REACTION OF POLYFLUORINATED α-HALO-β-KETO ESTERS WITH AMMONIA

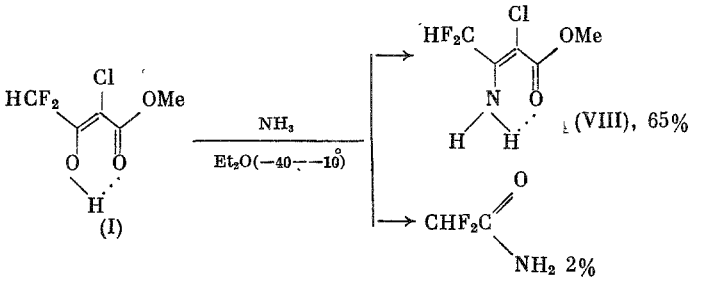
K. I. Pashkevich, A. É. Skryabina, and V. I. Saloutin

UDC 542.91:547.488.4'261:546.171.1

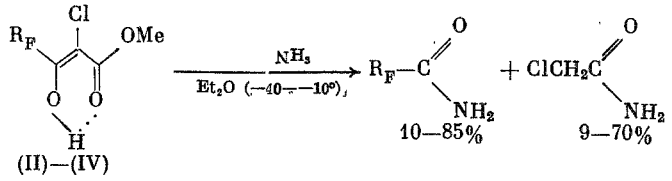
The action of NH_3 on acetoacetate and 4,4,4-trifluoroacetoacetate esters gives aminocrotonate esters [1, 2], while the action of NH_3 on 2,2-dibromoacetoacetate esters gives cleavage with the formation of dibromoacetamide [3]. The action of NH_3 on pentabromoacetoacetamide gives a haloform-like cleavage and formation of bromoform and the diamide of dibromomalonic acid [4]. The reaction of fluorinated α-halo-β-keto esters with ammonia has not yet been reported.

In the present work, we studied the reaction of NH_3 with the methylesters of fluorinated α-chloro- (I)-(IV) and α,α-dibromo-β-keto acids (V)-(VII).

The methyl ester of 2-chloro-4,4-difluoroacetoacetic acid (I) reacts with a threefold excess of ammonia in anhydrous ether at from −40 to −10°C to give the methyl ester of 2-chloro-4,4-difluoro-3-aminocrotonic acid (VIII) and the liberation of a small amount of difluoroacetamide.



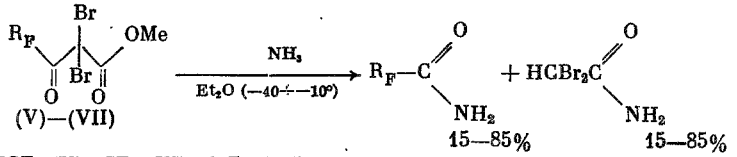
Thus, (I), similar to acetoacetate [1] and trifluoroacetoacetate esters [2], reacts with NH_3 at the carbonyl electrophilic site, although the reaction is accompanied by partial cleavage. In contrast, fully fluorinated α-chloro-β-keto esters (II)-(IV) react with NH_3 to form the products of alkaline cleavage of β-keto esters, namely, amides of fluorocarboxylic and chlorocarboxylic acids for 1:1 and 1:3 reagent ratios. In this case, formation of aminocrotonate esters (VIII) does not occur. The amides obtained were identified by comparison with authentic samples.



$R_F = CF_3$ (II), $H(CF_2)_2$ (III), C_4F_9 (IV).

The conversion of (II), (III), and (IV) depends on the reaction time.

Independently of the type of fluoroalkyl subsituent, the methyl esters of 2,2-dibromo-β-keto acids (V)-(VII) react with NH_3 to undergo cleavage and form amides of fluorocarboxylic and dibromoacetic acids in the case of reagent ratios 1:1 and 1:3. The reaction products were identified by comparison with authentic samples.



$R_F = HCF_2$ (V), CF_3 (VI), C_4F_9 (VII).

Institute of Chemistry, Urals Science Center, Academy of Sciences of the USSR, Sverdlovsk.
Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 5, pp. 1190-1192, May, 1985. Original article submitted June 20, 1984.

0568-5230/85/5405-1089$09.50

As in the case of (II)-(IV), the conversion of (V)-(VII) is a function of the reaction time. We should note that (V)-(VII) react with NH_3 similarly to 2,2-dibromoacetoacetate ester [3] and not to pentabromoacetoacetamide [4], which undergoes a haloform-like cleavage upon the action of NH_3. This apparently indicates high stability for the leaving tribromethyl anion relative to fluoroalkyl anions.

Since the major product of the reaction of (I) with excess NH_3 is (VIII), we may conclude that the initial attack of NH_3 occurs at the carbon atom bound to the fluoroalkyl substituent. The further course of this reaction depends both on the structure and electron-withdrawing capacity of the substituent in the β position and on the extent of halogenation of the α-carbon of the β-keto ester. Thus, going from CHF_2 to CF_3 and other fluoroalkyl substituents leads to the alkaline cleavage of polyfluorinated α-chloro-β-keto esters (II)-(IV) as the major reaction pathway. This same effect is observed upon the introduction of two halogen atoms to the α-carbon atom of a β-keto ester such as in 2,2-dibromoacetoacetate ester [3] and (V)-(VII).

EXPERIMENTAL

The IR spectra were taken on a UR20 spectrometer as a Vaseline oil mull. The PMR spectra were taken on a Tesla BS-567A spectrometer at 100 MHz in DMSO-d_6 and acetone-d_6. The gas–liquid chromatographic analysis was carried out on an LKhM-72 8-MD chromatograph using a katharometer detector and helium as the carrier gas on a 1 m × 3 mm steel column packed with 15% Carbowax 20M on Chromaton N-AW-DMCS at 150°C.

The fluorinated α-chloro- and α,α-dibromo-β-keto esters (I)-(VII) were obtained according to our previous precedures [5]. The amides of difluoroacetic, trifluoroacetic, teterafluoropropionic, and nonafluorovaleric acids were prepared according to Lovelace et al. [6]. Dibromoacetamide was prepared according to Steinkopf [7], while chloroacetamide was prepared according to Becker [8].

Reactions of fluorinated α-chloro- and α,α-dibromo-β-keto esters with ammonia. A sample of 0.01 mole β-ketoester in 50 ml anhydrous ether was added to a three-necked flask equipped with a stirrer, bubbler, and low-temperature condenser cooled by a mixture of dry ice and acetone. The flask was placed in a bath cooled with dry ice–acetone to −10 to −40°C. An equimolar amount of threefold excess of ammonia was bubbled into the flask with stirring. Then, the mixture was stirred for 3 h and left to warm to about 20°C. The precipitate of chloro- or dibromoacetamide was filtered off, washed with ether or acetone, and dried. Ether was distilled off the mother liquor, and the crystalline residue was sublimed to give amides of fluorocarboxylic acids.

The amides of the fluorocarboxylic acids and chloro- and dibromoacetamides were identical to samples reported in the literature relative to melting point and IR and PMR spectra 6-8 .

In the case of (I), the precipitate after sublimation was identified as the methyl ester of 2-chloro-4,4-difluoro-3-aminocrotonic acid (VIII) (65% yield), mp 103-105°C. Found: C 32.62; H 3.85; N 7.49; F 19.80; Cl 18.17%. Calculated for $C_5H_6ClF_2O_2N$: C 32.36; H 3.26; N 7.55; F 20.48; Cl 19.11%. IR spectrum (ν, cm^{-1}): 1650 (CO), 3200 (NH_2, stretching), 1520 (NH_2, def.). PMR spectrum (δ, ppm, J, Hz, DMSO-d_6): 3.52 (3H, MeO), 3.70 (2H, NH_2), 7.02 (1H, CHF_2, J = 56.15).

CONCLUSIONS

1. The reaction of polyfluorinated α-chloro-β-keto esters with ammonia in the case of a difluoromethyl substituent gives 2-chloro-4,4-difluoro-3-aminocrotonic ester as the major product. When CF_3 and higher fluoroalkyl substituents are present at the β-carbon of the β-keto ester, the esters are cleaved by NH_3 to amides of fluorocarboxylic acids and chloroacetamide.

2. Fluoroalkyl derivatives of 2,2-dibromo-β-keto esters undergo cleavage by the action of NH_3 to give amides of fluorocarboxylic acids and dibromoacetamide, regardless of the type of fluoroalkyl substituent.

LITERATURE CITED

1. S. A. Glickman and A. C. Cope, J. Am. Chem. Soc., 67, 1017 (1945).
2. F. Swarts, Bull. Soc. Acad. Roy. Belg., 12, 679 (1926).
3. M. Conrad and L. Schmidt, Ber., 29, 1046 (1896).
4. H. N. Stokes and H. V. Pehman, Ber., 19, 2698 (1886).
5. V. I. Saloutin, Z. E. Skryabina, M. N. Rudaya, and K. I. Pashkevich, Izv. Akad. Nauk SSSR, Ser. Khim., 1106 (1984).
6. A. M. Lovelace et al., Aliphatic Fluorine Compounds, Van Nostrand—Reinhold (1958).
7. W. Steinkopf, Ber., 38, 2695 (1905).
8. H. Becker, Laboratory Textbook in Organic Chemistry [Russian translation], Vol. 2, Mir, Moscow (1979), p. 86.