SYNTHESIS OF OPTICALLY ACTIVE CYCLOPROPYL-SUBSTITUTED IMIDAZOLIN-2-ONE BASED ON (+)-4-α-ACETYLCAR-2-ENE

M. A. Klimkin, V. G. Kasradze, O. S. Kukovinets, and F. Z. Galin

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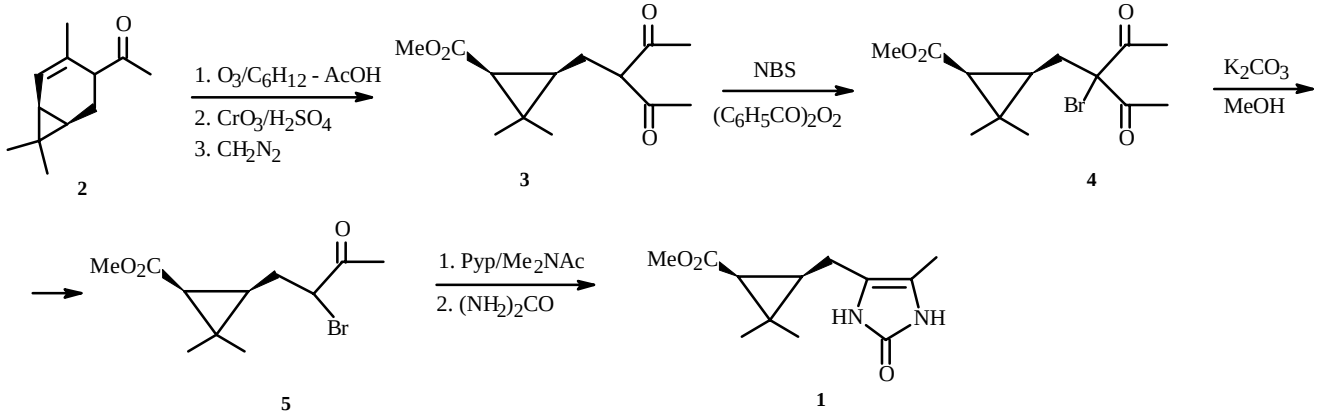
Cyclopropyl-substituted imidazolin-2-one was synthesized based on the ozonolysis of (+)-4-α-acetylcar-2-ene using the condensation of α-bromoketone and urea as a key step.

Key words: imidazolin-2-one, (+)-4-α-acetylcar-2-ene, (+)-(1S,3R)-2,2-dimethyl-3-(2-bromo-3-oxobutyl)cyclopropanecarboxylic acid methyl ester, urea, condensation.

Functionally substituted cyclopropanes are widely distributed in nature [1]. Unique pentacyclopropane nucleosides that are effective fungicides have been isolated from living organisms and identified [2].

We previously reported the synthesis of optically active derivatives of 2,2-dimethylcyclopropanecarboxylic acid that contain pyrazole and oxazole moieties [3]. In continuation of this research, we synthesized optically active cyclopropyl-substituted imidazolin-2-one (**1**) from **5**, prepared by transformation of the product from ozonolysis of (+)-4-α-acetylcar-2-ene (**2**) [4]. Diketoester **3** was synthesized as described earlier [3]. Bromination of **3** with an equimolar amount of NBS in CCl_4 converts at most 70% (a 1.5-fold excess of NBS is required for complete conversion).



2 **3** **4** **5** **1**

Bromoketone **5** was prepared in 98% yield from **4** using K_2CO_3 in MeOH. Condensation of **5** with urea under the literature conditions [5] gave chiral heterocycle **1**, which contains the cyclopropane fragment, in 42% yield.

EXPERIMENTAL

IR spectra were recorded on a Specord M-80 instrument as thin layers or in nujol. ^1H and ^{13}C NMR spectra were obtained on a Bruker AM-300 spectrometer (working frequency 300 and 75.46 MHz, respectively) in $CDCl_3$ with TMS internal standard. The specific rotation was measured in $CHCl_3$ on a Perkin—Elmer 241 MS polarimeter. GLC analysis was performed

Institute of Organic Chemistry, Ufa Scientific Center, Russian Academy of Sciences, 450054 Ufa, pr. Oktyabrya, 71, fax (3472) 35 60 66. Translated from Khimiya Prirodnykh Soedinenii, No. 6, pp. 488-489, November-December, 2000. Original article submitted February 6, 2000.

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on a Chrom-5 chromatograph [1.2 m × 3 mm column, silicone SE-30 (5%) on chromaton N-AW-DMCS (0.16-0.20 mm) stationary phase, working temperature 50-300°C] with He carrier gas.

(+)-(1S,3R)-2,2-Dimethyl-3-(2-acetyl-3-oxobutyl)cyclopropanecarboxylic Acid Methyl Ester (3). Prepared in 52% yield by the literature method [3].

(+)-(1S,3R)-2,2-Dimethyl-3-(2-acetyl-2-bromo-3-oxobutyl)cyclopropanecarboxylic Acid Methyl Ester (4). A mixture of **3** (1 g, 0.004 mol) in dry CCl_4 (15 mL), freshly recrystallized benzoyl peroxide (0.01 g), and N-bromosuccinimide (1.12 g, 0.0062 mol) was refluxed until succinimide was no longer evolved. Succinimide was filtered off. CCl_4 was evaporated. The solid was treated with ethylacetate (150 mL), washed successively with saturated $NaHCO_3$ and NaCl solutions, and dried with Na_2SO_4. The solvent was evaporated to give a solid (1.4 g) that was chromatographed (SiO_2, eluent petroleum ether:ethylacetate 7:1). Yield of **4**, 1.03 g, 78%, n_D^{20} 1.4751, $[\alpha]_D^{20}$ +5.2° (*c* 1.8).

IR spectrum (KBr, ν, cm^{-1}): 530 (C–Br), 1380, 1385 [$C(CH_3)_2$], 1715 ($COCH_3$), 1735 (CO_2CH_3).

PMR (δ, ppm, J/Hz): 1.15 (3H, s, CH_3-2), 1.18 (3H, s, CH_3-2), 1.52 (1H, d, J = 6, H-1), 1.36 (1H, $W_{1/2}$ = 18, H-3), 2.40 (6H, s, $2CH_3CO$), 2.53 (2H, $W_{1/2}$ = 18, CH_2), 3.64 (3H, s, CH_3O).

^{13}C NMR (δ, ppm): 14.33, 28.72 (q, q, CH_3-2), 25.29 (s, C-2), 26.94 (d, C-3), 26.96 (q, 2CO**C**H_3), 28.49 (d, C-1), 30.09 (t, CH_3), 51.47 (q, CH_3O), 74.36 (s, CBr), 171.94 (s, CO_2), 200.56, 200.30 (s, s, 2C=O).

(+)-(1S,3R)-2,2-Dimethyl-3-(2-bromo-3-oxobutyl)cyclopropanecarboxylic Acid Methyl Ester (5). A mixture of **4** (1 g, 0.003 mol) and K_2CO_3 (0.21 g, 0.0015 mol) in absolute MeOH (15 mL) was stirred for 3 h. The MeOH was evaporated. The solid was treated with ethylacetate (60 mL), washed with saturated $NaHCO_3$ and NaCl solutions, and dried with Na_2SO_4. The solvent was evaporated to give pure **5** according to GLC. Yield 0.85 g (98%), n_D^{20} 1.4925, $[\alpha]_D^{20}$ +13.2° (*c* 1.5).

IR spectrum (KBr, ν, cm^{-1}): 590 (C–Br), 1380, 1385 [$C(CH_3)_2$], 1705 (C=O), 1720 (CO_2CH_3).

PMR (δ, ppm, J/Hz): 1.25 (3H, s, CH_3-2), 1.31 (3H, s, CH_3-2), 1.53 (1H, d, J = 6, H-1), 2.27 (3H, $W_{1/2}$ = 18, CH_2CH), 2.40 (3H, s, CH_3CO), 3.64 (3H, s, CH_3O), 4.21 (1H, HCBr).

^{13}C NMR (δ, ppm): 14.20, 28.59 (q, CH_3), 25.65, 25.29 (s, C-2), 26.34 (q, CO**C**H_3), 27.61 (t, CH_2), 28.36, 28.17 (d, d, C-1), 30.71, 30.55 (d, d, C-3), 51.27 (q, OCH_3), 54.83, 53.79 (d, CBr), 171.94 (s, CO_2), 201.76, 201.67 (s, s, C=O).

(+)-(1S,3R)-2,2-Dimethyl-3-[(5-methyl-2-oxo-2,3-dihydro-1H-imidazol-4-yl)methyl]cyclopropanecarboxylic Acid Methyl Ester (1). A mixture of **5** (0.25 g, 0.0009 mol), N,N-dimethylacetamide (1 mL), and piperidine (0.183 mL, 0.00185 mol) was stirred for 1 h at room temperature, treated with urea (0.367 g, 0.0061 mol), $ZnCl_2$ (0.018 g, 0.00013 mol), and $MgCO_3$ (0.183 g, 0.0022 mol), again stirred at 170°C for 2 h, cooled to room temperature, treated with AcOH (2 mL, 10%), left for 24 h at -8°C, and diluted with ethylacetate (100 mL). The organic layer was separated, washed with saturated $NaHCO_3$ and NaCl solutions, and dried over Na_2SO_4. The solvent was evaporated. The solid was chromatographed (SiO_2, eluent petroleum ether:ethylacetate 1:1) to give **1**, 0.1 g, 42%, $[\alpha]_D^{20}$ +7.8° (*c* 0.00276).

IR spectrum (KBr, ν, cm^{-1}): 1380, 1385 [$C(CH_3)_2$], 1660 (C=C), 1700 (C=O), 1730 (CO_2CH_3), 2940, 2970.

PMR (δ, ppm, J/Hz): 1.16 (6H, s, CH_3-2), 1.29 (6H, s, CH_3-2), 1.36 (1H, $W_{1/2}$ = 14, H-3), 1.5 (1H, d, J = 6, H-1), 2.03 (3H, s, CH_3-5′), 2.93 (2H, d, J = 6, CH_2), 3.64 (3H, s, CH_3O).

^{13}C NMR (δ, ppm): 13.87 (q, CH_3-5′), 14.15, 28.76 (q, CH_3-2), 25.67 (t, CH_2), 28.24 (d, C-1), 28.41 (s, C-2), 31.67 (d, C-3), 51.22 (s, CH_3O), 129.96 (s, C-4′), 145.82 (s, C-5′), 159.24 (s, C=O), 172.11 (s, CO_2).

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