2-C-Methyl-erythritol, a New Branched Alditol from *Convolvulus glomeratus*

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The Convolvulaceae family is known to contain a number of resin glycosides. Their building blocks are short chain volatile acids, long chain hydroxy-fatty acids and carbohydrates. The carbohydrates isolated so far are D-glucose, L-rhamnose, D-fucose, D-glucovose and presumably 6-deoxyglucose. Fractionation of extracts of *Convolvulus glomeratus* Choisy afforded in addition to some hydrocarbons and steroids which were not further characterized, 2-C-methyl-d- or L-erythritol (I) which was identified by 1H and 13C NMR spectroscopy. Biosynthetically the alditol I may arise from isoprenoid or amino acid precursors. Carbohydrate precursors such as the aldoses 2 or 3 or the ketose 4 are also possible.

The molecular formula of I was established as being C6H10O4 on the basis of the proton decoupled 13C NMR spectrum which reveals the presence of five carbon atoms, and the elemental analysis. The mass spectrum of the tetra-O-trimethylsilylether (5) shows no molecular ion peak. However, characteristic peaks due to the ions [M−CH2OSiMe3]? and C6H11SiO4? are of high abundance.

From the off-resonance decoupled 13C NMR spectrum one quartet, two triplets, one doublet, and one singlet are clearly visible thus showing that the alditol I contains one methyl group, two methylene groups, one methine group and one fully substituted carbon atom. The 1H NMR spectrum was not very informative, except for the resonance of the methyl group (δ 1.12). However, on addition of europium nitrate to the solution one AB-pattern and one ABX-pattern became clear. On acetation the alditol I furnished a tri- (6) and a tetraacetate (7). The 1H NMR spectrum of the triacetate is particularly informative. Beside the resonances of the methyl group (1.23) and the three acetyl groups (2.02, 2.09, 2.06), the AB (νA = 4.15, νB = 3.91, JAB = 11.5 Hz) and the ABX patterns (νA = 4.57, νB = 4.16, νX = 5.20, JAB = 12.0, JAX = 3.0, JBX = 7.5 Hz) were seen.

The two spin patterns established the presence of one CH3−OH group and one HO−CH2−OH group in the molecule and thus confirmed the conclusion based upon the 13C NMR spectrum. Moreover, the resonance of the methyl group was shifted downfield in the tetraacetate and this suggested the structural element HO−CH2−CH3. This established the constitution of I as that of a 2-C-methyltetritol, but did not distinguish between the erythro or threo configuration.

This information could possibly be sought in the lanthanide induced shift 1H NMR spectra, since erythro forms are reported to give much smaller induced shifts than the threo forms. However, in order to draw safe conclusions on this background it seemed necessary to investigate the shift curves of both the threo and the erythro form.

To answer the stereochemical question we carried out a synthesis of racemic I from citraconic acid (8).

Methylation gave dimethylcitrateconate (9) which on oxidation with potassium permanganate furnished a dihydroxy diester (10). This was converted into I by lithium aluminium hydride reduction. The 1H NMR spectrum of the synthetic compound and its triacetate were identical with those of I and its triacetate.

Further studies on the lanthanide induced shifts and synthetic compounds related to I are in progress.

Experimental. The NMR spectra were recorded on Varian A-60A (1H, 60 MHz) and Jeol PS-100 (13C, 25.1 MHz, PPT). Chemical shifts are given in ppm relative to TMS in CDCl3 or dioxane solutions and relative to sodium 3-(trimethylsilyl)-propane sulfonate in D2O.

Mass spectra were obtained with AEI MS 902. Combustion analysis was performed by Alfred Bernhardt, Elbach über Engelakirchen, Germany.

Isolation of the alditol I. *Convolvulus glomeratus* (roots and shoots) was collected in April and May in Sind, Pakistan. The plant was cut into small pieces, dried and ground. The ground material (12 kg) was refluxed with light petrolatum for 6 h. The extract was filtered and evaporated to dryness under vacuum to yield a thick dark green oil (113 g, 1 %) which was shown mainly to consist of hydrocarbons.

The residue was dried and refluxed with

ethanol (95 %) for 6 h. The extract was filtered and evaporated to dryness under vacuum to yield a dark green gum (1125 g, 9.4 %). This material was mixed with filter-aid and successively Soxhlet-extracted with light petroleum, benzene, chloroform, ethyl acetate, and ethanol to yield five extracts: 91.5, 19.5, 312, 151.5, and 646 g, respectively. The light petroleum extract was found to consist mainly of steroids. So far no further compounds have been identified from the benzene, chloroform and ethanol extracts. The ethyl acetate extract was applied to an alumina column and eluted with chloroform-ethyl acetate (1:1), ethyl acetate and ethanol. The green mass obtained from the ethyl acetate fractions was shaken with hexane which removed most of the coloured material. The semi-solid material was left at room temperature for a few months and the additio I crystallized. Repeated recrystallizations from hot hexane gave colourless crystals (12.5 g, m.p. 82–88 °C, [α]D = +24.8° (H2O c 7.0). (Found: C 44.87; H 8.86. Calc. for C8H10O2: C 44.11; H 8.89.) 1H NMR (D2O): ð 1.12 (3 H, s, tertiary methyl), 3.45 and 3.57 (AB pattern, JAB = 11.0 Hz, −CH2OH), 3.5–4.0 (ABC pattern, HO−CH−CH2OH).

3.5 NMR (dioxane): ð 29.0 (q, methyl carbon), 63.5 and 67.8 (both t, two methylene carbons), 75.6 (s, quaternary carbon), 76.4 (d, methine carbon).

Acetylation. The additio I yields both a tri- and a tetraacetoxy on treatment with acetic anhydride and pyridine. The relative yields of the two acetates depended on the conditions of acetylation. The two acetates were easily separable on TLC. In 65 % ether in light petroleum the Rf-values were 0.28 (triacetoxy) and 0.66 (tetraacetoxy).

Triacetoxy (6). The additio I (175 mg) was dissolved in a mixture of 2 ml pyridine and 2 ml acetic anhydride and left at room temperature for 3 h. After evaporation to dryness and purification on TLC it furnished a colourless oil (320 mg), [α]D = −26.5° (CHCl3, c 18.4). 1H NMR (CDCl3): ð 1.23 (3H s, tert. methyl), 2.02, 2.09 and 2.09 (all 3H and s, three acetyl groups), 4.15 and 3.91 (AB pattern, JAB = 11.5 Hz, −CH2−OAc), 4.57 (A), 4.16 (B) and 5.20 (X) (ABX pattern, JAB = 12.0, JAX = 3.0 and JBX = 7.5, AcoO−CH−CH2OAc), 2.76 (s, OH conc. dependent).

MS: M+ 262 absent, m/e 189 (6 %, M−CH2OAc), (Calc. for C10H12O4 189.0762; found 189.0771), 159 (55 %, M−60−43), 129 (90 %, m/e 189−60, m* 88.0), 117 (100 %, AcoOCH−C(CHO) + OH).

Tetraacetoxy (7). The additio I (183.5 mg) was dissolved in a mixture of 1.8 ml pyridine and 2 ml acetic anhydride and the mixture was refluxed for 3 h. Evaporation to dryness yielded a yellow oil (321 mg) which was purified on TLC to yield pure oily tetraacetate.

1H NMR (CDCl3): ð 1.51 (s, tert. methyl), 2.01, 2.01, 1.99 and 1.99 (all 3H and s, four acetyl groups, 4.45 and 4.30 (AB pattern, JAB = 12.0 Hz, −CH2OAc), 4.48 (A), 4.05 (B) and 5.36 (X) (ABX pattern, JAB = 12.0, JAX = 3.0 and JBX = 7.5, AcoO−CH−CH2OAc). MS: M+ 304 absent, m/e 231 (24 %, M−CH2OAc), (Calc. for C18H18O6 231.0869, found 231.0863), 189 (14 %, 231−42, m* 154.5), 189 (43 %, 231−72, m* 109.6, and AcoOCH−C(CHO) = +OAc), 129 (100 %, 189−60, m* 88.0).

Tetra-O-trimethylsilyl ether (5). To a solution of I (40 mg) in pyridine (5 ml) was added hexamethyldisilazane (0.5 ml) and trimethylchlorosilane (0.5 ml). The mixture was left overnight and evaporated in vacuum. The residue was dissolved in carbon tetrachloride (1 ml), filtered and dried over sodium sulfate. The product was used directly for mass spectrometry. M+ 424 (absent), m/e 409 (0.7 %, M−Me), 321 (7.9 %, M−CH3OSiMe3), 213 (100 %, Me3SiOCH−C(CHO) = +OSiMe3). (Calc. for C27H34Si2O2 419.2136 as found), 73 (52.2 %, +SiMe3).

Dimethyl citraconate (9). To citraconic acid (8) (20 g) was added an excess of thionyl chloride (ca. 50 ml) and the mixture was kept at 50 °C for 3 h. Excess of thionyl chloride was distilled off under reduced pressure and the resulting citraconoyl dichloride methanol (10 ml) was added without further purification. This mixture was kept at 50 °C for 2 h. Excess methanol was removed and the crude dimethyl citraconate was distilled under vacuum (12 mm, 96−98 °C, yield 13.4 g oily diester). 1H NMR (CDCl3): ð 2.04 (d, J = 1.7 Hz, olefinic methyl), 3.78 and 3.66 (both s, two methoxyls), 5.89 (q, J = 1.7 Hz, olefinic H). rmax (CHCl3) 1725 cm−1.

Dimethyl 2-C-methyl-erythro-tartrate (10). A solution of dimethyl citraconate (10 g, 0.063 mol) in water (200 ml) was kept at 5 °C and pH 13. Potassium permanganate (10 g, 0.063 mol) in water solution (300 ml) was added and the mixture was stirred for 20 min. The solution was decolorized by addition of sodium hydrogen sulfite and after saturation with sodium chloride it was extracted with ethyl acetate three times. The combined extracts were dried over sodium sulfate and evaporated to dryness (yield 1.8 g). Recrystallization from hot ethyl acetate gave colourless crystals (1.5 g, m.p. 93 °C). 1H NMR (CDCl3): ð 1.53 (s, quaternary methyl), 3.75 and 3.81 (both s, two methoxyls), 3.80 (s, two hydroxyls), 4.40 (s, methine H), rmax (KBr) 1740 and 3370 cm−1. MS: M+ absent, m/e 133 20 %, (M−CO2CH3), m/e 90 100 %, (McLaugherty rearr. CH3OCH2).
temperature for 2 h and then poured into water (60 ml). The solid material was removed in a centrifuge. The solution was evaporated almost to dryness, mixed with methanol–water (1:1, 50 ml) and solid carbon dioxide was added. The residue that appeared was filtered off and the filtrate evaporated to dryness to yield a solid material (0.5 g) which was difficult to crystallize. The NMR spectra of this compound and its triacetate were identical with the corresponding spectra of the alditol 1 and its triacetate, respectively.

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N-Vinyl as N-H Protecting Group.
A Convenient Synthesis of Myosmine

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We here describe a convenient synthesis of the minor tobacco alkaloid myosmine (I), starting with a condensation of N-vinylpyrrolidone with ethyl nicotinate. The condensation product 2 is treated with boiling concentrated hydrochloric acid without prior purification and, after extraction of bases and distillation, I is obtained in a 63% yield.

This synthesis of myosmine is similar to previous ones in which the N–H group in 2-pyrrolidone was protected as an N-acyl or N-trimethylsilyl derivative, but preparation of the N–H protected pyrrolidone is here avoided by using the commercially available N-vinylpyrrolidone. Reports on the use of vinlyc groups as protective groups for N–H are scanty. 2-Acyl-1-methylnvinyl groups have for instance found application in peptide syntheses.

Experimental. A solution of freshly distilled N-vinylpyrrolidone (Fluka) (20 g, 0.18 mol) and ethyl nicotinate (25.0 g, 0.17 mol) in dry toluene (200 ml) was added to a stirred suspension of sodium hydride (0.26 mol, introduced as 10.4 g of a 60% suspension in mineral oil) in dry toluene (100 ml). The mixture was then refluxed for 1.5 h. A light green precipitate was formed at the beginning of the heating. The cooled reaction mixture was poured under stirring into dilute hydrochloric acid (100 ml of conc. acid + 180 ml of water). After 5 min the pH was adjusted to 4 with concentrated sodium hydroxide solution, the toluene layer was separated, and the aqueous layer was extracted with chloroform–ethanol (3:2, 3 × 200 ml). The organic layers were combined and dried (Na₂SO₄), and the solvent was evaporated giving a residue which was treated with refluxing concentrated hydrochloric acid (250 ml, 14 h). The tar formed was discarded and the remaining solution was made alkaline (pH 10) with concentrated sodium hydroxide solution and then extracted with chloroform (3 × 150 ml). After drying (Na₂SO₄), concentration and distillation, 1 was obtained as a pale yellow liquid (15.1 g, 63%), b.p. 113–115 °C (0.4 kPa), which solidified in the receiver, m.p. 39–42 °C. These values, as well as the IR absorption max at 1618 cm⁻¹ (film), agree well with those previously given for myosmine.

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