ADDITION OF AMINES TO ETHYL α-FLUOROACRYLATE AND PHENYL α-FLUOROVINYL KETONE

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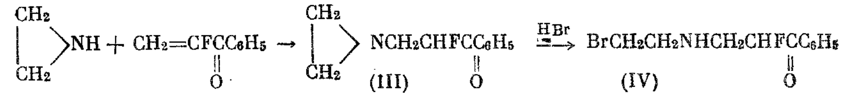
The ester of α-chloro- and α-bromoacrylic acids react with amines to give mainly the addition products of the amines to the double bond [1]; the reaction of ethyl α-fluoroacrylate (I) with NH_3 and ethylamine leads only to the corresponding α-fluoroacrylic acid amides [2]. It proved that (I) reacts with diethylamine, piperidine, ethylenimine, and cyclohexylamine to give the ethyl esters of N-substituted α-fluoro-β-alanines $R^1R^2NH + CH_2 = CF \cdot COOC_2H_5 \rightarrow R^1R^2NCH_2CHFCOOC_2H_5$. The formation of α-fluoroacrylic acid amides was not observed.

(I) (II a-d)

$R^1R^2 = (C_2H_5)_2$ (a); $(CH_2)_5$ (b); $(CH_2)_2$ (c); $R^1 = H$, $R^2 =$ cyclo-C_6H_{11} (d)

Ethylenimine also adds easily to phenyl α-fluorovinyl ketone. The addition product (III) reacts with HBr with an opening of the ring.


(III) (IV)

In the NMR spectra of the addition products of the amines to the α-fluorovinyl group the ^{19}F signal represents a doublet of triplets; the spin–spin coupling constant (SSCC) with the geminal proton is ~50 Hz, and with the vicinal protons it is ~30 Hz. The diastereotopicity of the vicinal protons is not manifested in the spectra.

EXPERIMENTAL

The GLC determination conditions were: Tswett 4-67 chromatograph, detector based on the heat conductivity, carrier gas = helium, adsorbent = Chromosorb W, and liquid phases = Rheoplex-400 (30%) and SE-30 (15%).

The IR spectra were obtained on an IRS-14 instrument; the ^{19}F NMR spectra were recorded on a Hitachi H-60 instrument at an operating frequency of 56.4 MHz for ^{19}F, and CF_3COOH as the external standard.

Ethyl Ester of α-Fluoro-β-diethylaminopropionic Acid (IIa). With cooling in water, to a solution of 5.9 g (0.05 mole) of (I) [3] in 10 ml of abs. ethanol was added 3.65 g (0.05 mole) of diethylamine in 10 ml of abs. ethanol, and the mixture was refluxed for 3 h. After distilling off the alcohol we obtained 5.7 g (60%) of (IIa), bp 86-88° (5 mm); n_D^{20} 1.4220. Found: C 56.64; H 9.11; N 7.74%. $C_9H_{18}FNO_2$. Calculated: C 56.76; H 9.45; N 7.29%. Infrared spectrum (ν, cm^{-1}): 1729, 1753 (C=O). ^{19}F NMR spectrum: δ 115.4 ppm; $J_{F-H(gem)} = 48.6$, $J_{F-H(vic)} = 25.9$ Hz.

Ethyl Ester of α-Fluoro-β-pentamethyleneiminopropionic Acid (IIb). Obtained in a similar manner from 5.2 g (0.04 mole) of (I) and 3.7 g (0.04 mole) of piperidine. Yield 4.7 g (53.1%); bp 96° (13 mm); n_D^{20} 1.4470. Found: C 59.86; H 8.39; N 7.25%. $C_{10}H_{18}FNO_2$. Calculated: C 59.11; H 8.86; N 6.89%. Infrared spectrum (ν, cm^{-1}): 1729, 1753 (C=O). ^{19}F NMR spectrum: δ 114.0 ppm; $J_{F-H(gem)} = 48.6$, $J_{F-H(vic)} = 25.9$ Hz.

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Ethyl Ester of α-Fluoro-β-ethyleniminopropionic Acid (IIc). A solution of 11.8 g (0.1 mole) of (I) and 6 ml of ethylenimine in 30 ml of abs. ether was refluxed for 4 h. Distillation gave 2.6 g (30%) of (IIc), bp 81-82° (10 mm); n_D^{20} 1.4317; d_4^{20} 1.019. Found: F 10.00; N 8.73%. $C_7H_{12}FNO_2$. Calculated: F 10.78; N 8.69%. Infrared spectrum (ν, cm^{-1}): 1755 (C=O). ^{19}F NMR spectrum: δ 118.0 ppm; $J_{F-H(gem)} = 48.6$, $J_{F-H(vic)} = 25.9$ Hz. Oxalate, mp 162-163° (decomp.). Found: N 6.02%. $C_9H_{14}FNO_6$. Calculated: N 5.57%.

Ethyl Ester of α-Fluoro-β-cyclohexylaminopropionic Acid (IId). From 5.9 g (0.05 mole) of (I) and 5 g (0.05 mole) of cyclohexylamine in 20 ml of abs. ethanol (3 h under reflux) we obtained 4.5 g (41%) of (IId), bp 113° (7 mm); n_D^{20} 1.4570. Found: C 60.20; H 9.09; N 7.05%. $C_{11}H_{20}FNO_2$. Calculated: C 60.83; H 9.21; N 6.45%; IR spectrum (ν, cm^{-1}): 1729, 1753 (C=O). ^{19}F NMR spectrum: δ 120.0 ppm; $J_{F-H(gem)} = 48.6$, $J_{F-H(vic)} = 25.9$ Hz.

α-Fluoro-β-ethyleniminopropiophenone (III). A solution of 8.5 g (0.05 mole) of phenyl α-fluorovinyl ketone [4] and 3.3 g of ethylenimine in 30 ml of abs. ether was refluxed for 1 h and then left to stand overnight, after which the ether was distilled off and the residue was vacuum distilled. We obtained 10.4 g (95.4%) of (III), bp 128-130° (3.5 mm); n_D^{20} 1.4860. Found: C 68.76; H 6.23; N 6.78%. $C_{11}H_{12}FNO$. Calculated: C 68.73; H 6.25; N 7.25%. Infrared spectrum (ν, cm^{-1}): 1895 (C=O). ^{19}F NMR spectrum: δ 113.1 ppm; $J_{F-H(gem)} = 50.2$, $J_{F-H(vic)} = 27.5$ Hz. Oxalate, mp 120°. Found: N 5.23%. $C_{13}H_{14}FNO_5$. Calculated: N 4.94%.

The reaction of (III) with HBr in ether gives compound (IV), mp 127° (from ethyl acetate). Found: Br 22.24; F 5.93; N 3.89%. $C_{11}H_{13}BrFNO$. Calculated: Br 22.50; F 5.35; N 3.94%.

CONCLUSIONS

The reaction of diethylamine, piperidine, ethylenimine, and cyclohexylamine with ethyl α-fluoroacrylate, and also of ethylenimine with phenyl α-fluorovinyl ketone, leads to the addition of the amines to the α-fluorovinyl group with the formation of α-fluoro-β-aminopropionic acid derivatives.

LITERATURE CITED

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