

ORGANIC FLUORINE COMPOUNDS.

4-AMINO-FLUOROCROTONIC ACID AND 5-AMINO-2-FLUORO-2-PENTENOIC ACID

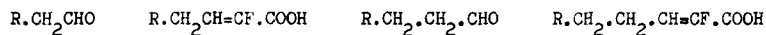
Ernst D. Bergmann and Amnon Cohen

Department of Organic Chemistry, Hebrew University

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Tolman and Vereš^V have recently published in this Journal (1) a synthesis of 4-amino-2-fluorocrotonic acid from 4-bromo-2-fluorocrotonic acid via the 4-phthalimido compound. We have prepared the same acid by a different route, using the method of Bergmann and Shahak (2). Phthalimid-oacetaldehyde (I), m.p. 113.5-114° (18.8 g), which was prepared in 86% yield by an improvement of the method of Siedel and Nahn (3), was dissolved in xylene (70 ml.) and added to the sodioenolate of diethyl oxalofluoroacetate (from ethyl fluoroacetate (10.6 g.) in xylene (2) and the mixture refluxed for 30 min. and poured into water. The xylene solution was washed with water and distilled in vacuo. Ethyl 2-fluoro-4-phthalimidocrotonate (II) (13 g. 46%) boiled at 191°/1 mm and melted at 54° (after recrystallization from a mixture of benzene and hexane) (Calcd. for $C_{14}H_{12}FNO_4$: C, 60.7; H, 4.3; F, 6.9; N, 5.0. Found : C, 60.9; H, 4.4; F, 6.7; N, 4.7%). Hydrolysis with boiling dilute hydrochloric acid gave 2-fluoro-4-phthalimidocrotonic acid, from water m.p. 162-163° (Calcd. for $C_{12}H_8FNO_4$: C, 57.8; H, 3.6; F, 7.6; N, 5.7. Found : C, 58.1; H, 3.5; F, 7.9; N, 5.5%), whilst hydrolysis with boiling concentrated hydrochloric acid and a little glacial acetic acid yielded 4-amino-2-fluorocrotonic acid hydrochloride in 30% yield, from glacial acetic acid m.p. 190° (dec.) lit. (1) : 172-178° (dec.). (Calcd. for $C_4H_9ClFNO_2$: C, 30.9; H, 4.5; F, 12.2; N, 9.0. Found : C, 31.2;

H, 4.8; N, 8.7%).

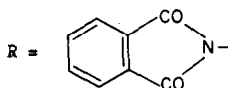


I

II

III

IV



Analogously, condensation of β -phthalimidopropionaldehyde (III) (4) with diethyl oxalofluoroacetate gave ethyl 2-fluoro-5-phthalimido-2-pentenoate (IV) in 45% yield, from ethyl acetate-petroleum ether m.p. 80° (Calcd. for C₁₅H₁₄FNO : F, 6.5. Found; F, 6.8%) and its hydrolysis with boiling concentrated hydrochloric acid 5-amino-2-fluoro-2-pentenoic acid hydrochloride (yield, 50%), from glacial acetic acid m.p. 185° (Calcd. for C₅H₇ClFNO₂ : 35.4; H, 5.3; F, 11.2. Found : C, 35.1; H, 5.1; F, 11.2%).

These unsaturated fluorinated amino-acids may be of some biological interest, as 4-aminocrotonic acid is a metabolite of histidine (5).

References.

- 1) V. Tolman and K. Vereš, Tetrahedron Letters, 1967 (1964).
- 2) E.D. Bergmann and I. Shahak, J. Chem.Soc., 5261 (1960); 4033 (1961).
- 3) W. Siedel and H. Nahm, German Patent 928,711; Chem.Abstr., 52, 5471 (1958).
- 4) R.O. Atkinson and F. Poppelsdorf, J.Chem.Soc., 244 (1952).
- 5) T.A. Goryukhena, Biokhimiya, 21, 90 (1956); Chem.Abstr., 50, 10239 (1956).