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

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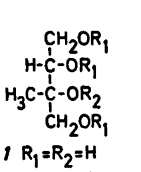
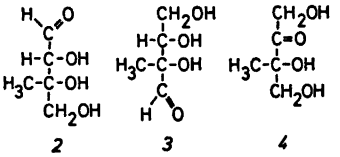
The Convolvulaceae family is known to contain a number of resin glycosides.[1] Their building blocks are short chain volatile acids, long chain hydroxy-fatty acids and carbohydrates. The carbohydrates isolated so far are D-glucose, L-rhamnose, D-fucose, D-quinovose and presumably 6-deoxygulose. Fractionation 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 (*1*) which was identified by ^{1}H and ^{13}C NMR spectroscopy. Biosynthetically the alditol *1* may arise from isoprenoid or amino acid precursors. Carbohydrate precursors such as the aldoses *2* or *3* or the ketose *4* are also possible.

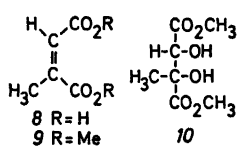
The molecular formula of *1* was established as being $C_5H_{12}O_4$ on the basis of the proton decoupled ^{13}C NMR spectrum which reveals the presence of five carbon atoms, and the



1 $R_1=R_2=H$
5 $R_1=R_2=SiMe_3$
6 $R_1=Ac$ $R_2=H$
7 $R_1=R_2=Ac$



2 *3* *4*



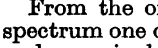
8 R=H
9 R=Me

10

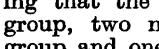
elemental analysis. The mass spectrum of the tetra-*O*-trimethyl-silylether (*5*) shows no molecular ion peak. However, characteristic peaks due to the ions $[M-{\cdot}CH_2OSiMe_3]^+$ and $C_9H_{23}Si_2O_2^+$ are of high abundance.

From the off-resonance decoupled ^{13}C NMR spectrum one quartet, two triplets, one doublet, and one singlet are clearly visible thus showing that the alditol *1* contains one methyl group, two methylene groups, one methine group and one fully substituted carbon atom. The ^{1}H 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 acetylation the alditol *1* furnished a tri- (*6*) and a tetraacetate (*7*). The ^{1}H 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, 2.09), the AB (ν_A = 4.15, ν_B = 3.91, J_{AB} = 11.5 Hz) and the ABX patterns (ν_A = 4.57, ν_B = 4.16, ν_X = 5.20, J_{AB} = 12.0, J_{AX} = 3.0, J_{BX} = 7.5 Hz) were seen.

The two spin patterns established the presence of one $-CH_2-OH$ group and one



group in the molecule and thus confirmed the conclusion based upon the ^{13}C NMR spectrum. Moreover, the resonance of the methyl group was shifted downfield in the tetraacetate and this suggested



the structural element. This established the constitution of *1* 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 ^{1}H NMR spectra, since *erythro* forms are reported to give much smaller induced shifts than the *threo* forms.[2,3] 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 *1* from citraconic acid (*8*).

Methylation gave dimethylcitraconate (*9*)[4] which on oxidation with potassium permanganate furnished a dihydroxy diester (*10*). This was converted into *1* by lithium aluminium hydride reduction. The ^{1}H NMR spectrum of the synthetic compound and its triacetate were identical with those of *1* and its triacetate.

Further studies on the lanthanide induced shifts and synthetic compounds related to *1* are in progress.

Experimental. The NMR spectra were recorded on Varian A-60A (^{1}H, 60 MHz) and Jeol PS-100 (^{13}C, 25.1 MHz, PFT). Chemical shifts are given in ppm relative to TMS in $CDCl_3$ or dioxane solutions and relative to sodium 3-(trimethylsilyl)-propane sulfonate in D_2O.

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

Isolation of the alditol 1. *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 petroleum 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 645 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 alditol *1* crystallized. Repeated recrystallizations from hot acetone gave colourless crystals (12.5 g, m.p. 82 – 83 °C, $[\alpha]_D^{22}$ = 21.4° (H_2O *c* 7.0). (Found: C 44.87; H 8.86. Calc. for $C_5H_{12}O_4$: C 44.11; H 8.89). ^{1}H NMR (D_2O): δ 1.12 (3 H, *s*, tertiary methyl), 3.45 and 3.57 (AB pattern J_{AB} = 11.0 Hz, $-CH_2OH$), 3.5 – 4.0 (ABC pattern, HO – CH – CH_2OH). ^{13}C NMR (dioxane): δ 20.0 (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 alditol *1* yields both a tri- and a tetraacetate 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 R_F-values were 0.28 (triacetate) and 0.66 (tetraacetate).

Triacetate (6). The alditol *1* (178 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), $[\alpha]_D^{20}$ = +18.1° ($CHCl_3$, *c* 18.4). ^{1}H NMR (CCl_4): δ 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, J_{AB} = 11.5 Hz, $-CH_2-OAc$), 4.57 (A), 4.16 (B) and 5.20 (X) (ABX pattern, J_{AB} = 12.0, J_{AX} = 3.0 and J_{BX} = 7.5, AcO – CH – CH_2OAc), 2.76 (*s*, OH conc. dependent). MS: M^+ 262 absent, *m/e* 189 (6 %, M – $\cdot CH_2OAc$), (Calc. for $C_8H_{13}O_5$ 189.0762; found 189.0771), 159 (55 %, M – 60 – 43), 129 (90 %, *m/e* 189 – 60, *m** 88.0), 117 (100 %, $AcOCH_2-C(CH_3)=^+OH$).

Tetraacetate (7). The alditol *1* (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. ^{1}H NMR (CCl_4): δ 1.51 (*s*, tert. methyl), 2.01, 2.01, 1.99 and 1.99 (all 3 H and *s*, four acetyl groups, 4.45 and 4.30 (AB pattern, J_{AB} = 12.0 Hz, $-CH_2OAc$), 4.48 (A), 4.05 (B) and 5.36 (X) (ABX pattern, J_{AB} = 12.0, J_{AX} = 3.0 and J_{BX} = 7.5, AcO – CH – CH_2OAc). MS: M^+ 304 absent, *m/e* 231 (24 %, M – $\cdot CH_2OAc$); (Calc. for $C_{10}H_{15}O_6$ 231.0869, found 231.0863), 189 (14 %, 231 – 42, *m** 154.5), 159 (43 %, 231 – 72, *m** 109.6, and $AcOCH_2-C(CH_3)=^+OAc$), 129 (100 %, 189 – 60, *m** 88.0).

Tetra-O-trimethylsilyl ether (5). To a solution of *1* (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 spectroscopy. M^+ 424 (absent), *m/e* 409 (0.7 %, M – Me), 321 (7.9 %, M – $\cdot CH_2OSiMe_3$), 219 (100 %, $Me_2SiOCH_2-C(CH_3)=^+OSiMe_3$), (Calc. for $C_9H_{23}Si_2O_2$ 219.1236 as found), 73 (52.2 %, $^+SiMe_3$).

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 to 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). ^{1}H NMR ($CDCl_3$) δ 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). ν_{max} ($CHCl_3$) 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 decolourized 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). ^{1}H NMR ($CDCl_3$) δ 1.53 (*s*, quaternary methyl), 3.75 and 3.81 (both *s*, two methoxyls), 3.80 (*s*, two hydroxyls), 4.40 (*s*, methine H), ν_{max} (KBr) 1740 and 3370 cm^{-1}. MS: M^+ absent, *m/e* 133 20 %, ($M - CO_2CH_3$), *m/e* 90 100 %, (McLafferty rearr. $C_3H_6O_3^+$).

2-C-Methyl-DL-erythritol (racemic 1). A solution of the ester *10* (1.5 g) in dry tetrahydrofuran was added to a solution of lithium aluminium hydride (1.1 g) in dry tetrahydrofuran (20 ml). The mixture was stirred at room

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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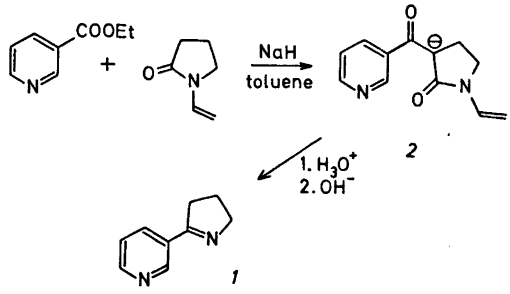
We here describe a convenient synthesis of the minor tobacco alkaloid myosmine (*1*), starting with a condensation of *N*-vinylpyrrolidone with ethyl nicotinate. The condensation product 2 is treated with boiling concentrated hydrochloric acid without prior purification and, after extraction of bases and distillation, *1* 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 [1] or *N*-trimethylsilyl [2] derivative, but preparation of



the N–H protected pyrrolidone is here avoided by using the commercially available *N*-vinylpyrrolidone. Reports on the use of vinylic groups as protective groups for N–H are scanty. 2-Acyl-1-methylvinyl groups have for instance found application in peptide syntheses.[3]

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 (Na_2SO_4), 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 (Na_2SO_4), 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.[1]

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