* (**1**). — 5-(D-*galacto*-Pentitol-1-yl)tetrazole[2] (2.0 g) was dissolved at room temperature in concentrated nitric acid (10 mL), and the solution was kept in a covered dish. After 5 days, crystals appeared, and after 10 days, water was added, and the product was filtered off and washed with water. Recrystallized from water, **1** (1.67 g, 70%) was obtained as rhombic plates, m.p. 200–201°, $[\alpha]_D$ +21.7° (*c* 1, water); ^{1}H-n.m.r. (270 MHz; $HCONMe_2$-d_7): δ 5.51 (d, 1 H, $J_{1,2}$ 1.3 Hz, H-1), 4.50 (d, 1 H, $J_{3,4}$ 1.3 Hz, H-4), 4.17 (dd, 1 H, $J_{2,3}$ 9.6 Hz, H-3), and 3.98 (dd, 1 H, H-2).

Anal. Calc. for $C_6H_{10}N_4O_6$: C, 30.77; H, 4.30; N, 23.93. Found: C, 30.90; H, 4.47; N, 24.27.

*5-[4-(Ethoxycarbonyl)-*D-galacto-*tetritol-1-yl]tetrazole* (**2**). — Compound **1** (0.50 g) in ethyl alcohol (13 mL) and sulfuric acid (0.1 mL) was boiled under reflux for 24 h, and cooled to room temperature, whereupon compound **2** crystallized.

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Recrystallized from ethanol, it gave 0.45 g (80.5%) of **2** as needles, m.p. 180–181°, $[\alpha]_D$ +34.4° (*c* 1, *N*,*N*-dimethylformamide), $[\alpha]_D$ +19.5° (*c* 1, water).

Anal. Calc. for $C_8H_{14}N_4O_6$: C, 36.64; H, 5.38; N, 21.37. Found: C, 36.56; H, 5.70; N, 21.70.

5-[4-Methoxycarbonyl)-D-galacto-*tetritol-1-yl]-tetrazole* (**3**). — Compound **1** (0.50 g) in methyl alcohol (13 mL) and sulfuric acid (0.1 mL) was boiled under reflux for 24 h, and cooled to room temperature, and compound **3** crystallized. Recrystallized from methanol, it gave 0.32 g (60%) of **3** as rectangular plates, m.p. 210–213°, $[\alpha]_D$ +33.1° (*c* 0.9, *N*,*N*-dimethylformamide). $[\alpha]_D$ +23° (*c* 1, water).

Anal. Calc. for $C_7H_{12}N_4O_6$: C, 33.57; H, 4 87; N, 22.58. Found: C, 33.65; H. 4.93; N, 22.29.

5-{4-[(2-Hydroxyethyl)aminocarbonyl]-D-galacto-*tetritol-1-yl}tetrazole* (**4**). — A solution of compound **3** (0.50 g) in 2-aminoethanol (3 mL) was kept in a closed vessel for 4 weeks at room temperature. Evaporation under diminished pressure at room temperature gave a white powder. Recrystallized from ethanol, 0.38 g (64%) of **4** was obtained as needles, m.p. 178–180°, $[\alpha]_D$ +25° (*c* 1, water).

Anal. Calc. for $C_8H_{15}N_5O_6$: C, 34.64; H, 5.41; N, 25.27. Found: C, 34.91; H, 6.80; N, 25.00.

5-[4-(Dimethylaminocarbonyl)-D-galacto-*tetritol-1-yl]tetrazole* (**5**). — Compound **3** (0.30 g) was dissolved in dimethylamine (3 mL), and the solution was kept in a closed vessel for 4 weeks at room temperature. Evaporation under diminished pressure at room temperature gave a white powder. Recrystallized from 3:2 ethanol–water twice, it gave 0.20 g (61%) of **5** as needles, m.p. 163–164°, $[\alpha]_D$ +6.1° (*c* 1, water).

Anal. Calc. for $C_8H_{15}N_5O_5 \cdot 0.5\ H_2O$: C, 35.56; H, 5.93; N, 25.92. Found: C, 35.73; H, 6.93; N, 25.76.

5-[4-(Morpholinocarbonyl)-D-galacto-*tetritol-1-yl]tetrazole* (**5**). — Compound **3** (0.30 g) was dissolved in morpholine (3 mL), and treated as described for compound **4**. Recrystallized twice from ethanol, 0.33 g (70%) of **5** was obtained as hexagonal plates, m.p. 190–192° (dec.), $[\alpha]_D$ +31.1° (*c* 1, water).

Anal. Calc. for $C_{10}H_{17}N_5O_6 \cdot C_4H_9NO$: C, 43.07; H, 6.66; N, 21.54. Found: C, 43.05; H, 7.00; N, 21.58.

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