SOME PROPERTIES OF POLYFLUORINATED CHROMONES

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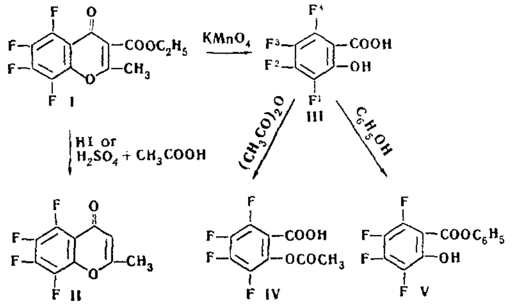
It has been shown that polyfluorinated chromones, unlike their nonfluorinated analogs, give normal derivatives at the carbonyl group. It has been found that the oxidation of 3-ethoxycarbonyl-2-methyl-5, 6, 7, 8-tetrafluorochromone gives a good yield of tetrafluorosalicylic acid.

We have recently shown that the condensation of pentafluorobenzoyl chloride with magnesioethoxyacetoacetic ester gives a good yield of 3-ethoxycarbonyl-2-methyl-5,6,7,8-tetrafluorochromone (I) [1]. This compound is of definite interest, since derivatives of 3-chromonecarboxylic acid, which are cyclic β-keto esters, have been studied to a considerably smaller extent than derivatives of 2-chromonecarboxylic acid. In addition, it was of interest to find how the polyfluoroaromatic ring affects the properties of the γ-pyrone ring condensed with it. As is well known, in the chromones, the γ-pyrone ring mostly has a cryptoionic structure, which leads to the suppression of the electrophilic properties of the carbonyl group. Thus, for example, chromones do not react with phenylhydrazine [2] and possess reduced activity with respect to hydroxylamine, hydrazine, etc., the attack being directed predominantly to the C_2 atom and leading to the opening of the ring. At the same time, a characteristic feature of the chromones is the formation of an oxonium salt with hydrogen chloride [3] and of a perbromide [4]. As compared with the nonfluorinated chromones, the carbonyl group in I possesses increased electrophilic properties, obviously because of the presence of the polyfluoroaromatic ring and the ethoxycarbonyl group. Compound **I** reacts with hydroxylamine hydrochloride in acetic acid, smoothly giving an oxime [1], and with phenylhydrazine it forms a phenylhydrazone in almost quantitative yield. At the same time, **I** does not react either with bromine or with hydrogen chloride, [1], apparently because of the strong effects of the conjugation of the unshared pair of electrons of the oxygen atom with the polyfluorinated ring. The γ-pyrone ring in I proved to be extremely resistant to opening under the action of the reagents generally used for this purpose. Thus, the reaction of I with benzylamine formed N-benzyl-2-methyl-5, 6, 7, 8-tetrafluoro-3-chromonecarboxamide [5 ,6]; in an attempt at ring opening by heating the substance with aqueous alkali, a mixture of products was formed, fluorine being split off [7]. On being heated with HI, I undergoes ketonic decomposition with the formation of 2-methyl-5 ,6 ,7,8-tetrafluorochromone (II) [8]; compound II is also formed in almost quantitative yield when I is heated with a mixture of acetic and sulfuric acids. It is an interesting fact that in **II** the carbonyl group retains considerable electrophilicity. Thus, it is possible to obtain a phenylhydrazone from II by heating to 180° C. The γ-pyrone ring in II is not opened by the action of HI or by heating with Pd/C in Tetralin [9], and its reaction with benzylamine forms products of nucleophilic replacement of the fluorine. We were able to cleave the γ-pyrone ring only by oxidizing I with a solution of $KMnO_4$ in acetone at room temperature. The main product of this process was the previously unknown tetrafluorosalicylic acid (III). The structure of III was confirmed by the results of analyses, spectra, and chemical reactions. In the F^{19} NMR spectrum [internal standard— p-bis(trifluoromethyl)-benzene], four signals of approximately equal intensity are observed. The nature of the splitting and a comparison with the calculated values of the chemical shifts made it possible to assign the signals in the following way: 73.3 ppm, F^4; 87.9 ppm, F^2; 102.5 ppm, F^1; and 110 ppm, F^3. When III was acetylated with acetic acid, o-acetyltetrafluorosalicylic acid (IV) was obtained, and its reaction with phenol formed phenyl tetrafluorosalicylate (V).



EXPERIMENTAL

2-Methyl-5, 6, 7, 8-tetrafluorochromone (II). Five grams (16.5 mM) of 3-ethoxycarbonyl-2-methyl-5, 6, 7, 8-tetrafluorochromone (I) was heated with a mixture of 13 ml of CH_3COOH, 10 ml of water, and 1.6 ml of conc H_2SO_4 at 130° C for 4 hr, after which the evolution of CO_2 had ceased. The reaction mixture was cooled and made alkaline. The crystals that deposited were filtered off with suction and washed with water, giving 3.5 g of II (92%), mp 102–104° C (from petroleum ether). Found, %: C 51.54, 51.52; H 1.51, 1.40; F 32.51, 32.81. Calculated for $C_{10}H_4F_4O_2$, %: C 51.73; H 1.73; F 32.73. IR spectrum (in KBr), cm^{-1}: 1008 s (C–F), 1115 s (C–O–C), 1498 s and 1526 s (polyfluorinated aromatic ring), 1613 s (C=C, conjugated with C=O), 1668 s (C=O in chromones). UV spectrum (in ethanol): λ_{max} 224 and 296 nm (log ε 4.316 and 3.82). The F^{19} NMR spectrum [internal standard—p-bis(trifluoromethyl)benzene] had four signals of approximately equal intensity: 80.8 ppm, F^4; 88.3 ppm, F^2; 96.9 ppm, F^1; and 100.6 ppm, F^3. Compound II was also obtained in 76% yield by heating I with HI at 140–160° C for 4 hr. To obtain the phenylhydrazone, 2.5 g (10.7 mm) of II and 1.2 g (10.7 mM) of phenylhydrazine were mixed and heated at 170–180° C for 10 min. The precipitate that formed was filtered off with suction and was washed with water and a minimum amount of ether. This gave 1.84 g of a mixture of stereoisomeric phenylhydrazones (52.6%). Recrystallization from hexane gave 0.69 g of an isomer with mp 152–154° C. Found, %: C 59.19, 59.20; H 3.08, 2.98; F 23.35, 23.36; N 9.02, 8.91. Calculated for $C_{16}H_{10}F_4N_2O$, %: C 59.62; H 3.11; F 23.60; N 8.69. UV spectrum (in ethanol): λ_{max} 264 and 290 nm (log ε 4.266 and 3.894). The part of the precipitate insoluble in hexane was recrystallized from benzene, giving 1 g of an isomer with mp 215–217° C. Found, %: C 59.40, 59.79; H 2.95, 2.98; F 23.26, 23.34; N 9.08, 9.09. UV spectrum (in ethanol) : λ_{max} 246 nm (log ε 4.114).

3-Ethoxycarbonyl-2-methyl-5,6,7,8-tetrafluorochromone phenylhydrazone. A mixture of 0.5 g (1.65 mM) of I and 0.18 g (1.65 mM) of phenylhydrazine was heated at 180° C for 5 min and cooled, and 1 ml of water and 1 ml of ether were added. The mixture was triturated until a precipitate formed. The precipitate was filtered off with suction and washed with water to give 0.62 g (96%) of the phenylhydrazone, mp 167–169° C (from CCl_4). Found, %: C 58.31, 58.16; H 3.32, 3.43; F 19.20, 18.83; N 7.43, 7.52; OC_2H_5 12.07, 12.25. Calculated for $C_{19}H_{14}F_4N_2O_3$, %: C 57.91; H 3.58; F 19.25; N 7.11; OC_2H_5 11.40.

Tetrafluorosalicylic acid (III). Solutions of 5 g (16.5 mM) of I in 20 ml of acetone and of 5.2 (33 mM) of $KMnO_4$ in 180 ml of acetone were mixed, and the mixture was stirred at room temperature for 16 hr. The acetone was distilled off, the residue was boiled with water, and the precipitate of manganese dioxide was filtered off and washed several times with boiling water. The filtrate was evaporated, acidified, and extracted continuously with ether for 15 hr. This gave 2.2 g (64%) of III, mp 168.5–170° C (from water). Found, %: C 40.17, 40.19; H 1.16, 1.00; F 36.31, 36.21; mol. wt. 207, 212. Calculated for $C_7H_2F_4O_3$, %: C 40.03; H 0.95; F 36.19; mol. wt. 210. IR spectrum (in CCl_4), cm^{-1}; 1010 s (C–F), 1500 s (polyfluorinated aromatic ring), 1690 s (C=O, bound), 1710 s (C=O, free), 3085 broad (OH, bound), 3500 m (OH, free). UV spectrum (in ethanol): λ_{max} 228 and 300 nm (log ε 3.903 and 3.48).

o-Acetyltetrafluorosalicylic acid (IV). A mixture of 0.3 g (1.4 mM) of I, 0.7 ml of acetic anhydride, and 3 drops of conc H_2SO_4 was heated for a few minutes. After cooling, 3 ml of water were added and the precipitate formed was filtered off, washed with water, and dried. This gave 0.19 g of IV (53%), mp 104–106° C (from a mixture of hexane and benzene). Found, %: C 43.40, 43.35; H 1.68, 1.77; F 30.59, 30.29. Calculated for $C_9H_4F_4O_4$, %: C 43.07; H 1.58; F 30.03. IR spectrum (in KBr), cm^{-1}: 1000 s (C–F), 1260 s (C–O in esters), 1500 s and 1535 s (polyfluorinated aromatic ring). UV spectrum (in ethanol): λ_{max} 268 nm (log ε 2.954).

Phenyl tetrafluorosalicylate (V). A mixture of 0.7 g (3.3 mM) of III and 0.32 g (3.3 mM) of phenol was heated to 165° C, 0.2 g of $POCl_3$ was added, and the mixture was kept at this temperature for 1 hr. Then it was cooled to 60° C and poured into water; the precipitate that separated was filtered off with suction and washed with water. This gave 0.73 g (77%) of V, mp 81–82.5° C (from ethanol). Found, %: C 54.58, 54.82; H 2.12, 2.05; F 26.33, 26.71. Calculated for $C_{13}H_6F_4O_3$, %: C 54.65; H 2.09; F 26.52. IR spectrum (in KBr), cm^{-1}: 1010 s (C–O in esters), 1500 s and 1540 s (polyfluorinated aromatic ring), and 1700 s (C=O in esters). UV spectrum (in ethanol): λ_{max} 274, 280, and 312 nm (log ε 3.474, 3.447, and 3.477).

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