Chemistry

E. M. ROKHLIN, N. P. GAMBARYAN, CHEN CHIN-YUN, and Academician I. L. KNUNYANTS

1960

SovietRxiv

Abstract

Full Text

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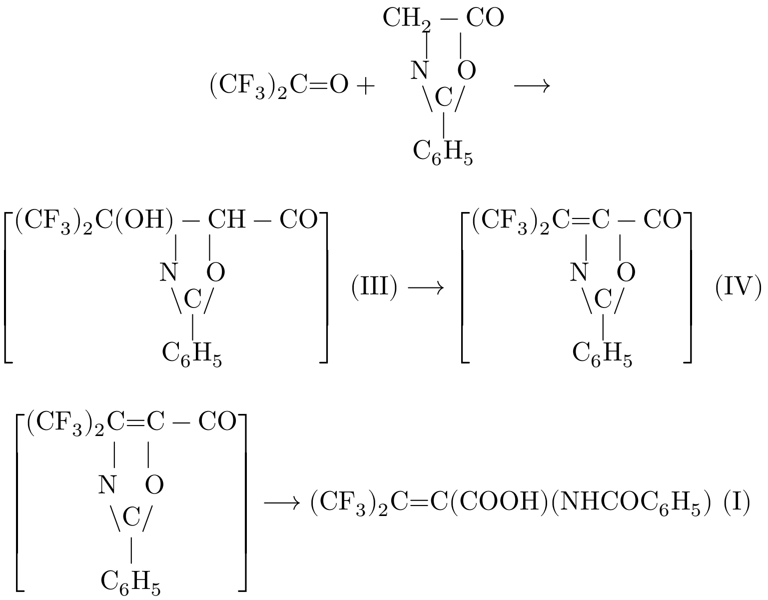
I. L. KNUNYANTS

2-PHENYL-4-HEXAFLUOROISOPROPYLIDENEOXAZOLONE-5

As a result of reactions of hexafluoroacetone with compounds containing active methylene groups, oxy compounds are usually obtained which do not undergo dehydration even under severe conditions ($^{1-3}$).

$$(CF_3)_2C{=}O + CH_2XY \longrightarrow (CF_3)_2C(OH) - CHXY$$

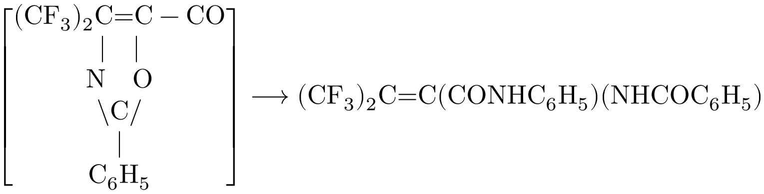
However, in the interaction of hexafluoroacetone with 2-phenyloxazolone-5, α-benzamidohexafluorodimethylacrylic acid (I) was obtained. If the reaction mixture is treated with an excess of aniline, the anilide of α-benzamidohexafluorodimethylacrylic acid (II) is obtained. Evidently, the ease of dehydration of the intermediate oxyoxazolone (III) is explained by the realization of the strongly conjugated system of 2-phenyl-4-hexafluoroisopropylideneoxazolone-5 (IV):



$$(CF_3)_2C{=}O + \begin{array}{c} CH_2 - CO \\ |\quad\;| \\ N \quad O \\ \backslash C/ \\ | \\ C_6H_5 \end{array} \longrightarrow$$

$$\left[\begin{array}{c} (CF_3)_2C(OH) - CH - CO \\ |\quad\;| \\ N \quad O \\ \backslash C/ \\ | \\ C_6H_5 \end{array}\right] (III) \longrightarrow \left[\begin{array}{c} (CF_3)_2C{=}C - CO \\ |\quad\;| \\ N \quad O \\ \backslash C/ \\ | \\ C_6H_5 \end{array}\right] (IV)$$

$$\left[\begin{array}{c} (CF_3)_2C{=}C - CO \\ |\quad\;| \\ N \quad O \\ \backslash C/ \\ | \\ C_6H_5 \end{array}\right] \longrightarrow (CF_3)_2C{=}C(COOH)(NHCOC_6H_5)\ (I)$$

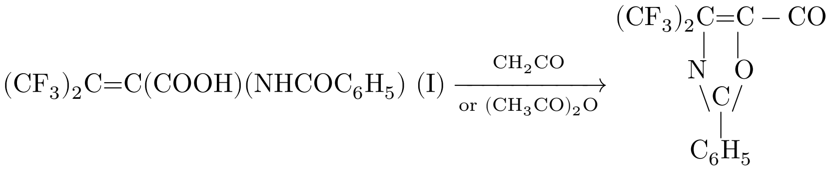


$$\left[\begin{array}{c}\mathrm{(CF_3)_2C{=}C-CO}\\ |\quad|\\ \mathrm{N}\quad\mathrm{O}\\ \backslash\mathrm{C}/\\ |\\ \mathrm{C_6H_5}\end{array}\right]\longrightarrow \mathrm{(CF_3)_2C{=}C(CONHC_6H_5)(NHCOC_6H_5)}\ \text{(II)}$$

α-Benzamidohexafluorodimethylacrylic acid (I) was also obtained under the conditions of the Erlenmeyer reaction (^{4}) from hexafluoroacetone and hippuric acid:

$$\mathrm{(CF_3)_2C{=}O + CH_2(COOH)(NHCOC_6H_5)} \xrightarrow[\mathrm{(CH_3CO)_2O}]{\mathrm{CH_3COONa}} \mathrm{(CF_3)_2C{=}C(COOH)(NHCOC_6H_5)}\ \text{(I)}$$

Acid I, under the action of ketene or acetic anhydride, is readily converted into 2-phenyl-4-hexafluoroisopropylideneoxazolone-5 (IV):



$$\mathrm{(CF_3)_2C{=}C(COOH)(NHCOC_6H_5)}\ \text{(I)} \xrightarrow[\text{or }\mathrm{(CH_3CO)_2O}]{\mathrm{CH_2CO}} \begin{array}{c}\mathrm{(CF_3)_2C{=}C-CO}\\ |\quad|\\ \mathrm{N}\quad\mathrm{O}\\ \backslash\mathrm{C}/\\ |\\ \mathrm{C_6H_5}\end{array}\qquad \text{(IV)}$$

Cyclization of α-benzamidohexafluorodimethylacrylic acid also takes place under the action of hexafluoroacetone.

Table 1

Interaction of 2-phenyl-4-hexafluoroisopropylideneoxazolone-5 with nucleophilic reagents

Nucleophilic compound	Reaction product	Solvent	Reaction duration, h	Yield of theory, %	M.p., °C	Found, % C	Found, % H	Found, % F	Found, % N	Calculated, % C	Calculated, % H	Calculated, % F	Calculated, % N
Water	α-Benzamidohexafluorodimethylacrylic acid * (I)	Ether	190	57	164 – 166 (with decomp.)(from dichloroethane)	44,30 44,19	2,16 2,15	35,25 34,30	4,38	44,04	2,16	34,84	4,28
Methanol	Methyl ester of α-benzamidohexafluorodimethylacrylic acid ** (V)	Benzene ***	20	93,5	86 – 86,5(from hexane)	46,04 45,94	2,71 2,67	34,41 33,96	4,45	45,76	2,66	33,41	4,11
Ethanol	Ethyl ester of α-benzamidohexafluorodimethylacrylic acid (VI)	Benzene ***	24	95	57 – 57,5(from hexane)	47,34 47,10	3,02 3,09	32,25 32,45		47,33	3,12	32,09	3,94
Ammonia	Amide of α-benzamidohexafluorodimethylacrylic acid (VII)	Ether	5	37	147 – 147,5(from benzene)	44,30 44,50	2,46 2,36	34,28 34,90	8,91	45,18	2,47	34,95	8,59
Ammonia ****	Amide of α-amino-α-benzamido-bis(trifluoromethyl)propionic acid * (XI)	Benzene,	0,3	91,8	140 – 145 (with decomp.)(from benzene)	42,34 42,33	3,23 3,41	31,58 31,28	12,26 12,14	41,99	3,23	33,21	12,25

Nucleophilic compound	Reaction product	Solvent	Reaction duration, h	Yield of theory, %	M.p., °C	Found, % C	Found, % H	Found, % F	Found, % N	Calculated, % C	Calculated, % H	Calculated, % F	Calculated, % N
Aniline	Anilide of α-benzamidohexafluorodimethylacrylic acid * (II)	Benzene	0,1	60	215—215,5 (with decomp.)(from aq. alcohol)	53,65	3,07	28,29	6,94	53,74	3,01	28,34	6,97
Benzylamine	Benzylamide of α-benzamidohexafluorodimethylacrylic acid (VIII)	Benzene	0,1	86	180—181 (from alcohol)	54,67	[illegible]	28,97	28,71	54,81	3,39	27,38	6,73
Thiophenol	Thiophenyl ester of α-benzamidohexafluorodimethylacrylic acid * (IX)	Ether	2	47,6	115,5—117,5(from hexane)	51,89	[illegible]	[illegible]	26,41	51,54	2,64	27,18	3,34
Ethyl ester of glycine	Ethyl ester of N-(α-benzamidohexafluorodimethylacrylyl)glycine (X)	Ether	24	77,3	133,5—135(from benzene)	46,34	[illegible]	[illegible]	[illegible]	46,61	3,42	27,65	6,80

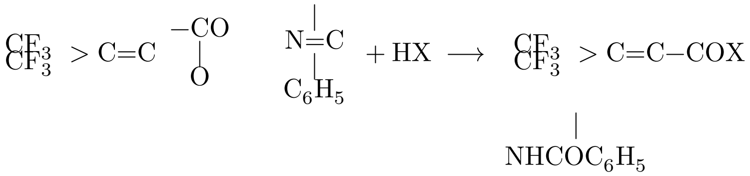
* 2-Phenyl-4-isopropylideneoxazolone-5 does not react under the same conditions.

** V was also obtained by treating I with diazomethane in ether solution.

*** In the presence of catalytic amounts of triethylamine; the reaction also oc-

curs without catalyst in excess alcohol, but the product is obtained in poorer yield.
**** Excess ammonia.

2-Phenyl-4-hexafluoroisopropylideneoxazolone-5 (IV) proved to be much more reactive than its nonfluorinated analog, 2-phenyl-4-isopropylideneoxazolone-5. Even at room temperature and without catalysts it readily enters into reactions with nucleophilic compounds (water, alcohols, ammonia*, aniline, benzylamine, thiophenol, ethyl glycinate), forming the corresponding derivatives of α-benzamidohexafluorodimethylacrylic acid (I, II, V–X)



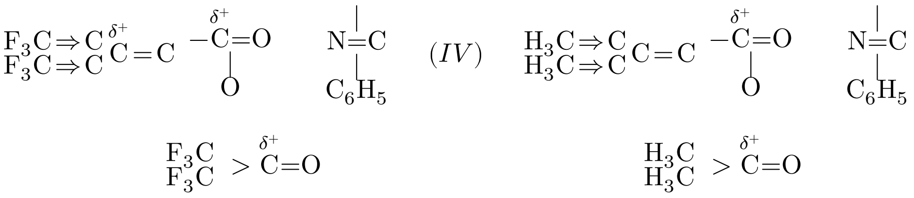
$$\begin{array}{l}CF_3\\CF_3\end{array} > C{=}C\begin{array}{c}-CO\\ |\\ O\end{array}\quad\begin{array}{c}|\\N{=}C\\|\\C_6H_5\end{array} + HX \longrightarrow \begin{array}{l}CF_3\\CF_3\end{array} > \begin{array}{c}C{=}C{-}COX\\ |\\ NHCOC_6H_5\end{array}$$

	I	V	VI	VII	II	VIII	IX	X
$X =$	OH	OCH_3	OC_2H_5	NH_2	NHC_6H_5	$NHCH_2C_6H_5$	SC_6H_5	$NHCH_2COOC_2H_5$

The nonfluorinated analog, 2-phenyl-4-isopropylideneoxazolone-5, reacts with similar compounds under much more severe conditions—on heating or in the presence of catalysts (acids and alkalis) ($^{6-14}$).

The ease with which 2-phenyl-4-hexafluoroisopropylideneoxazolone-5 (IV) reacts with nucleophilic agents is probably explained by the fact that the presence of electron-acceptor trifluoromethyl groups decreases the electron density at the carbonyl carbon atom through the combined action of the conjugation effect and the inductive effect, whereas in 2-phenyl-4-isopropylideneoxazolone-5 the electron-donor methyl groups act in the opposite direction. Oxazolone IV may be regarded as a vinylog of hexafluoroacetone; the latter, as is known, reacts with nucleophilic compounds much more readily than acetone (^{1},^{2}):

hexafluoroacetone vinylog (IV): acetone analog:



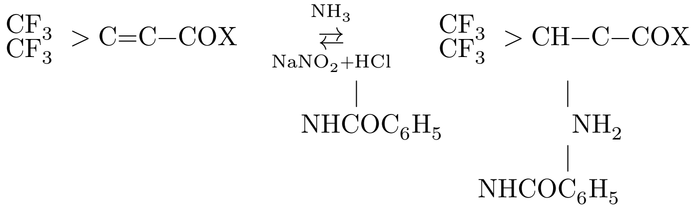
$$\begin{array}{l}F_3C\Rightarrow C\\F_3C\Rightarrow C\end{array}\overset{\delta^+}{C}=C\begin{array}{c}-\overset{\delta^+}{C}=O\\|\\O\end{array}\quad\begin{array}{c}|\\N=C\\|\\C_6H_5\end{array}\quad (IV)\quad\begin{array}{l}H_3C\Rightarrow C\\H_3C\Rightarrow C\end{array}C=C\begin{array}{c}-\overset{\delta^+}{C}=O\\|\\O\end{array}\quad\begin{array}{c}|\\N=C\\|\\C_6H_5\end{array}$$

$$\begin{array}{l}F_3C\\F_3C\end{array} > \overset{\delta^+}{C}=O \qquad\qquad \begin{array}{l}H_3C\\H_3C\end{array} > \overset{\delta^+}{C}=O$$

Experimental part

α-Benzamidohexafluorodimethylacrylic acid (I). 38 g of hexafluoroacetone was passed into a solution of 18.8 g of 2-phenyloxazolone-5 in 80 ml of pyridine with cooling by ice water. After being kept at room temperature for 1 hour, the mixture was poured into dilute hydrochloric acid with cooling. The oil was extracted with ether, the ethereal extract was dried, and the ether and the excess hexafluoroacetone hydrate were distilled off. Yield: 21.69 g (56.8% of theory) of I; m.p. and the results of elemental analysis are given in Table 1. The same acid was obtained from hexafluoroacetone and hippuric acid on heating to 50–60° in acetic anhydride in the presence of sodium acetate.

* With excess ammonia, the amide of α-amino-α-benzamido-bis(trifluoromethyl)propionic acid (XI) is obtained. Ammonia also readily adds to the methyl ester of α-benzamidohexafluorodimethylacrylic acid, forming the methyl ester of α-amino-α-benzamido-bis(trifluoromethyl)propionic acid (XII); it is of interest that, on treatment with nitrous acid, these compounds eliminate ammonia and are converted into the starting unsaturated compounds (V):



$$\begin{matrix} CF_3 \\ CF_3 \end{matrix} > C{=}\underset{\substack{| \\ NHCOC_6H_5}}{C}{-}COX \underset{NaNO_2+HCl}{\overset{NH_3}{\rightleftarrows}} \begin{matrix} CF_3 \\ CF_3 \end{matrix} > CH{-}\underset{\substack{| \\ NH_2 \\ | \\ NHCOC_6H_5}}{C}{-}COX$$

(V) $X = OCH_3$; XII $X = NH_2$ (XII) $X = OCH_3$; XI $X = NH_2$

For the order of addition to an unsaturated system containing two trifluoromethyl groups, see ([3],[5]).

Anilide of α-benzamidohexafluorodimethylacrylic acid (II). Into a solution of 0.52 g of α-benzamidohexafluorodimethylacrylic acid (I) in 4 ml of pyridine, 2.8 g of hexafluoroacetone was passed. On cooling, 2 ml of aniline was added; the mixture was kept at room temperature for 20 min and then poured into dilute hydrochloric acid; the resulting solid was recrystallized from aqueous alcohol. Yield 0.11 g (17.4% of theory); m.p. and results of elemental analysis, see Table 1.

II is also formed on treatment with aniline of a pyridine solution of 2-phenyl-4-hexafluoroisopropylideneoxazolone-5 (IV), obtained from hexafluoroacetone and 2-phenyloxazolone-5 (see preparation of I).

2-Phenyl-4-hexafluoroisopropylideneoxazolone-5 (IV). An excess of ketene (about 7 g) was passed into a solution of 7.0 g of α-benzamidohexafluorodimethylacrylic acid (I) in 30 ml of absolute ether over the course of 30 min. After removal of the solvent, 6.1 g (92% of theory) of IV was obtained, m.p. 82-84° (from hexane).

Found, %:	C 46.43; H 1.60; F 36.37; N 4.53
$C_{12}H_5F_6O_2N$. Calculated, %:	C 46.61; H 1.63; F 36.87; N 4.53

IV was also obtained by heating acid I with acetic anhydride on a boiling water bath.

Interaction of 2-phenyl-4-hexafluoroisopropylideneoxazolone-5 (IV) with nucleophilic reagents. All the nucleophilic reagents tested react with 2-phenyl-4-hexafluoroisopropylideneoxazolone-5 at room temperature without a catalyst in ether or benzene solution; the reagents were usually taken in equimolar amounts (hydrolysis of IV with water was carried out by shaking its ether solution with an excess of water).

The yields, melting points, and results of elemental analysis of the products obtained are given in Table 1.

Methyl ester of α-amino-α-benzamido-bis(trifluoromethyl)propionic acid (XII). Into a solution of 6.82 g of the methyl ester of α-benzamidohexafluorodimethylacrylic acid (V) in 50 ml of absolute ether, a large excess of gaseous ammonia was passed at room temperature. By cooling the solution to −70°, XII was isolated; yield 5.0 g (69.7% of theory), m.p. 99.5-103.5° (from hexane).

Found, %:	C 43.10; 43.24; H 3.33; 3.31; F 31.23; 31.16; N 7.83; 7.81
$C_{13}H_{12}F_6O_3N_2$. Calculated, %:	C 43.58; H 3.37; F 31.82; N 7.82

On treatment of a solution of XII in dilute hydrochloric acid with sodium nitrite, V was obtained, m.p. 84-86° (from hexane); a mixture with an authentic sample of V gives no depression of the melting point.

Institute of Organoelement Compounds
Academy of Sciences of the USSR

Received
26 V 1960

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Note: Figure translations are in progress. See original paper for figures.