# POLYFLUORINATED HETEROCYCLIC COMPOUNDS

## III. 3-Substituted Tetrafluorocoumarins*

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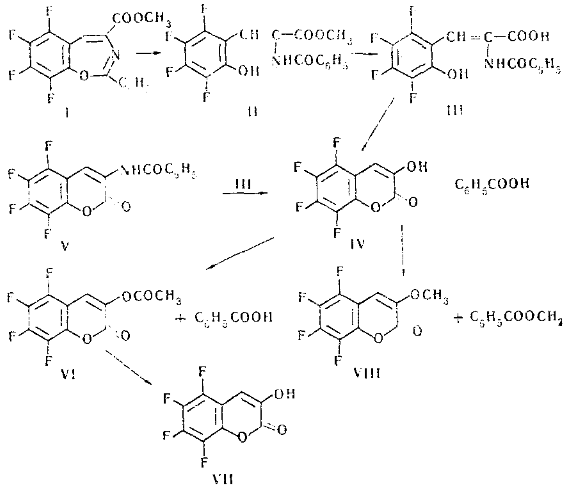
The treatment of 2-phenyl-4-carbomethoxy-6,7,8,9-tetrafluorobenz[f]oxazepin-1,3 (I), 3-benzamido-5,6,7,8-tetrafluorocoumarin (V), and α-benzamido-β-(2-hydroxy-3,4,5,6-tetrafluorophenyl)-acrylic acid (III) with a mixture of glacial acetic acid and a mineral acid gave (IV), the π-complex of 3-hydroxy-5,6,7,8-tetrafluorocoumarin (VII) and benzoic acid. Treatment of (IV) with acetic anhydride gave 3-acetoxy-5,6,7,8-tetrafluorocoumarin (VI) and benzoic acid. Treatment with diazomethane gave 3-methoxy-5,6,7,8-tetrafluorocoumarin (VIII) and methyl benzoate. IV was also obtained from an equimolar mixture of its components. A mechanism for the formation of IV from I is proposed.

In the preceding paper [1] we have shown that treatment of methyl α-benzamido-β-pentafluorophenyl) acrylate with potassium in dimethylformamide gave 2-phenyl-4-carbomethoxy-6, 7, 8, 9-tetrafluorobenz [f] oxazepin-1, 3 (I) in which the heterocyclic ring is readily opened by both acid and alkali.

In the present work we have studied the effects of acids to give not only ring opening of I but a whole series of other reactions. We have investigated these additional products. For example boiling I with a mixture of glacial acetic acid and sulfuric acid or hydrogen chloride or bromide gave a product of composition $C_{16}H_8F_4O_5$ (IV). The nitrogen was shown to be removed as ammonia during the reaction. The IR spectrum of the product had intense absorptions at 1704 $cm^{-1}$, (acid C=O) and 1752 $cm^{-1}$ (ester C=O). The intense sharp band at 3486 $cm^{-1}$ may be assigned as an O–H stretch.

The enolic nature of the hydroxyl group was shown by the qualitative reaction with iron (III) chloride solution. These data indicate that (IV) is an equimolar mixture of 3-hydroxy-5, 6, 7, 8-tetrafluorocoumarin (VII) and benzoic acid. However it was not possible to separate the components by normal methods. The product could be recrystallized from organic solvents or sublimed. The components of IV were separable only by chemical methods. Thus acetylation of IV with acetic anhydride in the presence of perchloric acid gave 3-acetoxy-5, 6, 7, 8-tetrafluorocoumarin (VI) which is easily separated from benzoic acid. The IR spectrum of VI contains an intense absorption at 1780 $cm^{-1}$ (ester C=O), but the 3486 $cm^{-1}$ O–H stretch of compound IV is absent from VI. Acid hydrolysis of VI converts it to 3-hydroxy-5, 6, 7, 8-tetrafluorocoumarin (VII). The structure of the latter is confirmed by the intense IR absorption bands at 3486 (O–H stretch) and 1750 $cm^{-1}$ (ester C=O).

Treatment of IV with diazomethane gave an easily separated mixture of 3-methoxy-5, 6, 7, 8-tetrafluorocoumarin (VIII) and methyl benzoate. Methyl benzoate was identified chromatographically, while the absence of an O–H stretch and the presence of intense bands at 1780 and 1250 $cm^{-1}$ (ester C=O and C–O–C) in the IR spectrum of VIII confirmed its structure.



The structure of IV was also confirmed by its formation from an equimolar mixture of the coumarin VII and benzoic acid. While the IR spectrum of IV contains only the bands of VII and benzoic acid, its UV spectrum is not the sum of the UV spectra of its components (see figure). This observation and the difficulty of separating IV into its components indicates that IV is a π-complex of the coumarin VII and benzoic acid. However further study is needed for a definitive decision on the nature of IV. According to Erlenmeyer and Standlin [2], 3-hydroxycoumarin and benzoic acid formed from the hydrolysis of 3-benzamidocoumarin are easily separable.

The molecular complex IV is also formed on heating the coumarin V [1] or α-benzamido-β-(2-hydroxy-3, 4, 5, 6-tetrafluorophenyl)acrylic acid (III) [1] with a mixture of glacial acetic acid and concentrated hydrochloric acid. It may therefore be suggested that the acid III and the coumarin V are intermediates in the conversion of I to IV. If it is further remembered that I is converted to the ester of α-benzamido-β-(2-hydroxy-3, 4, 5, 6-tetrafluorophenyl)acrylic acid (II) [1] under mildly acidic conditions, then the conversion of I and IV can be pictured in terms of the sequence of reactions shown in the diagram.

The new polyfluorinated derivatives of coumarin may have useful physiological properties, particularly since it is known that a number of coumarin derivatives have antibacterial activity [3, 4].

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*For part II, see [1].

## EXPERIMENTAL

**UV Spectra** were recorded on an SFD-2 spectrometer in ethanol at a concentration of $1 \cdot 10^{-4}$ M and a thickness of 0.5 cm. **IR spectra** were recorded on a UR-10 spectrometer.

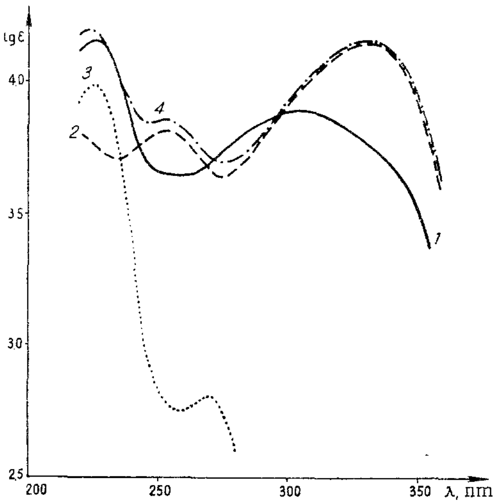
**The molecular complex of 3-hydroxy-5,6,7,8-tetrafluorocoumarin and benzoic acid (IV).** a) 1.5 g (4.4 mmoles) of I, 7 ml of glacial acetic acid, and 8 ml of conc. HCl were boiled for 7 hr. Water (15 ml) was added to the cooled mixture and the precipitate (0.86 g) was filtered off. Another 0.21 g was obtained by evaporation of the filtrate: total yield 70%, after sublimitation in vacuo in a water-cooled vessel, the mp 132.5°–133.5° C (sealed capillary). Found, %: C 53.84, 53.56; H 1.98, 1.90; F 22.12, 22.09. Calculated for $C_9H_2F_4O_3 \cdot C_7H_6O_2$, %: C 54.00; H 2.25; F 21.40. $\lambda_{max}$ I 226 nm (lg ε 4.16); $\lambda_{max}$ II 306 nm (lg ε 3.89). Compound IV was similarly obtained from III and V.

b) Equimolar quantities of VII and benzoic acid were dissolved in methanol, the methanol evaporated, and the residue sublimed to give IV, mp 130.5°–131.5° C (sealed capillary).

**3-Acetoxy-5,6,7,8-tetrafluorocoumarin (VI).** 0.14 g (0.39 mmole) of sublimed IV, 0.6 ml of glacial acetic acid, 0.6 ml of acetic anhydride, and 3 drops of conc. $HClO_4$ were kept at room temperature for 90 min. The mixture was poured into water, the solid filtered off, washed with water, stirred with soda solution, filtered again, washed with water and dried to give 0.08 g VI, mp 101.5°–102° C. Found, %: C 47.86, 48.13; H 1.52, 1.55; F 27.43, 27.60. Calculated for $C_{11}H_4F_4O_4$, %: C 47.85; H 1.45; F 27.59. $\lambda_{max}$ 278 nm (lg ε 4.09).

**3-Hydroxy-5,6,7,8-tetrafluorocoumarin (VII).** 0.27 g (0.1 mmole) VI, 2 ml conc. HCl, and 2 ml. glacial acetic acid were boiled for 4 hr. Water (6 ml) was added to the cooled mixture and the precipitate was filtered off—0.17 g (75%) of VII, mp after vacuum sublimation, 152.5°–153° C (sealed capillary). Found, %: C 46.66, 46.83; H 0.63, 0.88; F 32.06, 32.32. Calculated for $C_9H_2F_4O_3$, %: C 46.20; H 0.86; F 32.45. $\lambda_{max}$ I 254 nm (lg ε 3.81); $\lambda_{max}$ II 330 nm (lg ε 4.15).

**3-Methoxy-5,6,7,8-tetrafluorocoumarin (VIII).** 0.15 g (0.42 mmole) IV was treated with diazomethane in the normal way. A product of 0.12 g with a strong smell of methyl benzoate was obtained. Recrystallization from methanol gave VIII, mp 136.5°–138° C. Found, %: C 48.84, 48.77; H 1.46, 1.92; F 30.11, 30.15; M 249, 251. Calculated for $C_{10}H_4F_4O_3$, %: C 48.40; H 1.61; F 30.65; M 248. $\lambda_{max}$ 290 nm (lg ε 4.08).



UV absorption spectra: 1) the molecular complex (IV) of 3-hydroxy-5,6,7,8-tetrafluorocoumarin (VII) and benzoic acid; 2) 3-hydroxy-5,6,7,8-tetrafluorocoumarin (VII); 3) benzoic acid. 4) sum of the curves for VII and benzoic acid.

## REFERENCES

1. T. D. Petrova, V. P. Mamaev, G. G. Yakobson, and N. N. Vorozhtsov Jr., ZhGS, 771, 1968.

2. E. Erlenmeyer and W. Stadlin, Ann., 337, 290, 1904.

3. G. Rodighiero and C. Antonello, Boll. chim. farm., 97, 592, 1958, C.A., 43, 9201a, 1959.

4. R. Selleri, O. Caldini, and G. F. Ferretti, Boll. chim. farm., 104, 248, 1965.

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