Communications to the Editor

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STEREOSELECTIVE SYNTHESIS OF gem-BISTRIFLUOROMETHYLCYCLOPROPANE DERIVATIVES

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gem-Bistrifluoromethylcyclopropanecarboxylic acids were synthesized through the inter- and intramolecular cyclopropanation of bistrifluoromethylethylenic compounds with sulfonium ylids. The trans-cyclopropane (10) was converted to the hexafluorocypermethrin (13).

KEYWORDS—— cyclopropane; trifluoromethyl; sulfonium ylid; cypermethrin

Introduction of fluorine into bioactive compounds has attracted attention because of the augmented activity or selectivity of their functions compared with those of the parent compound. A number of chemical modifications of chrysanthemic acid and related compounds have been synthesized and their structure-activity relationship has been investigated.[1,2] Some of the fluorine-modified analogs were highly active.[3,4]

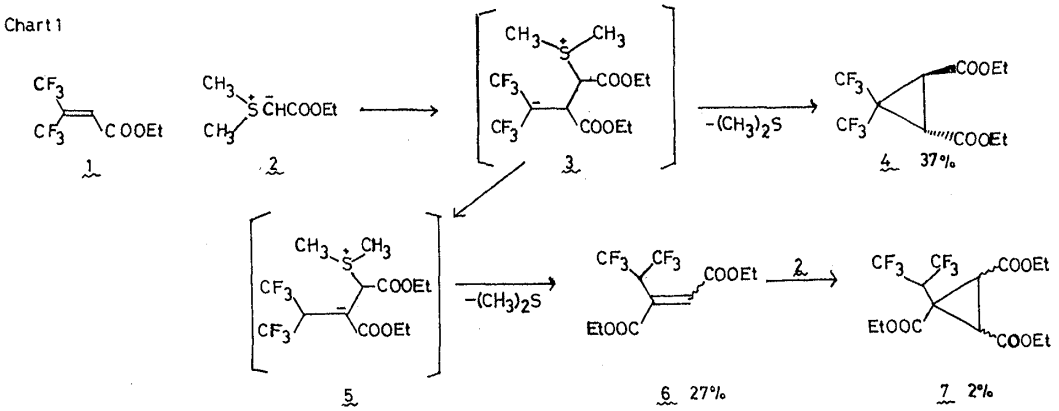
In this paper we report the synthesis of gem-bistrifluoromethylcyclopropane derivatives through the cyclopropanation of bistrifluoromethylethylenic compounds with sulfonium ylid in a stereoselective manner,[5] and the conversion of the trans-isomer to the hexafluorocypermethrin (13).

Owing to the electron-withdrawing character of the trifluoromethyl group, bistrifluoromethylethylenic compounds were reported to react as a Michael acceptor with amines[6] and as a 1,3-dipolarophile with diazo or azide compounds.[7]

The reaction of ethyl hexafluorosenecionate (1)[8] with sulfonium ylid (2) was investigated under a variety of reaction conditions, but gave the desired trans-cyclopropane (4)[9] in relatively low yield accompanied by the olefinic compounds (6) and the cyclopropane derivative (7). The formation of 6 may be explained by the proton transfer from the initial adduct 3 to the carbanion (5) stabilized by the ester group, followed by the β-elimination of dimethylsulfide (Chart 1).

To avoid the competitive proton transfer the ester group of 1 was converted to a hydroxyl group. The allyl alcohol (8) was obtained by treatment of 1 with DIBAL-H in 70-80% yield. As expected, the reaction of the benzoate (9) with 2 (DMF, r.t., 16h) gave the trans-cyclopropane (10) in 44% yield as the only product isolated. The trans-stereochemistry of 10 was confirmed by the following transformation to the

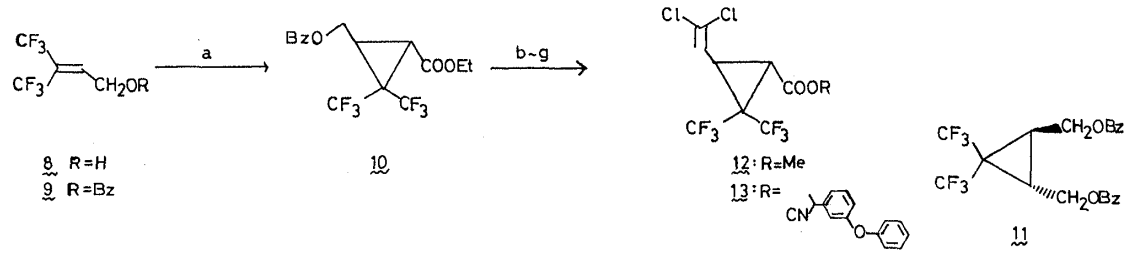
Chart 1



diol derivative (11). Reduction of the ester group of 10 (DIBAL-H, ether) and the subsequent esterification (PhCOCl, Py) afforded the dibenzoate [11, ^{1}H-NMR($CDCl_3$)δ 2.43 (2H, m), 4.53 (4H, m). ^{19}F-NMR($CDCl_3$)δ -3.3 (s)],[10] whose physical data are identical with those of the dibenzoate derived from the diester (4) (DIBAL-H then PhCOCl, Py). ^{19}F-NMR of either 4 or 11 showed one single peak due to their C_2-symmetrical structure.

The trans-cyclopropane (10) was converted to the hexafluorocypermethrin (13). Thus, the Swern oxidation[11] (step d in Chart 2) of the hydroxy ester afforded an unstable aldehyde, which was subjected to the Wittig reaction to form the dichloride (12, 51% yield from the hydroxy ester). Saponification of 12 to the acid (mp 85.8°C, 92% yield) and the subsequent reaction with the bromonitrile gave the hexafluorocypermethrin (13) as a diastereomeric mixture [13, 59% yield. ^{1}H-NMR ($CDCl_3$)δ 2.83 (1H, dm, J=7.2 Hz), 3.27 (1H, tm, J=7.2 Hz), 5.75 (1H, dm, J=7.2 Hz), 6.31 and 6.35 (1H, each s), 6.88-7.50 (9H, m). ^{19}F-NMR($CDCl_3$)δ +2.0 (qm, J=8.5 Hz), +1.4 (qm, J=8.5 Hz)][12] (Chart 2).

Chart 2



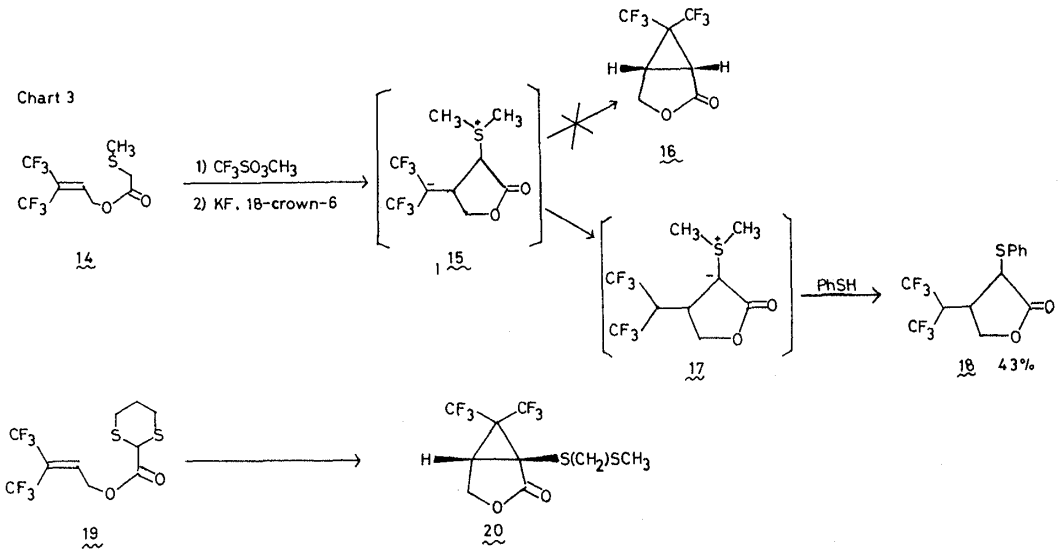
a) 2, DMF b) KOH, MeOH c) CH_2N_2 d) DMSO, $(COCl)_2$, Et_3N, CH_2Cl_2 e) $CBrCl_3$, $(Me_2N)_3P$, CH_2Cl_2, -100°C

f) KOH, MeOH g) $BrCH(CN)C_6H_4$-OC_6H_5, Et_3N, acetone

For the synthesis of cis-isomer (16) intramolecular cyclopropanation to form a [3,1,0] ring system was examined.[13] First, the methylthioacetate (14) was used as starting material. Thus, S-methylation ($CF_3SO_3CH_3$, 0°C, 1h) followed by the subsequent treatment with base (KF or Et_3N eg) gave no cyclopropane (16), but in the presence of benzenethiol (KF, 18-crown-6, CH_2Cl_2 then PhSH, CH_2Cl_2) the phenylsulfide (18) was obtained in 43% yield. This suggests the initial formation of the adduct (15), which was easily transformed to the sulfonium ylid (17). To prevent the ylid formation through the proton-transfer, the α-hydrogen atom was replaced with a sulfur atom. Indeed the 1,3-dithiane-2-carboxylate (19) was found to give the cyclopropane (20) by the similar reaction [a) $CF_3SO_3CH_3$, 0°C, b) KF, 18-crown-6, CH_2Cl_2-

DMF, r.t.] in 43% yield. Several attempts were made to convert 20 to 16, but failed. Thus, instead of the dithiane derivative another functional group should be used (Chart 3).

Chart 3



In conclusion, using γ,γ-bistrifluoromethylallyl alcohol (8) as the starting material gem-bistrifluoromethylcyclopropane derivatives are synthesized in stereoselective manner through inter- and intramolecular cyclopropanation with sulfonium ylid.

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9) 4: ^{1}H-NMR($CDCl_3$)δ: 1.28 (6H, t, J=7.5 Hz), 3.10 (2H, s), 4.27 (4H, q, J=7.5 Hz). ^{19}F-NMR($CDCl_3$)δ:[10] +0.27 (6F, s).
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