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SHORT COMMUNICATIONS

New Chiral Dihydroxycyclopropane Block from L-Tartaric Acid

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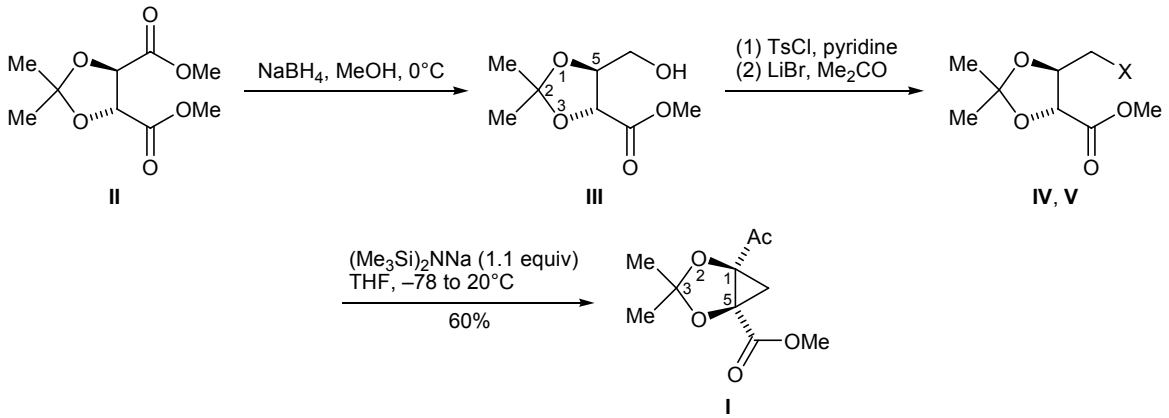
Functionalized hydroxycyclopropane derivatives attract interest as binding units and building blocks in organic synthesis [1, 2]. In this connection, widely used Kulinkovich reaction (transformation of RCO_2Me into R-cyclopropanol) should be noted [3]. The present communication reports on the synthesis of a new chiral dihydroxycyclopropane derivative **I** with the use of accessible L-tartaric acid as source of chirality. The scheme of synthesis of compound **I** includes the following steps. Reduction of known L-tartaric acid dimethyl ester acetonide **II** [4] with sodium tetrahydridoborate gave alcohol **III** in a moderate yield [5]. Compound **III** was converted first into *p*-toluenesulfonate **IV** and then into bromide **V**. The latter underwent intramolecular cyclization to produce target product **I** by the action of hexamethyldisilazane sodium salt in THF (yield ~60%).

The configuration of the new chiral center in compound **I** is determined by configuration of C^5 in bromide **V**, which is not involved in ring closure, for the formation of dioxabicyclo[3.1.0]hexane structure with *trans*-junction of the three and five-membered rings is exceptionally unfavorable.

Methyl (1*S*,5*R*)-3,3-dimethyl-2,4-dioxabicyclo-[3.1.0]hexane-1-carboxylate (I). A solution of 0.2 g (0.79 mmol) of compound **V** in 2 ml of tetrahydrofuran was cooled to –78°C, 0.6 ml (1.2 mmol) of a 2 M solution of hexamethyldisilazane sodium salt in THF was added dropwise, and the mixture was stirred for 1.5 h at that temperature, allowed to warm up to room temperature, and treated with a saturated solution of ammonium chloride. Tetrahydrofuran was evaporated, and the residue was extracted with chloroform. The combined extracts were dried over $MgSO_4$ and evaporated, and the residue was purified by column chromatography on silica gel using petroleum ether–ethyl acetate (2 : 1) as eluent. Yield 0.09 g (~61%), light yellow oily substance, $[\alpha]_D^{20}$ = +94.6° (*c* = 2.44, $CHCl_3$). IR spectrum, ν, cm^{-1}: 2992, 2955, 2937, 1749, 1730, 1441, 1375, 1358, 1306, 1267, 1240, 1211, 1196, 1159, 1136, 1107, 1014, 978, 868, 833, 795, 741, 548. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.39 s (3H),



IV, X = OTs; **V**, X = Br.

1.41 s (3H, CH_3), 1.47 d.d (1H, CH_2, J = 3.2, 6.5 Hz), 1.70 d (J = 4.6 Hz), 1.74 d (1H, CH_2, J = 5.6 Hz), 3.76 s (3H, OMe), 4.30 d.d (1H, 5-H, J = 3.4, 5.2 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 24.82 and 25.96 (CH_3), 33.12 (CH_2), 52.44 (OMe), 63.09 (C^5), 63.63 (C^1), 123.02 (C^3), 171.23 (**C**O_2Me). Found, %: C 55.01; H 6.87. $C_8H_{12}O_4$. Calculated, %: C 55.81; H 7.02.

Methyl (4*R*,5*S*)-5-hydroxymethyl-2,2-dimethyl-1,3-dioxolane-4-carboxylate (III) was synthesized according to the procedure described in [5]. Its specific optical rotation and other spectral parameters were consistent with the data given in [5].

Methyl (4*R*,5*S*)-2,2-dimethyl-5-(4-methylphenylsulfonyloxymethyl)-1,3-dioxolane-4-carboxylate (IV). A solution of 0.9 g (4.72 mmol) of compound **III** in 5 ml of anhydrous pyridine was cooled to 0°C, 1.08 g (7.0 mmol) of *p*-toluenesulfonyl chloride was added under stirring, and the mixture was stirred for 4–5 h at room temperature, poured into ice water, and extracted with chloroform (3×20 ml). The extracts were combined, washed with cold water and a saturated solution of sodium chloride, dried over $MgSO_4$, filtered, and evaporated. The residue was subjected to column chromatography on silica gel using petroleum ether–ethyl acetate (2:1) as eluent. Yield 1.26 g (70%), colorless crystals, mp 40–43°C, $[\alpha]_D^{20}$ = –20.0° (c = 2.71, $CHCl_3$). IR spectrum, ν, cm^{-1}: 2989, 2954, 1761, 1738, 1597, 1438, 1367, 1292, 1251, 1211, 1176, 1107, 985, 928, 852, 831, 818, 791, 665, 555. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.40 s (6H, 2-CH_3), 2.46 s (3H, 4′-CH_3), 3.78 s (3H, OMe), 4.19 d.d (1H, OCH_2, J = 5.0 Hz), 4.30–4.36 m (3H, OCH_2, 4-H, 5-H), 7.37 d (2H, H_{arom}, J = 8.0 Hz), 7.82 d (2H, H_{arom}, J = 8.3 Hz). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 21.55 (CH_3), 25.69 and 26.55 (2-CH_3), 52.53 (OMe), 68.32 (OCH_2), 74.94 (C^5), 76.23 (C^4), 112.08 (C^2), 127.94, 129.82, 132.57, 145.04 (C_6H_4), 170.14 (**C**O_2Me). Found, %: C 51.79; H 5.56; S 8.91. $C_{15}H_{20}O_7S$. Calculated, %: C 52.31; H 5.85; S 9.31.

Methyl (4*R*,5*R*)-5-(bromomethyl)-2,2-dimethyl-1,3-dioxolane-4-carboxylate (V). Freshly calcined lithium bromide, 0.38 g (4.42 mmol), was added to a solution of 0.56 g (1.40 mmol) of compound **IV** in 30 ml of diethyl ketone, and the mixture was heated for 5–6 h under reflux. The mixture was cooled, the precipitate was filtered off, and the filtrate was evaporated. The residue was dissolved in 10 ml of methylene chloride, the solution was washed with a saturated solution of sodium chloride, dried over $MgSO_4$, and evaporated, and the residue was subjected to column chromatography on silica gel using petroleum ether–ethyl acetate (2:1) as eluent. Yield 0.31 g (83%), $[\alpha]_D^{20}$ = –11.75° (c = 4.56, $CHCl_3$). IR spectrum, ν, cm^{-1}: 2989, 2939, 1763, 1734, 1437, 1380, 1288, 1211, 1157, 1103, 1015, 889, 831, 765. ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.44 s and 1.50 s (6H, CH_3), 3.54 d.t (J = 1.4, 1.6 Hz), 3.58 d.d (1H, CH_2, J = 3.8, 0.5 Hz), 3.65 q (1H, CH_2, J = 1.4 Hz), 3.79 s (3H, CO_2Me), 4.41–4.42 m (2H, 4-H, 5-H). ^{13}C NMR spectrum ($CDCl_3$), δ_C, ppm: 25.87 and 26.86 (CH_3), 32.40 (CH_2), 52.51 (OMe), 77.45 (C^5), 77.60 (C^4), 111.99 (C^2), 170.40 (**C**O_2Me). Found, %: C 37.30; H 4.79; Br 32.17. $C_8H_{13}BrO_4$. Calculated, %: C 37.96; H 5.18; Br 31.57.

The IR spectra were recorded on a Shimadzu IR Prestige-21 spectrometer from samples prepared as thin films. The ^1H and ^{13}C NMR spectra were measured on a Bruker AM-300 instrument at 300.13 and 75.47 MHz, respectively, using tetramethylsilane as internal reference. The optical rotations were measured on a Perkin–Elmer-341 instrument. The progress of reactions was monitored by TLC on Sorbfil plates (Russia); spots were developed by treatment with a solution of 4-methoxybenzaldehyde in ethanol containing sulfuric acid, followed by heating at 120–150°C. L-Tartaric acid (99%) was commercial product (from Aldrich).

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