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Brief Communications

2-Polyfluoroalkylchromones
13.* Synthesis and nitration of 6,8-dibromo-2-trifluoromethylchromone

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The nitration of 6,8-dibromo-2-trifluoromethylchromone depends on the reaction conditions and affords 6,8-dibromo-5-nitro- or 3,6,8-tribromo-5-nitro-2-trifluoromethylchromones. The structures of these compounds were determined from the ^{1}H and ^{13}C NMR spectroscopic data.

Key words: 6,8-dibromo-2-trifluoromethylchroman-4-one, 6,8-dibromo-2-trifluoromethylchromone, nitration, 6,8-dibromo-5-nitro- and 3,6,8-tribromo-5-nitro-2-trifluoromethylchromones, ^{1}H and ^{13}C NMR spectroscopy.

The introduction of electron-withdrawing groups into the benzene ring of 2-polyfluoroalkylchromones enhances the reactivity of these molecules toward amines[2—4] and makes them attractive for further investigations. In this connection, the synthesis of new nitro derivatives of 2-polyfluoroalkylchromones becomes an urgent task, which should be solved in the nearest future. We have recently described the nitration of monosubstituted 2-trifluoromethylchromones[2,5] and 5,7-dimethyl-2-polyhaloalkylchromones[1] and have shown that, in the latter case, the reaction proceeds *via* the formation of the 6-nitro derivative, which can be isolated and affords 5,7-dimethyl-6,8-dinitro-2-polyhaloalkylchromones. This work is devoted to the synthesis of 6,8-dibromo-2-trifluoromethylchromone and establishment of the direction of electrophilic attack during its nitration. 6,8-Dibromo-5-hydroxy-2-phenyl(styryl)chromones have previously[6] been synthesized by the bromination of chromones in DMSO.

Results and Discussion

The condensation of 3,5-dibromo-2-hydroxyacetophenone with ethyl trifluoroacetate in the presence of LiH in THF afforded 6,8-dibromo-2-hydroxy-2-trifluoromethylchroman-4-one (**1**) in 85% yield, whose dehydration on boiling in AcOH with an addition of concentrated HCl results within 3 min in the formation of 6,8-dibromo-2-trifluoromethylchromone (**2**). The treatment of chromone **2** with a nitrating mixture at 75 °C during 10 min affords mononitro derivative **3** in 75% yield. Its structure

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* For Part 12, see Ref. 1.

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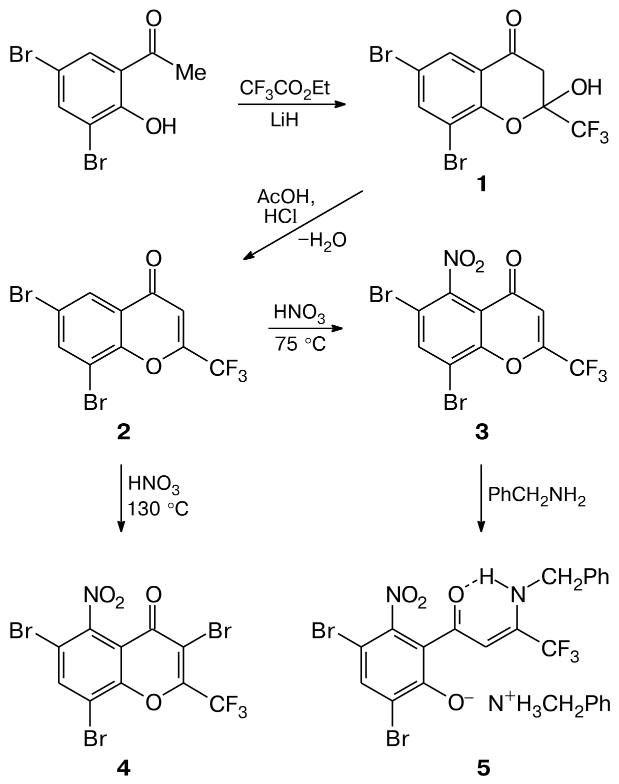
was unambiguously established from a comparison of the ^{13}C NMR spectra of compounds **2** and **3** recorded without ^1H decoupling.

Scheme 1



The signals from carbon atoms in the ^{13}C NMR spectrum of chromone **2** were assigned from the data for 2-trifluoromethylchromone[1] and 6,8-dibromo-5-hydroxyflavone[6] taking into account the $^nJ_{C,H}$ constants (n = 1—4). The introduction of the NO_2 group into precisely position 5 can easily be established considering the multiplicity of the weakest-field signal, which belongs to the carbonyl carbon atom. For chromone **2**, the signal from this atom manifests a doublet of doublets with the constants $^3J_{C,H}$ = 3.9 Hz and $^2J_{C,H}$ = 1.8 Hz, and for compound **3** it appears as a doublet with $^2J_{C,H}$ = 1.5 Hz. The signal from the C(8) atom is manifested as a doublet of doublets with $^2J_{C,H}$ = 4.4 Hz and $^4J_{C,H}$ = 1.8 Hz in **2** and as a doublet with $^2J_{C,H}$ = 3.9 Hz in **3**. Therefore, the nitration of chromone **2**, like 6-chloro-2-trifluoromethylchromone,[2] affords 5-nitrochromone **3** with high regioselectivity. The increments (Δδ) of the NO_2 group were 18.3 ppm (*ipso*-C), −8.3 and −4.5 ppm (*o*-C), −1.1 ppm (*p*-C), and −0.1 and 0.8 ppm (*m*-C). For *o*-C and *p*-C these values differ substantially from the standard Δδ values of the sterically non-hindered nitro group[7] and are close to their values in sterically overcrowded chromones,[1] which suggests the nonplanar conformation of the *peri*-NO_2 group in compound **3**.

When attempted to synthesize the dinitro derivative of chromone **2** under more drastic conditions of nitration, we observed an unusual formation of chromone **4**, *i.e.*, bromination at the pyrone ring along with the nitration of the benzene ring. The study of this reaction in more detail showed that the treatment of chromone **2** with the nitrating mixture at 130 °C during 1 h afforded a crystalline product, whose recrystallization from butyl alcohol produced a mixture of chromones **4** and **3** in a ratio of 88 : 12. The analytically pure sample of chromone **4** was obtained in 30% final yield after repeated recrystallization from isopropyl alcohol. According to the ^1H NMR spectroscopic data, the nitration of chromone **2** for 1 h at 100 and 160 °C afforded the same mixture of chromones **4** and **3** in ratios of 75 : 25 and 70 : 30, respectively. Thus, at 100—160 °C chromone **2** undergoes oxidative destruction to molecular bromine along with transformation into **3**. Molecular bromine brominates mononitro derivative **3** to form compound **4**. The ^1H NMR spectrum of chromone **4** contains a singlet from the H(7) proton at 8.32 ppm, which exhibits a downfield shift only by 0.02 ppm compared to the signal from H(7) in **3**, and does not contain a singlet from the ethylene H(3) proton, indicating that the latter was substituted during the reaction at elevated temperatures.

We have previously[2,8] shown that the reaction of benzylamine with 2-CF_3-chromones bearing a substituent in position 5 ceases at the stage of nucleophilic addition at the C(2) atom, which was explained by the destabilization of the open aminoenone form due to the repulsive interaction between this substituent and the vinyl hydrogen atom. We found that the treatment of an ethanolic solution of chromone **3** with benzylamine at ~20 °C, despite the presence of the NO_2 group in position 5, resulted in the pyrone ring opening and formation of salt **5**. This is related, most likely, to the elevated acidity of the phenol hydroxyl group, which is involved, in this case, in the formation of the salt with the second benzylamine molecule rather than in cyclization to form the chromanone structure.

Thus, 6,8-dibromo-2-trifluoromethylchromone (**2**) at 75 °C is nitrated at position 5 to form chromone **3**, and under more drastic conditions it partially decomposes to yield molecular bromine, which brominates chromone **3** at the pyrone ring to form compound **4**. The specific feature of chromone **3** is its ready opening under the action of benzylamine to form salt **5**.

Experimental

IR spectra were recorded on an IKS-29 instrument in Nujol. ^1H and ^{13}C spectra were recorded on a Bruker DRX-400 spectrometer with working frequencies of 400.13 and 100.62 MHz, respectively, for solutions in $CDCl_3$. The internal standard for ^1H and ^{13}C NMR spectra was Me_4Si.

6,8-Dibromo-2-hydroxy-2-(trifluoromethyl)chroman-4-one (1) was synthesized according to a described procedure[2] in 85% yield with m.p. 162—163 °C (toluene—hexane, 1 : 1). Found (%): C, 30.83; H, 1.03. $C_{10}H_5Br_2F_3O_3$. Calculated (%): C, 30.80; H, 1.29. IR, ν/cm^{-1}: 3380 (OH), 1695 (C=O), 1590 (arom.). ^1H NMR, δ: 3.09 (AB system, Δδ 0.02, 2 H, CH_2, J_{AB} = 16.8 Hz); 4.27 (s, 1 H, OH); 7.93 (d, 1 H, H(7) or H(5), J_m = 2.4 Hz); 7.99 (d, 1 H, H(5) or H(7), J_m = 2.4 Hz).

6,8-Dibromo-2-(trifluoromethyl)chromone (2) was synthesized by a described procedure[2] in 86% yield with m.p. 115—116 °C. Found (%): C, 32.28; H, 0.89. $C_{10}H_3Br_2F_3O_2$. Calculated (%): C, 32.29; H, 0.81. IR, ν/cm^{-1}: 3075 (=CH), 1680 (C=O), 1590, 1550 (arom.). ^1H NMR, δ: 6.78 (s, 1 H, =CH); 8.11 (d, 1 H, H(7) or H(5), J_m = 2.3 Hz); 8.28 (d, 1 H, H(5) or H(7), J_m = 2.3 Hz). ^{13}C NMR, δ: 110.78 (dq, C(3), ^1J = 174.1 Hz, $^3J_{C,F}$ = 2.7 Hz); 113.33 (dd, C(8), ^2J = 4.4 Hz, ^4J = 1.8 Hz); 118.36 (qd, CF_3, $^1J_{C,F}$ = 274.5 Hz, ^3J = 3.4 Hz); 119.95 (t, C(6), ^2J = 3.9 Hz); 126.03 (dd, C(4a), ^3J = 3.8 Hz, ^2J = 1.0 Hz); 127.96 (ddd, C(5), ^1J = 174.1 Hz, ^3J = 6.0 Hz, ^4J = 0.9 Hz); 140.78 (dd, C(7), ^1J = 173.7 Hz, ^3J = 6.8 Hz); 151.48 (t, C(8a), ^3J = 8.8 Hz); 152.79 (qd, C(2), $^2J_{C,F}$ = 39.8 Hz, ^2J = 4.5 Hz); 174.98 (dd, C(4), ^3J = 3.9 Hz, ^2J = 1.8 Hz).

6,8-Dibromo-5-nitro-2-(trifluoromethyl)chromone (3). A mixture of concentrated H_2SO_4 (0.5 mL) and concentrated HNO_3 (0.5 mL) was added to a solution of chromone **2** (0.5 g, 1.3 mmol) in concentrated H_2SO_4 (2.0 mL). The reaction mixture was heated at 75 °C for 10 min with stirring. After cooling, the mixture was diluted with ice-cold water, and the precipitate was filtered off, washed with water, dried, and recrystallized from BuOH. The yield was 0.42 g (75%), m.p. 163—164 °C. Found (%): C, 28.79; N, 3.28. $C_{10}H_2Br_2F_3NO_4$. Calculated (%): C, 28.81; N, 3.36. IR, ν/cm^{-1}: 1680 (C=O), 1615, 1580 (arom.), 1565 (NO_2). ^1H NMR, δ: 6.83 (s, 1 H, =CH); 8.30 (s, 1 H, H(7)). ^{13}C NMR, δ: 111.42 (dq, C(3), ^1J = 176.3 Hz, $^3J_{C,F}$ = 2.7 Hz); 112.25 (d, C(8), ^2J = 3.9 Hz); 115.48 (d, C(6), ^2J = 4.6 Hz); 117.72 (dd, C(4a), ^3J = 4.1, ^4J = 1.2 Hz); 118.01 (qd, CF_3, $^1J_{C,F}$ = 274.7 Hz, ^3J = 3.4 Hz); 141.61 (d, C(7), ^1J = 177.1 Hz); 146.21 (br.s, C(5)); 151.39 (d, C(8a), ^3J = 9.5 Hz); 152.67 (qd, C(2), $^2J_{C,F}$ = 40.6 Hz, ^2J = 4.5 Hz); 171.68 (d, C(4), ^2J = 1.5 Hz).

3,6,8-Tribromo-5-nitro-2-(trifluoromethyl)chromone (4) was synthesized similarly to compound **3** with the only exception that the reaction was carried out at 130 °C for 1 h. According to the ^1H NMR spectrum, the product contained 12% chromone **3**, which was removed by additional recrystallization from Pr^iOH. The yield was 0.10 g (30%), m.p. 215—216 °C. Found (%): C, 24.48; N, 2.77. $C_{10}HBr_3F_3NO_4$. Calculated (%): C, 24.22; N, 2.77. IR, ν/cm^{-1}: 1680 (C=O), 1620, 1595 (arom.), 1560 (NO_2). ^1H NMR, δ: 8.32 (s, 1 H, H(7)).

Salt of 3-benzylamino-1-(3,5-dibromo-2-hydroxy-6-nitrophenyl)-4,4,4-trifluorobut-2-en-1-one with benzylamine (5). Benzylamine (0.15 g, 1.4 mmol) was added to a suspension of chromone **3** (0.12 g, 0.29 mmol) in ethanol (1 mL). The resulting mixture was stirred until the initial chromone completely dissolved and left for 5 min at ~20 °C, after which the mixture was diluted with 10 mL of water. The yellow crystals that formed were filtered off, washed with water, dried, and recrystallized from a hexane—toluene (1 : 1) mixture. Salt **5** was obtained in 72% yield (0.13 g) and contained, according to the ^1H NMR data, an ~12% admixture of compounds with an unknown structure. Compound 5, m.p. 135—140 °C (decomp.). Found (%): C, 46.07; H, 3.50; N, 6.63. $C_{24}H_{20}Br_2F_3N_3O_4$. Calculated (%): C, 45.67; H, 3.19; N, 6.66. IR, ν/cm^{-1}: 1655 (C=O), 1610, 1540. ^1H NMR, δ: 3.55 (br.s, 3 H, N^+H_3); 3.85 (s, 2 H, $CH_2—N^+H_3$); 4.65 (s, 2 H, CH_2—NH); 5.82 (s, 1 H, CH=); 7.23—7.43 (m, 10 H, 2 Ph); 7.86 (s, 1 H, arom.); 10.8 (br.s, 1 H, NH).

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