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# INVESTIGATION OF METHODS FOR THE SYNTHESIS OF AZIRIDINES AND AZIRINES ON THE BASIS OF ETHYL-β,β-BIS(TRIFLUOROMETHYL) ACRYLATE

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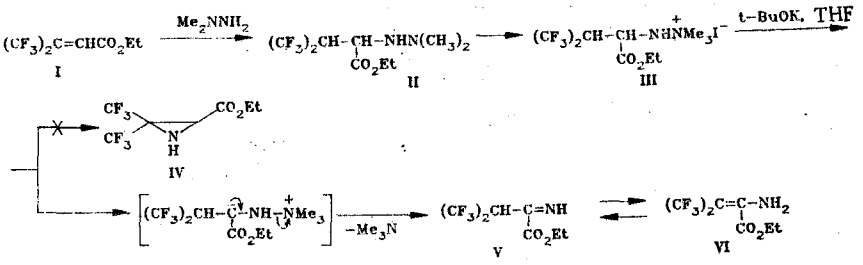
Various methods for the preparation of aziridines and azirines on the basis of ethyl β,β-bis(trifluoromethyl) acrylate were studied. Alkaline treatment of the products of addition of nucleophilic reagents to ethyl β,β-bis(trifluoromethyl) acrylate leads to the preparation of compounds of various classes that contain a hexafluoroisopropyl fragment.

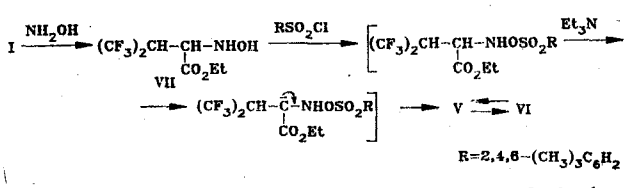
In the present research we attempted to synthesize 2-carbalkoxy-3,3-bis(trifluoromethyl)-aziridines and 2-carbalkoxy-3,3-bis(trifluoromethyl)azirines on the basis of ethyl β,β-bis-(trifluoromethyl) acrylate.

It is known that nucleophilic reagents attack the α position of ester I [1], where N-(2-carboxyethyl)-N',N'-dialkylhydrazine derivatives form the corresponding aziridines upon treatment with bases [2].

The reaction of ester I with N,N-dimethylhydrazine leads to addition product II, which forms hydrazinium salt III; the latter was assumed to undergo cyclization under the influence of tert-BuOK. However, instead of the expected aziridine IV, we obtained a mixture of imine V and enamine VI, which was separated by preparative liquid chromatography (Tables 1-3).



A similar transformation is observed in an attempt to cyclize hydroxylamine O-mesitylen-sulfonate (VII), which we obtained from ester I and hydroxylamine:



Mixtures of the imine and enamine in a ratio of VI:V = 9:1 (according to PMR data) are obtained in both cases after precipitation of the resulting salts and evaporation. After

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TABLE 1. Characteristics of II-XV

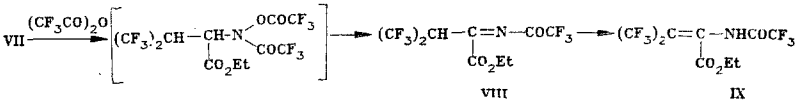
| Compound | bp (pressure, mm), mp, °C | ν, cm⁻¹ | | Found, % | | | Empirical formula | Calc., % | | | Yield, % |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | C=O | N–H | C | H | N | | C | H | N | |
| II | 59 (5,0) | 1740 | 3380 | 36,1 | 4,7 | 9,2 | $C_9H_{14}F_6N_2O_2$ | 36,5 | 4,8 | 9,5 | 85 |
| III | 145 | 1740 | 3220 | 27,0 | 3,8 | 6,9 | $C_{10}H_{17}F_6IN_2O_2$ | 27,4 | 3,9 | 6,4 | 90 |
| V } VI } | 80 (40) | 1735 | 3380 | 33,2 | 2,6 | 5,2 | $C_7H_7F_6NO_2$ | 33,5 | 2,8 | 5,6 | 70 |
| | | 1730 | 3250 | 33,3 | 2,7 | 5,1 | $C_7H_7F_6NO_2$ | 33,5 | 2,8 | 5,6 | |
| VII | 37 | 1725 | 3370 | 30,7 | 3,2 | 5,5 | $C_7H_9F_6NO_3$ | 31,2 | 3,3 | 5,2 | 72 |
| VIII } IX } | 30 (0,5) | — | — | — | — | — | $C_9H_6F_9NO_3$ | — | — | — | 79 |
| | | 1745 | | | | | | | | | |
| | | 1765 | 3240 | 30,6 | 1,5 | 3,8 | $C_9H_6F_9NO_3$ | 31,1 | 1,7 | 4,0 | |
| X | 79 (5,0) | 1740 | — | 36,2 | 4,2 | 9,1 | $C_9H_{12}F_6N_2O_2$ | 36,7 | 4,1 | 9,5 | 69 |
| XI | Oil | 1725 | — | 29,1 | 4,5 | 6,6 | $C_{10}H_8F_6N_2O_6S$ | 29,4 | 4,4 | 6,9 | 80 |
| XIII | 75 | 1735 | 3260 | 40,6 | 4,1 | 4,5 | $C_{11}H_{13}F_6NO_3$ | 40,9 | 4,0 | 4,4 | 30 |
| XIV | 47 | 1735 | — | 31,0 | 2,5 | 5,5 | $C_7H_7F_6NO_3$ | 31,5 | 2,6 | 5,2 | 60 |
| XV | 97 | 1740 | — | 42,1 | 3,7 | 3,2 | $C_{16}H_{17}F_6NO_5S$ | 42,7 | 3,8 | 3,1 | 45 |
| XVI | 36 | 1720 | 3310 | 31,1 | 2,7 | 5,2 | $C_7H_7F_6NO_3$ | 31,5 | 2,6 | 5,2 | 76 |
| XVII | 195* | — | 3270 | 17,4 | 2,2 | 6,6 | $C_3H_4F_6ClN$ | 17,7 | 2,0 | 6,9 | 68 |

*According to the data in [5] this compound had mp 200°C.

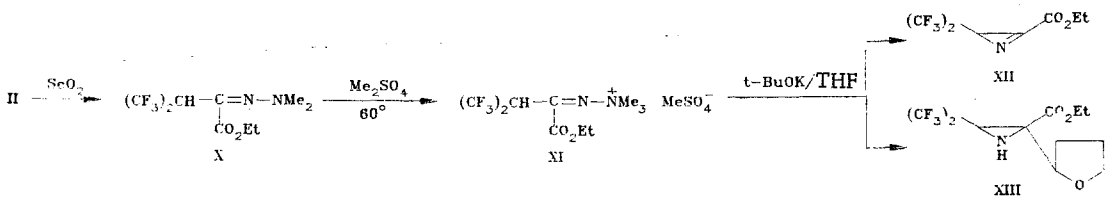
distillation of the mixture or after allowing the pure enamine V to stand for 2 weeks at 20°C, the V:VI ratio is 7:3, and does not change subsequently. When pyridine is added to this sample, the percentage of enamine VI increases up to the point of complete disappearance of imine V.

Preponderance of the enamine form in the enamine-imine equilibrium was also observed for a number of systems that contain electronegative substituents in the β position relative to the nitrogen atom [3]. It should be noted that hydrocarbon analogs of imine V and enamine VI do not undergo isomerization even under the influence of bases [4].

We were unable to obtain O-trifluoroacetyl derivatives of hydroxylamine VII, since the trifluoroacetylation of this compound leads to a mixture of imide VIII and enamide IX, and, after distillation, the VII:VIII ratio is 1:1 (according to PMR spectrosopy). When imide VIII is allowed to stand at 0°C for 1 month, it undergoes complete isomerization to enamide IX. This sort of transformation is characteristic for N-substituted imide-enamide systems [3].



The primary deprotonation of derivatives of III and VII is realized from the α position rather than from the β position with respect to the carboxy group, and this is a basic hindrance to alkaline cyclization of hydrazium salt III and hydroxylamine mesitylenesulfonate (VII). In order to circumvent this obstacle, to arrive at cyclization with the formation of the azirine, as in [6], we carried out the dehydrogenation of hydrazine II to hydrazone X and obtained hydrazonium salt XI. It should be noted that hydrazone X does not react with MeI (after 10 h at 80°C in MeCN) nor with methyl tosylate (after 2 days at 100°C without a solvent). In the alkaline cyclization of salt XI, instead of the expected azirine XII, we obtained 2-tetrahydrofuryl-substituted aziridine XIII (Tables 1-3).



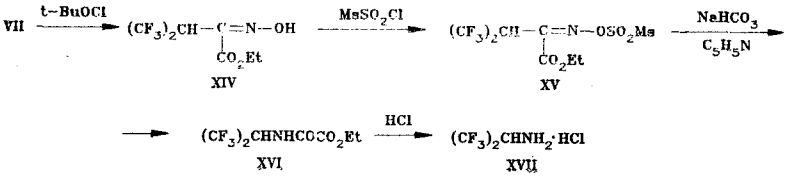
Similar transformations were carried out on the basis of hydroxylamine VII, which underwent dehydrogenation to oxime XIV in high yields under the influence of tert-butyl hypochlorite. Other oxidizing agents ($PbO_2$, $MnO_2$, $SO_2$) lead to the formation of complex mixtures of products. Oxime XIV gave O-mesitylenesulfonate XV, which, under the influence of a weak base ($NaHCO_3$ in pyridine), instead of the expected cyclization, underwent the Beckmann rearrange-

TABLE 2. Parameters of the PMR Spectra (δ, ppm; J, Hz)

| Compound | Et | | $HC(CF_3)_2$ | | | Other groups |
|---|---|---|---|---|---|---|
| | δ | $^3J_{HH}$ | δ | $^3J_{HF}$ | $^3J_{HH}$ | δ, J |
| II | 1,29; 4,27 | 6,4 | 3,67 | 8,4 | 2,6 | 3,1 (NH, $^3J_{HH}$=5,8); 4,05 (HCN); 2,41 ($Me_2N$) |
| III* | 1,27; 4,24 | 6,8 | 4,77 | 7,8 | 3,2 | 3,30 ($Me_3N$); 5,23 (HCN, $^3J_{HH}$=7,9); 7,3 (NH) |
| V | 1,37; 4,40 | 6,9 | 5,45 | 7,8 | — | 11,6 (NH) |
| VI | 1,34; 4,32 | 6,9 | — | — | — | 5,1 ($H_2N$) |
| VII | 1,25; 4,22 | 7,0 | 3,10 | 8,0 | 3,6 | 4,11 (HCN, $^3J_{HH}$=3,6); 5,93 (HN, HO) |
| VIII | 1,32; 4,40 | 6,6 | 5,02 | 7,0 | — | — |
| IX | 1,31; 4,35 | 6,6 | — | — | — | 6,95 (NH) |
| X | 1,30; 4,19 | 6,4 | 4,40 | 7,2 | — | 3,14 ($Me_2N$) |
| XI* | 1,33; 4,53 | 6,5 | 6,28 | 7,8 | — | 3,40 (MeO); 4,05 ($Me_3N$) |
| XIII | 1,26 | 6,8 | — | — | — | 1,6—2,2 (3′-and 4′-H); 3,6—3,9 (5′-H); 4,0—4,2 (2′-H); 2,36 (HN) |
| XIV | 1,33; 4,34 | 6,8 | 5,05 | 8,6 | — | 10,4 (OH) |
| XV | 1,24; 4,24 | 6,8 | 4,95 | 8,0 | — | 2,29 (4′-$CH_3$); 2,57 (2′-and 6′-$CH_3$); 6,95 (3′and5′-H) |
| XVI | 1,38; 4,38 | 7,0 | 5,23 | 7,0 | — | 7,55 (HN, $^3J_{HH}$=11,0) |
| XVII | — | — | 5,91 | 8,0 | — | 10,3 (HN, $^3J_{HH}$=10,0) |

*In $(CD_3)_2SO$.

ment to amide XVI. The structure of the latter was confirmed by spectral data and acidic hydrolysis to hexafluoroisopropylamine hydrochloride (XVII).




Consequently, the migrating group in this case is the hexafluoroisopropyl group rather than the carbethoxy group. A similar type of migration of fluoroalkyl groups is known in the Curtius rearrangement [7, 8].

Thus α-amino-3,3-bis(trifluoromethyl) propionic acid derivatives that contain easily leaving substituents attached to the nitrogen atom cannot be involved in alkaline cyclization with the participation of the carbanion in the β position. This is explained by the presence in the α position of a second readily deprotonated center. Liquidation of the latter in 2-imino-3,3-bis(trifluoromethyl) propionic acid derivatives that contain easily leaving substituents attached to the nitrogen atom does not lead to the desired cyclization. The Beckmann rearrangement is realized in one case, whereas in the other, one observes cyclization with involvement of the solvent, which is difficult to interpret on the basis of the available data.

## EXPERIMENTAL

The $^1H$ and $^{13}C$ NMR spectra were obtained with a Bruker WH-90 spectrometer (90 MHz). The substances were investigated in the form of 10% solutions of the samples in $CDCl_3$ or $D_6$-DMSO with tetramethylsilane as the internal standard. The IR spectra of KBr pellets of thin films of the substances were obtained with an IR-75 spectrometer. The constants and yields of the products are presented in Table 1, and the parameters of the PMR and NMR spectra are presented in Tables 2 and 3.

Ethyl-2-(N',N'-dimethylhydrazino)-3,3-bis(trifluoromethyl) Propionate (2). An 84-g (0.1 mole) sample of N,N-dimethylhydrazine was added to 23.6 g (0.1 mole) of ester I in 50 ml of absolute ether at −20°C, and the mixture was stirred for 30 min at this temperature. The mixture was then evaporated, and the residue was distilled.

N,N,N-Trimethyl-N'-[3,3,3-trifluoro-2-(trifluoromethyl)-1-(ethoxycarbonyl)propyl]hydrazinium Iodide (III). A 1.84-ml (0.03 mole) sample of methyl iodide was added to 3.16 g (0.01 mole) of hydrazine II. After 2 days, the crystalline product was removed by filtration and washed with ether.

TABLE 3. Parameters of the $^{13}C$ NMR Spectra (δ, ppm, J, Hz)

| Compound | Et | $C(CF_3)_2$ | | C—N | $CF_3$ | | Other groups |
|---|---|---|---|---|---|---|---|
| | δ | δ | $^2J_{CF}$ | δ | δ | $^1J_{CF}$ | |
| II | 14,2; 63,0 | 51,1 | 27,3 | 59,6 | 123,8 | 286,1 | 48,3 ($Me_2N$); 171,1 (CO) |
| V | 12,9; 63,8 | 48,7 | 29,5 | — | 121,8 | 285,3 | 157,9; 158,3 (CO, CN) |
| VI | 13,2; 63,5 | 88,8 | 33,8 | 147,2 | 122,8<br>123,8 | 268,9<br>270,4 | 163,8 (CO) |
| IX | 13,5; 64,8 | 109,8 | 33,0 | 139,4 | 121,1<br>121,7 | 278,0<br>278,0 | 115,6 ($CF_3CO$, $^1J_{CF}$=290); 155,3 ($COCF_3$, $^2J_{CF}$=42); 160,5 (CO) |
| X | 14,2; 61,7 | 52,5 | 30 | 112,6 | 123,7 | 280,0 | 48,3 ($Me_2N$); 161,3 (CO) |
| XIII | 13,5; 62,4 | 47,2 | 35,2 | 51,9 | 121,7 | 279,2 | 25,3; 28,6; 69,0; 76,9 (tetrahydrofuryl), (165,8 (CO) |
| XIV | 14,0; 63,9 | 46,1 | 32,4 | 138,7 | 122,0 | 280,9 | 161,5 (CO) |
| XVI | 13,2; 63,8 | 52,5 | 33,8 | — | 121,1 | 280,6 | 156,7; 159,0 (CO) |

Ethyl-2-amino-3,3-bis(trifluoromethyl) Acrylate (VI). A 1.12-g (0.01 mole) sample of tert-BuOK was added to a suspension of 4.38 g (0.01 mole) of salt III in absolute THF at 0°C, and the mixture was stirred at this temperature for 2 h. The mixture was then filtered, and the filtrate was evaporated. The residue was identified as a mixture of amine VI and imine V in a ratio of 9:1. Distillation yielded a V:VI ratio of 7:3. The reaction product was separated by preparative liquid chromatography [with a 250 mm by 21.2 mm Chrompack column with an EAK UV detector by elution with a propanol–hexane system (3:97)].

Ethyl-2-hydroxylamino-3,3-bis(trifluoromethyl) Propionate (VII). A solution of 3.3 g (0.1 mole) of the hydroxylamine base in 20 ml of absolute ethanol was added to 23.6 g (0.1 mole) of ester I in 50 ml of absolute ethanol at –20°C, and the mixture was stirred at this temperature for 1 h. The mixture was the evaporated, and the residue was dissolved in hot $CCl_4$. Crystalline hydroxylamine VII was obtained when the solution was allowed to stand in a refrigerator.

Ethyl 2-Trifluoroacetamido-3,3-bis(trifluoromethyl) Acrylate (IX). A 21.0-g (0.1 mole) sample of trifluoroacetic anhydride was added at 0°C to 2.69 g (0.01 mole) of hydroxylamine VII to 20 ml of absolute ether at 0°C, and the mixture was allowed to stand at this temperature for 1 h. The mixture was then evaporated and distilled *in vacuo*. According to the PMR spectrum, the acylation product was a mixture of imide VIII and enamide IX. In the course of a month VII underwent complete isomerization to IX.

Ethyl Bis(trifluoromethyl)Pyruvate Dimethylhydrazone (X) and Products of the Reaction of Hydrazone X with Dimethyl Sulfate (XI). A 1.66-g (0.015 mole) sample of $SeO_2$ was added to 2.96 g (0.01 mole) of hydrazine II in 50 ml of benzene, and the mixture was stirred for 2 h. The precipitated selenium was removed, and the mixture was evaporated. The residue was distilled *in vacuo* to give hydrazone X. A 3.78-g (0.033 mole) sample of dimethyl sulfate was added to a 2.94-g (0.01 mole) sample of hydrazone X, and the mixture was heated at 60°C for 2 days. The excess dimethyl sulfate was removed by vacuum distillation. The yellow residue — an uncrystallizable oil — was virtually pure salt XI.

2-Carbethoxy-2-(2-tetrahydrofuryl)-3,3-bis(trifluoromethyl)aziridine (XIII). A 1.12-g (0.01 mole) sample of tert-BuOK was added to 4.2 g (0.01 mole) of salt XI in 50 ml of absolute THF, and the mixture was heated at 50°C for 10 h. The solution was evaporated, and the residue was treated with ether–hexane (1:3). The precipitate was separated, and the solution was passed through a layer of silica gel (10 cm). The solution was evaporated, the residual oil was dissolved in hot $CCl_4$, and the solution was stored in a refrigerator. This procedure gave crystalline product XIII.

Ethyl 2-Oximino-3,3-bis(trifluoromethyl) Propionate (XIV). A 1.12-g (0.11 mole) sample of tert-butyl hypochlorite was added at 0°C to 2.69 g (0.01 mole) of hydroxylamine VII in 50 ml of ethyl acetate, and the mixture was maintained for 30 min at this temperature, afterwards it was evaporated, and the residual oil was dissolved in hot $CCl_4$. The storage of the solution in a refrigerator gave crystalline oxime XIV.

Ethyl 2-Mesitylenesulfonyloximino-3,3-bis(trifluoromethyl) Propionate (XV). A 1.35-g (0.01 mole) sample N,N-dimethylbenzylamine was added to a mixture of 2.67 g (0.01 mole) of oxime XV and 2.18 g (0.01 mole) of mesitylenesulfonyl chloride in 50 ml of absolute ether at 0°C, and the mixture was maintained at this temperature for 1 h. After separation of the precipitate, the solution was evaporated, and the residue was crystallized from $CCl_4$.

Ethyl N-Hexafluoroisopropoxyoxaminate (XVI). A 0.02-mole sample of $NaHCO_3$ was added at 0°C to a solution of 4.49 g (0.01 mole) of XV in 20 ml of pyridine, and the mixture was stirred at this temperature for 1 h. The pyridine was then removed *in vacuo*, the residue was extracted with $CCl_4$, the filtrate was evaporated, and the residual oil was dissolved in hot $CCl_4$. Cooling of the solution yielded crystalline ester XVI.

Hexafluoroisopropylamine Hydrochloride (XVII). A mixture of 2.67 g (0.01 mole) of oxaminate XVI and 10 ml of a 30% hydrochloric acid was allowed to stand for 8 h, after which it was evaporated. The crystalline reaction product was washed with ether.

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# PORPHYRINS. 18.* SYNTHESIS OF OCTAPROPYLPORPHYRIN BY THE METHOD OF MONOPYRROLE CYCLOTETRAMERIZATION OF 5-CARBOXY-2-METHOXYMETHYL-3,4-DIPROPYLPYRROLE. INVESTIGATION OF THE THERMOLYSIS OF meso-N-METHYLFORMALDIMINEOCTAPROPYLPORPHYRIN


A. M. Shul'ga and G. V. Ponomarev



UDC 547.749



The synthesis of octapropylporphyrin on the basis of 5-carboxy-2-methoxymethyl-3,4-dipropylpyrrole was realized. It was demonstrated that in the thermolysis of meso-N-methylformaldimineoctapropylporphyrin, $3^1,5^1$-cyclo-$3^1$-ethylidene- and $3^1,5^1$-cyclo-$3^1$-ethyl-$5^1$-(N-methylimine) derivatives are also formed in addition to $3^1,5^1$-cyclo-$3^1$-ethylhectaporphyrin.


In order to confirm the general character of the thermal decomposition of Schiff bases of meso-formylporphyrins to porphyrins with a cyclopentane ring [2] and to ascertain the effect of the length of the alkyl substituents in the pyrrole rings on the course of the thermolysis, we undertook the synthesis of octapropylporphyrin (I), from which we obtained, in 92% yield, the necessary Schiff base II. To obtain the starting porphyrin I and its derivatives we used the synthetic pathway proposed by Siedel and Winkler [4]† (see the scheme presented below).

*See [1] for Communication 17.

†In [4] it is erroneously assumed that pyrrole III upon oxidation by lead tetraacetate gives immediately the hydroxymethyl derivative, whereas the subsequent action of methanolic alkali leads not only to saponification of the carbothoxy group but also to cleavage of the carboxy group. However, it was subsequently demonstrated in other derivatives [10] that, in fact, the 2-acetoxymethyl group is, nevertheless, formed; however, the latter group may readily undergo alcoholysis in the case of brief heating in alcohol, as, for example, during recrystallization.


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