A new synthesis of *E*- and *Z*(−)(1*R*,3*S*)-2,2-dimethyl-3-(3,3,3-trifluoro-2-chloropropen-1-yl)cyclopropanecarboxylic acids from (+)-3-carene

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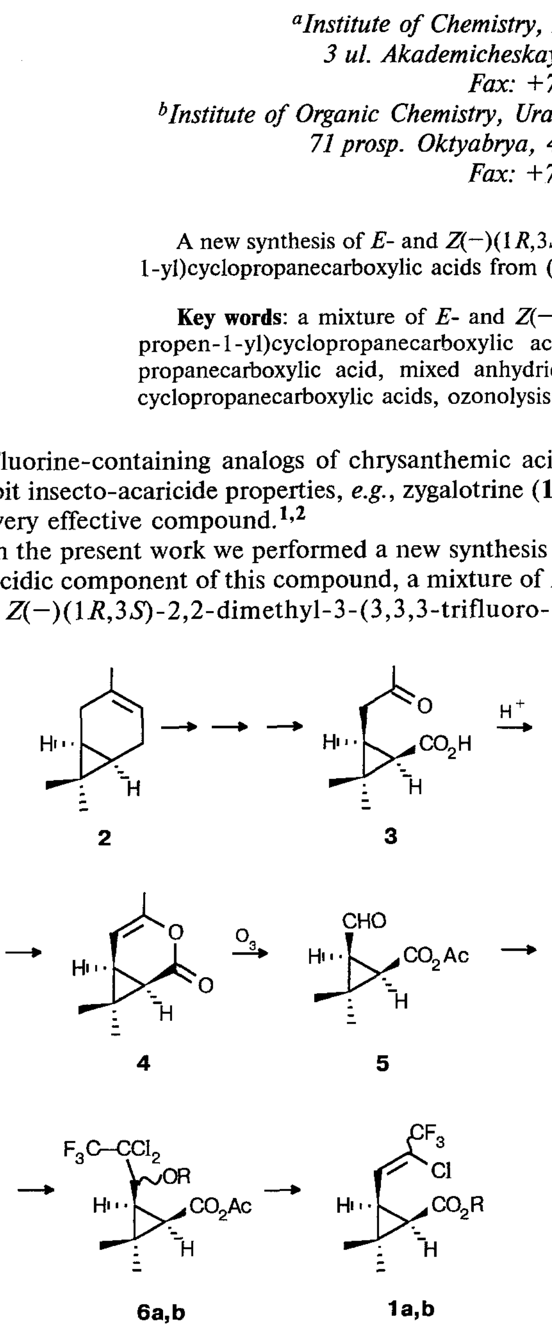
A new synthesis of *E*- and *Z*(−)(1*R*,3*S*)-2,2-dimethyl-3-(3,3,3-trifluoro-2-chloropropen-1-yl)cyclopropanecarboxylic acids from (+)-3-carene in 21 % total yield was carried out.

Key words: a mixture of *E*- and *Z*(−)(1*R*,3*S*)-2,2-dimethyl-3-(3,3,3-trifluoro-2-chloropropen-1-yl)cyclopropanecarboxylic acids, (1*R*,3*S*)-2,2-dimethyl-3-(2-oxopropyl)cyclopropanecarboxylic acid, mixed anhydride of acetic and (1*R*,3*S*)-2,2-dimethyl-3-formylcyclopropanecarboxylic acids, ozonolysis.

Fluorine-containing analogs of chrysanthemic acids exhibit insecto-acaricide properties, *e.g.*, zygalotrine (**1a**) is a very effective compound.[1,2]

In the present work we performed a new synthesis of the acidic component of this compound, a mixture of *E*- and *Z*(−)(1*R*,3*S*)-2,2-dimethyl-3-(3,3,3-trifluoro-2-chloropropen-1-yl)cyclopropanecarboxylic acids (**1b**), from (+)-3-carene (**2**) *via* the known ketoacid (**3**).[3,4,5]



1a: R = CH(CN)—C_6H_4—Ph
1b,6a: R = H
6b: R = Ac

Ketoacid **3** was converted into enololactone **4** according to the known procedures,[5,6] and compound **4** was transformed into anhydridoaldehyde **5**. The latter easily forms anhydridoalcohol (**6a**) by the action of an organozinc compound obtained from trichlorotrifluoroethane and Zn. Treatment of the anhydridoalcohol with acetic anhydride in pyridine afforded a mixture of epimeric acetates (**6b**) in almost quantitative yield. According to GLC analysis and judging by the integral intensity of the signals of the *gem*-dimethyl group protons in the 1.09—1.30 ppm region, the ratio of the isomers is 3 : 1.

Treatment of the mixture of acetates **6b** with zinc in DMF followed by hydrolysis gave the target product **1b**. Its ^{1}H NMR spectrum contains a double set of signals corresponding to *Z*- and *E*-isomers in the ratio of 9 : 1, which agrees with the literature data.[1]

The new feature of the synthetic scheme proposed here is the protection of the carboxy group as a mixed anhydride, whose mild hydrolysis allowed us to avoid epimerization at the C(1) atom. This type of protection was found to be relatively stable.

Experimental

Optical rotation was measured on a Perkin-Elmer-141 polarimeter in $CHCl_3$. IR spectra were recorded on a UR-20 instrument. NMR spectra were obtained on Tesla BS-487, Tesla BS-567 (^{1}H NMR), and Jeol FX-90 (^{13}C NMR, 22.5 MHz) instruments in $CDCl_3$ using $SiMe_4$ as the internal standard.

(+)-3-Carene (2), n_D^{20} = 1.4726, $[\alpha]_D^{20}$ +15.7° (pure compound).

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(−)(1*R*,3*S*)-2,2-Dimethyl-3-(2-oxopropyl)cyclopropanecarboxylic acid (3) was obtained from compound **2** according to the known procedure[3] as a colorless oil, $[\alpha]_D^{21}$ −2.71° (*c* 2.0).

(−)-4,7,7-Trimethyl-3-oxabicyclo[4.1.0]hept-4-en-2-one (4) was obtained from compound **3** according to the known procedure,[6] m.p. 44—46 °C (pentane), $[\alpha]_D^{20}$ −86°(*c* 2.0).

The mixed anhydride of acetic acid and (1*R*,3*S*)-2,2-dimethyl-3-(2,2-dichloro-3,3,3-trifluoro-1-hydroxypropyl)-cyclopropanecarboxylic acid (6a). CF_3CCl_3 (1.77 g, 9.4 mmol) was added dropwise under argon to a mixture of zinc powder (0.62 g, 8.6 mmol) and CuCl (40 mg, 0.4 mmol) in DMF (10 mL), and the mixture was stirred for 2 h. The reagent obtained was added portionwise to a stirred solution of aldehyde **5** (1.5 g, 7.9 mmol) in DMF (3 mL) and heated at 50—60 °C for 10 h. The solution was cooled to 0 °C and poured into a mixture of 150 mL of ether and 100 mL of ice water. The aqueous layer was extracted with ether (3×100 mL). The organic layer was washed with saturated aqueous NaCl and dried with Na_2SO_4. The solvent was distilled off to give 1.85 g (70 %) of product **6a** as an individual compound, according to TLC data (hexane—acetone, 3 : 1, Silufol). IR (CCl_4), ν/cm^{-1}: 675 (C—Cl), 1375, 1380 (Me_2C), 1395 (C—F), 1760, 1825 (—CO—O—CO—), 3450 br.s (OH).

The mixed anhydride of acetic acid and (−)(1*R*,3*S*)-2,2-dimethyl-3-(1-acetoxy-2,2-dichloro-3,3,3-trifluoropropyl)cyclopropanecarboxylic acids (6b). A mixture of alcohol **6a** (0.14 g, 1.8 mmol), Ac_2O (0.12 g, 1.2 mmol) and dry pyridine (0.14 g, 1.8 mmol) was kept for 20 h at room temperature, then diluted with 100 mL of ether and successively washed with H_2O (30 mL), 10 % H_2SO_4, and saturated aqueous NaCl (30 mL), and dried with $MgSO_4$. The solvents were distilled off to give 0.27 g of a residue which was chromatographed on SiO_2 (hexane—ether, 2 : 1, as the eluent) to yield 0.25 g (98 %) of product **6b** as a yellow liquid, n_D^{20} = 1.4741, $[\alpha]_D^{20}$ −17.8° (*c* 3.0). IR (CCl_4), ν/cm^{-1}: 675 (C—Cl), 1380, 1385 (Me_2C), 1395 (C—F), 1040, 1185, 1735 (Ac), 1760, 1820 (—CO—O—CO—). ^1H NMR, δ: 1.09, 1.15, 1.25, 1.3 (four s, 6 H, Me_2C), 1.51 (d, 1 H, HC(1), *J* = 7.8 Hz), 1.96 (s, 3 H, AcO), 2.15 (s, 3 H, CO_2Ac), 4.5—4.6 (m, 1 H, HC—C—OAc). Found (%): C, 41.10; H, 3.97; Cl, 18.51, $C_{13}H_{15}O_5Cl_2F_3$. Calculated (%): C, 41.18; H, 3.98; Cl, 18.70.

The mixture of *E*- and *Z*(−)(1*R*,3*S*)-2,2-dimethyl-3-(2-chloro-3,3,3-trifluoropropen-1-yl)cyclopropanecarboxylic acids (1b). Zinc powder (0.51 g, 7.9 mmol) was added to a solution of acetate **6b** (0.25 g, 0.65 mmol) in 3 mL of DMF. The mixture was stirred for 10 h, diluted with 100 mL of ether, and filtered. The filtrate was washed with 20 mL of saturated aqueous NaCl and dried with $MgSO_4$. The solvent was distilled off to give 0.2 g of a residue, which was then added to a mixture of 10 % aqueous NaOH (1 mL) and acetone (1 mL). The solution was stirred for 3 h, then 10 mL of H_2O was added. The solution was extracted with ether (3×50 mL). The pH of the aqueous layer was adjusted to 7 by adding 10 % H_2SO_4 with cooling (5 °C) and extracted with ether (3×100 mL). The extract was washed with saturated aqueous NaCl and dried with $MgSO_4$. The solvent was distilled off to give 0.15 g of product **1b** as a yellow oil, which was an individual compound according to TLC data (hexane—acetone—methanol, 4 : 2 : 1, Silufol). $[\alpha]_D^{20}$ −2.34° (*c* 3.0). IR (CCl_4), ν/cm^{-1}: 680 (C—Cl), 1380, 1385 (Me_2C), 1390 (C—F), 1710, 2600—3000 (CO_2H), 840, 1670 (C=C). ^1H NMR, δ: 0.96, 105 (two s, *E*) and 1.15, 1.3 (two c, *Z*) (6 H, Me_2C), 1.43 (d, *E*) and 1.63 (d, *Z*) (1 H, HC(1), *J* = 7.8 Hz), 1.86—2.33 (m, 1 H, HC(3)), 6.7 (d, *E*) и 6.8 (d, *Z*) (1 H, HC=C, *J* = 7.8 Hz). Found (%): C, 41.56; H, 4.33; Cl, 15.31. $C_8H_{10}O_2ClF_3$. Calculated (%): C, 41.66; H, 4.36; Cl, 15.37.

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