a method similar to that used to prepare benzyl S-aziridine-2-carboxylate [4], was added to a solution of 0.222 g (10 mmole) of acrylate IX, and the mixture was heated at 60°C for 8 h. The solution was then evaporated, and the residue was separated by preparative liquid chromatography.

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# ADDUCTS OF METHYL β,β-BIS(TRIFLUOROMETHYL)ACRYLATE WITH NUCLEOPHILES AND ALLYLIC REARRANGEMENT DURING THEIR DEHYDROFLUORINATION


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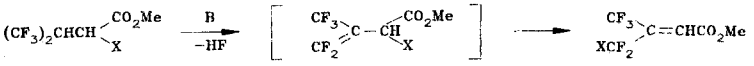
UDC 547.717'722.3



A number of adducts of methyl β,β-bis(trifluoromethyl)acrylate with various nucleophiles were synthesized. The boundaries of the allylic rearrangement of 2-substituted 3-trifluoromethyl-4,4-difluoro-3-butenoates, obtained by dehydrofluorination of the cited adducts, were investigated.

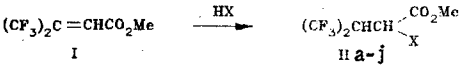

We have previously observed allylic rearrangement with migration of an aziridinyl substitutent [1]:



X = aziridino and 2-methylaziridino

In the present research we investigated the boundaries of this rearrangement as a function of the types of substituents in the 2 position of the aziridinyl residue, as well as other heteroatomic α-substituents X (X = $R^1R^2N$, MeO). For this, we synthesized adducts of β,β-bis(trifluoromethyl)acrylate I with a number of nucleophiles (Tables 1 and 2).

In addition to IIa, allylic rearrangement product III (12%) was isolated from the reaction mixture by high-performance liquid chromatography (HPLC) in the preparation of adducts IIa by heating an equimolar mixture of the starting reagents (50°C, MeCN), i.e., under the reaction conditions the dehydrofluorination of adduct IIa proceeds under the influence of nucleophile HX. Adducts IIb-i were obtained in 55-85% yields by the addition of the corresponding amines with cooling (−30°C, $Et_2O$). We were able to realize the addition of methanol only by heating (150°C) ester I in a sealed ampul with excess reagent in the presence of KF applied to $Al_2O_3$: adduct IId was obtained in 55% yield.



II a X = 2-methoxycarboxylaziridino; b X = 2,2-dimethylaziridino; X = $Me_2N$; dX = MeO; e X = azetidino; e X = pyrrolidino; g X = piperidino; h X = HOHN; i X = $H_2N$; j X = $Me_2NHN$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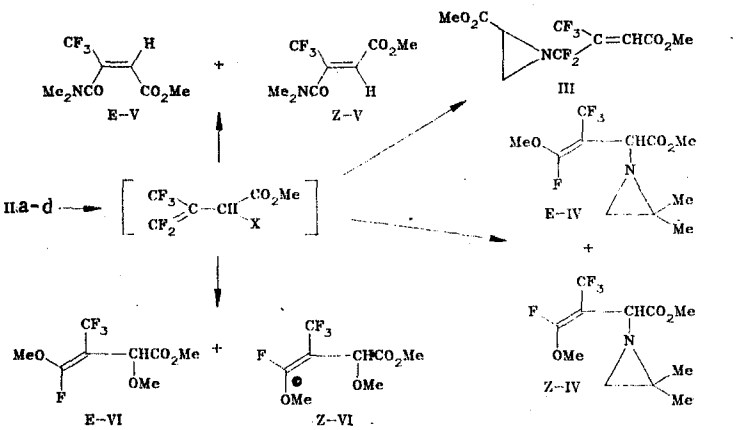
Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 10, pp. 1359-1362, October, 1985. Original article submitted January 23, 1985.

TABLE 1. Characteristics of the Synthesized Compounds

| Compound | bp (mm) or mp, °C[a] | $\nu_{C=O}$, $cm^{-1}$ | Calc., % | | | Empirical formula | Found, % | | | Yield, % |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | C | H | N | | C | H | N | |
| IIa | 50 (0,5) | 1745, 1762 | 37,1 | 3,4 | 4,4 | $C_{10}H_{11}F_6NO_4$ | 37,2 | 3,5 | 4,5 | 57 |
| IIb | 55 (5) | 1750 | 40,9 | 4,4 | 4,8 | $C_{10}H_{13}F_6NO_2$ | 40,5 | 4,5 | 4,9 | 79 |
| IIc | 45 (5) | 1745 | 35,9 | 4,1 | 5,2 | $C_8H_{11}F_6NO_2$ | 35,7 | 4,2 | 5,3 | 65 |
| IId | 78 (40) | 1755 | 33,1 | 3,1 | — | $C_7H_8F_6O_3$ | 33,3 | 3,2 | — | 55 |
| IIe | 50 (5) | 1761 | 38,7 | 3,9 | 5,0 | $C_9H_{11}F_6NO_2$ | 38,9 | 4,0 | 4,9 | 82 |
| IIf | 55 | 1765 | 40,9 | 4,4 | 4,8 | $C_{10}H_{13}F_6NO_2$ | 40,7 | 4,3 | 4,9 | 71 |
| IIf · HCl | 94 | 1766 | 36,4 | 4,2 | 4,2 | $C_{10}H_{14}ClF_6NO_2$ | 36,6 | 4,1 | 4,4 | 95 |
| IIg | 62 | 1768 | 43,0 | 4,9 | 4,6 | $C_{11}H_{15}F_6NO_2$ | 43,1 | 4,8 | 4,5 | 68 |
| IIg · HCl | 95 | 1760 | 38,4 | 4,7 | 4,1 | $C_{11}H_{16}ClF_6NO_2$ | 38,6 | 4,6 | 4,2 | 95 |
| IIh | 34 | 1750 | 28,2 | 2,7 | 5,5 | $C_6H_7F_6NO_2$ | 28,1 | 2,5 | 5,4 | 85 |
| IIi | 59 (12) | 1758 | 30,1 | 2,9 | 5,9 | $C_9H_7F_6NO_2$ | 30,2 | 2,8 | 5,8 | 76 |
| IIj | 70 (12) | 1740 | 34,0 | 4,3 | 9,9 | $C_8H_{12}F_6N_2O_2$ | 34,3 | 4,4 | 9,8 | 79 |
| III | 60 (0,5) | 1750, 1760 | 39,6 | 3,3 | 4,6 | $C_{10}H_{10}F_5NO_4$ | 39,9 | 3,2 | 4,7 | 12 |
| E-IV | | 1755 | 43,9 | 5,5 | 5,1 | $C_{11}H_{15}F_4NO_3$ | 43,4 | 5,3 | 5,2 | 21 |
| Z-IV | | 1755 | | | | | 43,7 | 5,4 | 5,3 | 12 |
| E-V | | 1740 | 42,7 | 4,4 | 6,2 | $C_8H_{10}F_3NO_3$ | 42,4 | 4,2 | 6,3 | 33 |
| Z-V | | 1740 | | | | | 42,6 | 4,3 | 6,1 | 11 |
| E-VI | | 1712 | 39,0 | 4,1 | — | $C_8H_{10}F_4O_4$ | 39,4 | 4,0 | — | 26 |
| Z-VI | | 1715 | | | | | 39,1 | 3,9 | — | 13 |

[a]The melting or boiling points for the E and Z isomers of IV-VI were not determined because of the small amounts (50 mg) of the substances.

The expected allylic migration is observed only in the case of IIc when adducts IIb-d are treated with ground potassium hydroxide in refluxing toluene; the rearrangement is accompanied by hydrolysis of the difluoromethylene group to a carbonyl group to give isomeric amides E- and Z-V:



Only vinyl substitution of the fluorine atom by a methoxy group in the intermediate olefin under the influence of the methanol formed in the hydrolysis of the ester group occurs in the case of adduct IIb to give isomeric esters E- (21%) and Z-IV (12%). In this case allylic migration of the 2,2-dimethylaziridinyl substituent is evidently hindered, and a competitive reaction with the less bulky nucleophile is therefore realized.

Only vinyl substitution of the fluorine atom by a methoxy group to give isomeric esters E- and Z-VI is also observed in the dehydrofluorination of adduct IId.

## EXPERIMENTAL

The PMR spectra of 10% solutions of the substances in $CDCl_3$ were recorded with Bruker WP-80-SY (80 MHz), WH-90 (90 MHz), and WM-400 (400 MHz) spectrometers with tetramethylsilane (TMS) as the internal standard. The $^{19}F$ NMR spectra were recorded with Perkin-Elmer R-12 (56 MHz) and Bruker WP-80-SY (75.39 MHz) spectrometers with $CF_3COOH$ as the external standard. The IR spectra were obtained with a Perkin-Elmer 580-B spectrometer. Analytical and preparative liquid chromatography was carried out with a Du Pont Prep LC chromatograph with a UV spectrophotometer as the detector and Zorbaz SIL 4.6 by 250 mm and Zorbaz SIL 22.7 by 250 mm columns.

The characteristics of the synthesized IIa-j, III, and the E and Z isomers of IV-VI are presented in Table 1.

TABLE 2. Parameters of the PMR and $^{19}F$ PMR Spectra of II-VI

| Compound | PMR spectrum | | | | | $^{19}F$ NMR spectrum | |
|---|---|---|---|---|---|---|---|
| | δ, ppm | | | | J, Hz | δ,* ppm | J, Hz |
| | COOMe | N—CH—CO | $CH(CF_3)_2$ | other groups | | | |
| IIa | 3,73; 3,82 | 2,87—3,20 | 3,91 | 1,66—2,18; 2,30—2,69 ($CH—CH_2$) | 8,0 ($^3J_{HF}$) | 14,91; 17,07 ($2CF_3$) | 9,0 ($^4J_{FF}$); 9,0 ($^3J_{FH}$) |
| IIb | 3,30 | 3,25 | 3,82 | 1,00 (2Me); 0,77—1,67 ($CH_2$) | 9,0 ($^3J_{HF}$); 2,7 ($^3J_{HH}$) | (A) 14,50; 18,40; (B) 15,70; 17,80 | 10,5 ($^4J_{FF}$); 9 ($^3J_{FH}$); 10,5 ($^4J_{FF}$); 9 ($^3J_{FH}$) |
| IIc | 3,79 | — | — | 3,70 ($ABX_3$); 2,31 ($Me_2N$) | 11,0 ($^3J_{HH}$); 7,3 ($^3J_{HF}$); $J_{AB}$=26,3 | 13,66—14,21; 14,71—15,53 ($3CF_3$) | |
| IId | 3,76 | — | 3,62 | 3,49 (MeO); 0,09 (HCO) | 7,0 ($^3J_{HF}$) | 12,82; 16,39 ($2CF_3$) | 8,54 ($^4J_{FF}$); 8,6 ($^3J_{FH}$) |
| IIe | 3,84 | — | — | 3,54—3,8 (CH—CH); 2,03; 3,67 (azetidino group) | | 13,80—14,30; 15,40—15,90 ($2CF_3$) | |
| IIf | 3,767 | — | — | 3,88 ($ABX_3$, $CF_3—CH—CH$); 1,72; 2,77; 2,58 (pyrrolidino group) | 10,5 ($^3J_{HH}$); 7,8 ($^3J_{HF}$); $J_{AB}$=97,5 | 13,50—14,00; 14,70—15,10 ($2CF_3$) | |
| IIf · HCl | 3,91 | 5,00 | 4,64 | 2,07—2,42; 3,22—3,67; 3,70—3,82 (pyrrolidino group) | 8,0 ($^3J_{HF}$) | 14,33; 18,22 ($2CF_3$) | 9,0 ($^4J_{FF}$); 9,0 ($^3J_{FH}$) |
| IIg | 3,78 | 3,49—3,69 | 3,74—3,98 | 1,23—1,71; 2,10—2,45; 2,49—2,87 (piperidino group) | | 13,80—14,10; 15,10—15,60 ($2CF_3$) | |
| IIg · HCl | 3,89 | 4,98 | 4,27 | 1,56—1,93; 1,98—2,40; 3,16—3,80 (piperidino group) | 7,0 ($^3J_{HF}$) | 13,41; 18,14 ($2CF_3$) | 9,3 ($^4J_{FF}$); 9,3 ($^3J_{FH}$) |
| IIh | 3,78 | 4,13 | 3,69 | 5,47 (NH, HO) | 8,0 ($^3J_{HF}$); 4,0 ($^3J_{HH}$) | | |
| IIi | 3,80 | 3,75 | 4,09 | 1,75 ($NH_2$) | 8,0 ($^3J_{HF}$); 6,0 ($^3J_{HH}$) | 13,09; 16,76 ($2CF_3$) | 8,5 ($^4J_{FF}$); 8,5 ($^3J_{FH}$) |
| IIj | 3,71 | 3,02 | 3,58 | 2,38 ($Me_2N$); 4,00 (NH) | 8,0 ($^3J_{HF}$); 6,0 ($^3J_{HH}$) | | |
| III | 3,78; 3,84 | — | — | 2,31; 2,45; 3,08 ($CH_2—CH$); 6,82 (CH) | 1,5 ($^4J_{HF}$) | | |
| E-IV | 3,76 | 3,59 | — | 1,22; 1,27 ($Me_2C$); 1,20—1,30; 1,58 ($CH_2$); 3,89 (MeOCF) | 1,1 ($^4J_{MeOF}$) | (A) 21,09 ($CF_3$); −2,54 (CF) (B) 21,82 ($CF_3$); −1,38 (CF) | 11,0 ($^4J_{FF}$) 10,0 ($^4J_{FF}$) |
| Z-IV | 3,77 | 3,59 | — | 1,22; 1,27 ($Me_2C$); 1,20—1,30; 1,56 ($CH_2$); 3,89 (MeOCF) | 1,1 ($^4J_{MeOF}$) | (A) 21,79 ($CF_3$); −0,85 (CF) (B) 22,76 ($CF_3$); −1,53 (CF) | 18,8 ($^4J_{FF}$) 20,0 ($^4J_{FF}$) |
| E-V | 3,79 | — | — | 2,97; 3,07 ($Me_2N$); 6,44 (CH) | | 11,78 ($CF_3$) 16,91 ($CF_3$) | 1,7 ($^4J_{HF}$) |
| Z-V | 3,84 | — | — | 3,04 ($Me_2N$); 6,24 (CH) | | 20,37 ($CF_3$); −1,02 (CF) | 11,4 ($^4J_{FF}$) |
| E-VI | 3,82 | — | — | 3,45; 3,91 (2MeO); 4,56 (CH) | | 21,02 ($CF_3$); 1,78 (CF) | 18,4 ($^4J_{FF}$) |
| Z-VI | 3,80 | — | — | 3,45; 3,91 (2MeO); 4,57 (CH) | | | |

*The letters A and B denote a diastereomeric pair; B/A = 2.6 for IIb (spectrum recorded at −10°C in $d_8$-toluene), and B/A = 1.7 for E- and Z-IV. Complex multiplets are observed for IIc, e, f, g.

Methyl 2-(2-Methoxycarbonylaziridino)-3-trifluoromethyl-4,4,4-trifluorobutanoate (IIa) and Methyl 3-Trifluoromethyl-4-(2-methoxycarbonylaziridino)-4,4-difluoro-2-butenoate (III). A mixture of 0.44 g (2 mmole) of methyl β,β-bis(trifluoromethyl)acrylate and 0.2 g (2 mmole) of methyl aziridine-2-carboxylate in 50 ml of acetonitrile was heated at 50°C for 8 h, after which it was evaporated, and the residue was separated by HPLC.

Methyl 2-(2,2-Dimethylaziridino)-3-trifluoromethyl-4,4,4-trifluorobutanoate (IIb). A solution of 10 mmole of 2,2-dimethylaziridine in 10 ml of ether was added at −30°C to 2.2 g (10 mmole) of methyl β,β-bis(trifluoromethyl)acrylate in 50 ml of ether, after which the mixture was maintained at this temperature for 0.5 h. It was then evaporated, and the residue was distilled in vacuo.

Adducts IIc, e-h, j were similarly obtained.

Methyl 2-Pyrrolidino-3-trifluoromethyl-4,4,4-trifluorobutanoate Hydrochloride (IIf•HCl) and Methyl 2-Piperidino-3-trifluoromethyl-4,4,4-trifluorobutanoate Hydrocloride (IIg•HCl). These compounds were obtained by passing gaseous HCl into solution of the corresponding adducts in absolute ether.

Methyl 2-Methoxy-3-trifluoromethyl-4,4,4-trifluorobutanoate (IId). A mixture of 22.2 g (100 mmole) of acrylate I, 30 g of MeOH, and 5 g of $KF/Al_2O_3$ in a sealed ampul was heated at 150°C for 10 h, after which the mixture was filtered, and the filtrate was distilled in vacuo.

Methyl 2-Amino-3-trifluoromethyl-4,4,4-trifluorobutanoate (IIi). This compound was obtained by the method in [2].

(Z)- and (E)-Methyl 2-(2,2-Dimethylaziridino)-3-trifluoromethyl-4-fluoro-4-methoxy-3-butanoates IV. A 2.8-g (50 mmole) sample of ground KOH was added to a solution of 2 mmole of adduct IIb in 20 ml of absolute toluene, and the mixture was refluxed for 5 min. It was then cooled and diluted with an equal volume of ether, and the diluted mixture was filtered through a 1-cm-thick layer of silica gel. The filtrate was evaporated, and the residue was separated by preparative liquid chromatography.

Compounds (Z)- and (E)-V and (Z)- and (E)-VI were similarly obtained.

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