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SHORT COMMUNICATIONS

Synthesis of *Z*-2-Methyl-6-*R*-1,2,3,4-tetrahydro-4-quinolinecarboxylic Acids

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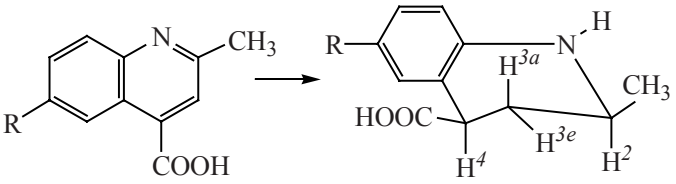
The known methods of reduction of quinolinecarboxylic acids not always give high yields of 1,2,3,4-tetrahydroquinolinecarboxylic acids and often involve a formation of product mixtures [1, 2].

We discovered an efficient procedure for the synthesis of 2-methyl- and 2,6-dimethyl-1,2,3,4-tetrahydro-4-quinolinecarboxylic acids (**I** and **II**).



I, II

R = H (**I**), CH_3 (**II**).

Compounds **I** and **II** were obtained by reducing 2-methyl- and 2,6-dimethyl-4-quinolinecarboxylic acids with Raney alloy at room temperature in alkaline medium. The final product we succeeded to isolate in the maximum yield by acidifying the reaction mixture with formic acid followed by extraction into chloroform. The yield attained 80–85%.

As shown by ^{1}H NMR spectroscopy the compounds obtained were individual *Z*-isomers. The establishment of the structure of compounds **I** and **II** was based on the coupling constants of the axial proton H^3. The appearance of two large coupling constants of H^3 (10.98–12.3 Hz) indicates equatorial orientation of both substituent at the atom C^4 and the substituent at C^2 thus proving the *cis*-orientation of 4-carboxy and 2-methyl groups [3, 4].

2-Methyl-1,2,3,4-tetrahydroquinoline-4-carboxylic acid (I). To a solution of 2 g (0.01 mol) of 2-methylquinoline-4-carboxylic acid in 10 ml of 10% sodium hydroxide was added by small portions at stirring within 1 h 1.6 g of Raney alloy, and the mixture was stirred for 1 h more at room temperature. The precipitate was filtered off, washed with hot water, formic acid was added to the filtrate to pH 3, and the reaction product was extracted into chloroform and dried over anhydrous sodium sulfate. Chloroform was evaporated to dryness, and the residue was recrystallized from 50% ethanol. Yield 1.6 g (80%), colorless crystals, mp 131–134°C. IR spectrum, ν, cm^{-1}: 1701 (CO), 2966 (CH_3), 3278 (NH). ^{1}H NMR spectrum, δ, ppm: 1.29 d (3H, CH_3, *J* 6.11 Hz), 2.01 d.d (1H, H^{3a}, *J* 12.21, 10.98 Hz), 2.26 d.d.d (1H, H^{3e}, *J* 10.98, 6.11, 2.44 Hz), 3.45 d.d.d (1H, H^{2a}, *J* 10.98, 6.11, 2.44 Hz), 4.01 d.d (1H, H^{4a}, *J* 12.21, 6.11 Hz), 6.56 d (1H, H^8, *J* 7.33 Hz), 6.71 t (1H, H^6, *J* 7.33 Hz), 7.07 t (1H, H^7, *J* 7.33 Hz), 7.14 d (1H, H^5, *J* 3.33 Hz). Mass spectrum, *m/z* (I_{rel}, %): 205 (44) $[M]^+$, 190 (28), 146 (91), 130 (100), 118 (9.5), 103 (4), 77 (19), 65 (8). Found, %: C 69.00; H 6.87; N 7.40. $C_{11}H_{13}NO_2$. Calculated, %: C 69.11; H 6.80; N 7.33.

2,6-Dimethyl-1,2,3,4-tetrahydroquinoline-4-carboxylic acid (II) was prepared similarly. Yield 85%, mp 136–140°C (50% ethanol). IR spectrum, ν, cm^{-1}: 1716 (CO), 2950, 2854 (CH_3), 3382 (NH). ^{1}H NMR spectrum, δ, ppm: 1.29 d (3H, CH_3, *J* 6.3 Hz), 1.8 d.d (1H, H^{3a}, *J* 12.3, 11.1 Hz), 2.11 s (3H, CH_3), 2.2 d.d.d (1H, $H^{3\varepsilon}$, *J* 11.3, 7.11, 2.6 Hz), 3.35 d.d.d (1H, H^{2a}, *J* 11.11, 6.58, 2.4 Hz), 3.85 d.d (1H, H^{4a}, *J* 12.5, 6.6 Hz), 6.4 d (1H, H^8, *J* 8.1 Hz), 6.8 d (1H, H^7, *J* 8.33 Hz), 7.4 s (1H, H^5). Mass spectrum, *m/z* (I_{rel}, %): 219 (45)

$[M]^+$, 204 (25), 160 (78), 144 (100), 143 (9.5), 103 (3), 91 (9.5), 71 (8), 65 (6). Found, %: C 70.10; H 7.30; N 6.85. $C_{12}H_{15}NO_2$. Calculated, %: C 70.24; H 7.32; N 6.83.

IR spectra were recorded on a spectrophotometer Shimadzu FTIR-8400S from pellets with KBr. ^1H NMR spectra were registered on a spectrometer Bruker AM 300 (300 MHz), internal reference TMS, solvent $CDCl_3$. Mass spectra were obtained on a GC-MS spectrometer Finnigan Trance DSQ with a direct admission of samples into the ion source, ionization energy 80 eV.

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