FLUORO-CONTAINING HETEROCUMULENES

COMMUNICATION 7.* REACTION OF BIS(TRIFLUOROMETHYL)KETENE WITH DIAZOMETHANE AND ISONITRILES

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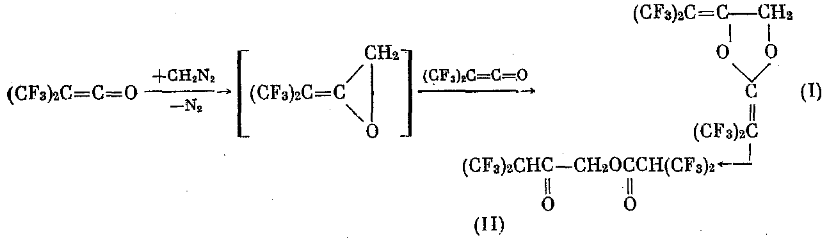
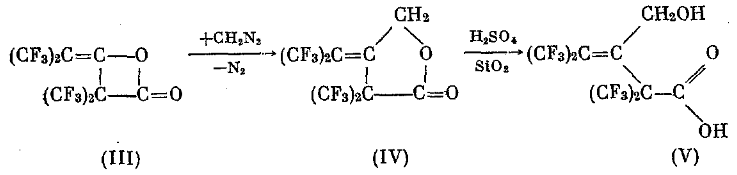
The reaction of dimethylketene with CH_2N_2 gives dimethylcyclopropanone [2]. In order to obtain a fluoro-containing cyclopropanone we reacted bis(trifluoromethyl)ketene with CH_2N_2 but the methylene insertion product could not be obtained. Apparently, this product is formed at low temperatures (GLC data), but even at 0°C it reacts with the next fluorinated ketene to give the substituted dioxolane (I)



The structure of adduct (I) was proved by its acid hydrolysis to acyloxy ketone (II), and also by the spectroscopic data. Absorption at 1685 cm^{-1} is observed in the IR spectrum of dioxalane (I), which corresponds to the band of the stretching vibrations of the C = C bond, and the absorption bands of the CO group are absent; the signals, observed in the ^{19}F NMR spectrum (multiplets at −183 and −21.4 ppm), correspond to the CF_3 with an sp^2 hybridized C atom (cf. [3]); finally, the chemical shift of the CH_2 group in the NMR spectrum (5.48 ppm) indicates that it enters into the composition of a five-membered, and not a three-membered ring (cf. [4]). Consequently, both bis(trifluoromethyl)ketene molecules react at the CO group in the formation of adduct (I).

It is known that bis(trifluoromethyl)ketene is dimerized under the influence of weak nucleophiles [5]. However, as the results obtained by us show, such dimerization fails to occur when reaction is with CH_2N_2. If the finished dimer (III) is reacted with CH_2N_2, then the product of inserting the CH_2 group into the β-lactone ring (IV) is formed.† The structure of the formed γ-lacetone (IV) follows from the spectral data and hydrolysis to acid (V)



Isonitriles react with bis(trifluoromethyl)ketene in the same manner as diazomethane. Both ketene molecules react at the CO group to give iminodioxolanes (VI), whereas perfluorinated ketenes react at the C = C bond [6]

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*See [1] for Communication 6.

†Data on the reaction of CH_2N_2 with β-lactones were not found in the literature.

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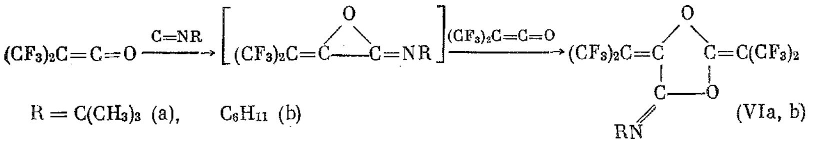
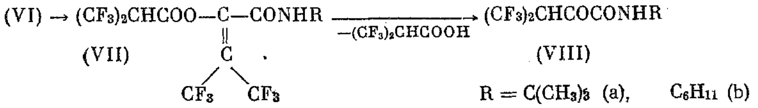


$R = C(CH_3)_3$ (a), C_6H_{11} (b)

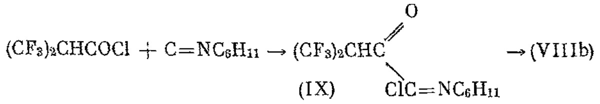
(VIa, b)

The structure of the (VI) dioxolanes was established by the IR, NMR and mass spectra. The obtained compounds are unstable and on long standing in the air, or when treated rapidly with conc. H_2SO_4, they add a molecule of water and change to the (VII) amides, which, in turn, are easily hydrolyzed to the amides of bis(trifluoromethyl)pyruvic acid (VIII).



(VII) (VIII) $R = C(CH_3)_3$ (a), C_6H_{11} (b)

Amide (VIIIb) was obtained by counter synthesis, by the reaction of hexafluoroisobutyryl chloride with cyclohexyl isonitrile and subsequent hydrolysis of the adduct (IX) (cf. [7]).



(IX)

This reaction is a convenient method for the preparation of fluoro-containing pyruvic acid derivatives, which can compete successfully with other methods [8].

As a result, the reactions of bis(trifluoromethyl)ketene with CH_2N_2 and isonitriles again illustrated the peculiar tendency of the fluorinated ketene to react at the C = O group (cf. [5]), whereas the reactions at the C = C bond are characteristic for the unfluorinated analogs.

EXPERIMENTAL METHOD

The IR spectra were taken on a UR-20 instrument. The NMR spectra were taken on a Perkin–Elmer R-12 instrument (60 MHz), using HMDS as the internal standard. The ^{19}F NMR spectra were taken on a Hitachi instrument (56.46 MHz). The chemical shifts are given in parts per million relative to CF_3COOH as the external standard.

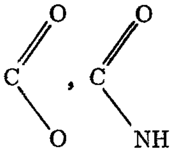
2,4-Bis(hexafluoroisopropylidene)-1,3-dioxolane (I). To a solution of 9 g of bis(trifluoromethyl)ketene in 15 ml of absolute ether was slowly added at –70° an ether solution of CH_2N_2 until decolorization ceased. GLC analysis of the cold reaction mixture disclosed the presence of a volatile component, which gradually changed to dioxolane (I) when the mixture was warmed up to 0°. After distilling off the ether we obtained 6.5 g (70%) of (I) with mp 58-59° (from CCl_4). Found: C 29.14; H 0.56; F 61.24%. $C_9H_2F_{12}O_2$. Calculated: C 29.19; H 0.54; F 61.62%. Infrared spectrum (ν, cm^{-1}): 1685 (C = C), 1750 (w). NMR spectrum (in C_6H_6): 5.48 (CH_2, singlet). ^{19}NMR spectrum: –18.3 [$(CF_3)_2C=$, multiplet]; –21.4 [$(CF_3)_2C=$, multiplet]. Molecular weight of (I) = 370 (mass spectrometry).

Hydrolysis of 1,3-Dioxolane (I). A mixture of 0.5 g of dioxolane (I) and 2 ml of conc. H_2SO_4 was shaken until the crystals dissolved. The next day the reaction mixture was poured over ice. We obtained 0.5 g (98%) of acyloxy ketone (II) with mp 39-41° (from CCl_4). Found: C 28.03; H 1.12; F 59.18%. $C_9H_4F_{12}O_3$. Calculated: C 27.83; H 1.54; F 58.75%. Infrared spectrum (ν, cm^{-1}): 1760, 1780 (C = O). NMR spectrum (in CH_3CN): 4.16 (CH_2, singlet); 3.38 (2[$(CF_3)_2CH$], heptet), J_{H-F} 8.0 Hz. ^{19}F NMR spectrum (in CH_3CN): –14.6 [$(CF_3)_2CH$, doublet], J_{FH} 8.0 Hz; –13.6 [$(CF_3)_2OH$, doublet], J_{FH} 8.0 Hz.

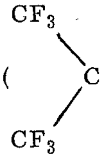
3-Bis(trifluoromethyl)-4-hexafluoroisopropylidene-γ-butyrolactone (IV). To a solution of 2.5 g of the β-lactone dimer (III) in 5 ml of absolute ether was slowly added at –78° an ether solution of CH_2N_2 until the decolorization ceased. The temperature was brought up to ~20°. We obtained 1.5 g (58%) of (IV) with bp 75° (40 mm). Found: C 29.09; H 0.52%. $C_9H_2F_{12}O_2$. Calculated: C 29.19; H 0.54%. Infrared spectrum (ν, cm^{-1}): 1650 (C = C), 1810 (C = O). NMR spectrum (in CCl_4): 4.67 (CH_2, singlet). ^{19}F NMR spectrum (in CCl_4): –19.4 ($CF_3C=$, multiplet); –18.4 ($CF_3C=$, quartet), J_{FF} 8.0 Hz; –16.3 [$(CF_3)_2C$, quartet], J_{FF} 12.8 Hz.

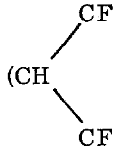
Hydrolysis of γ-Lactone (IV). A mixture of 1.23 g of γ-lactone (IV), 4 ml of conc. H_2SO_4 and 1 g of SiO_2 was heated at 100° for 9 h, cooled, and poured over ice. The obtained crystals were filtered and washed with water. We obtained 1 g (78%) of (V) with mp 66-68° (from CCl_4). Found: C 27.42; H 1.54; F 58.15%. $C_9H_4F_{12}O_3$. Calculated: C 27.83; H 1.54; F 58.75%. Infrared spectrum (ν, cm^{-1}): 1645 (C=C), 1730, 1760 (C=O). NMR spectrum (in C_6H_6): 4.88 (CH_2, singlet). ^{19}F NMR spectrum (in ether): −14.8 [$(CF_3)_2C$, multiplet]; −20.2 ($CF_3C=$, quartet), J_{FF} 9.6 Hz; −22.6 ($CF_3C=$, multiplet). Mol. wt. of (V) = 388 (mass spectrometry).

5-tert-Butylimino-2,4-bis(hexafluoroisopropylidene)-1,3-dioxolane (VIa). Into a solution of 2.7 g (0.03 M) of tert-butyl isonitrile in 15 ml of absolute ether at −40 to −30° was passed 11.6 g (0.06 M) of bis(trifluoromethyl)ketene. The temperature was brought up slowly to 0°, and by freezing with CO_2 we isolated 10.2 g (72%) of (VIa) with mp 67-69° (by freezing from hexane). Found: C 35.47; H 2.03; F 51.90; N 3.22%. $C_{13}H_9F_{12}NO_2$. Calculated: C 35.51; H 2.05; F 51.93; N 3.19%. Infrared spectrum (ν, cm^{-1}): 1680 (C=C), 1710 (C=N). ^{19} NMR spectrum (in CCl_4): −22.8 ($CF_3C=$, quartet), J_{FF} 10.6 Hz; −21.7 [$(CF_3)_2C$, multiplet]; −20 ($CF_3C=$, quartet), J_{FF} 10.6 Hz.

Hydrolysis of Dioxolane (VIa). a) The crude dioxolane (VIa) (3.6 g) was allowed to stand in a loosely stoppered flask for 2 months. We obtained 1.7 g (47%) of (VIIa) with mp 125-126° (from C_6H_6). Found: C 33.79; H 2.51; F 50.27%. $C_{13}H_{11}F_{12}NO_3$. Calculated: C 34.14; H 2.40; F 49.89%. Infrared spectrum (ν, cm^{-1}): 1550, 1680, 1790, 3310 (C=C,  $\mathrm{C(=O)O}$, $\mathrm{C(=O)NH}$). ^{19}F NMR spectrum (in CH_3CN): −13.7 [$(CF_3)_2 \cdot CH$, broad doublet]; −17.7 ($CF_3C=$, undeciphered multiplet); −19.1 ($CF_3C=$, quartet), J_{FF} 10.6 Hz.

b) To an ether solution of dioxolane (VIa) was added 1 drop of water. The next day the ether was evaporated, and the residue was recrystallized from C_6H_6. We obtained crystals with mp 125-126°, which were identical with those obtained in the proceding experiment.

5-Cyclohexylimino-2,4-bis(hexafluoroisopropylidene)-1,3-dioxolane (VIb). To a solution of 5.2 ml (0.04 M) of the ketene in 10 ml of absolute ether was added in drops, at −50°, 2.18 g (0.02 M) of cyclohexyl isonitrile in 10 ml of absolute ether. A part of the solvent was then distilled off, and by freezing we isolated 7.9 g (85%) of the (VIb) crystals with mp 51-55° (by freezing from hexane). Found: N 3.02%. $C_{15}H_{11}F_{12}NO_2$. Calculated: N 3.01%. Infrared spectrum (ν, cm^{-1}): 1680 (C=C), 1710 (C=N). ^{19}F NMR spectrum (in ether): −19.1 ($CF_3C=$, quartet); −21.7 ($CF_3C=$, quartet), J_{FF} 8.8 Hz; −20.8 ( $\mathrm{(CF_3)_2C=}$, multiplet). Mol. wt. of (VIb) = 465 (mass spectrometry).

Hydrolysis of dixolane (VIb). With cooling, 15 ml of conc. H_2SO_4 was added to 1.4 g of dioxolane (VIb). After 10 min the mixture was poured over ice and the obtained crystals were filtered. We obtained 1.2 g (82%) of the (VIIb) crystals with mp 125-126° (from CCl_4). Found: C 37.41; H 2.61; F 46.77%. $C_{15}H_{13}F_{12} \cdot NO_3$. Calculated: C 37.26; H 2.69; F 47.20%. Infrared spectrum (ν, cm^{-1}): 1580, 1670, 1690, 1787 (C=C, C=O, CONH), 3300 (NH). NMR spectrum (in acetone): 3.65 (CH, multiplet); 5.55 ( $\mathrm{CH(CF_3)_2}$, heptet), J_{HF} 8.0 Hz; 8.05 (NH, broad singlet). ^{19} NMR spectrum (in acetone): −13.4 [$(CF_3)_2CH$, broad doublet]; −17.7 (undeciphered multiplet); −19.4 ($CF_3C=$, quartet), J_{FF} 8.0 Hz. Mol. wt. of (VIIb) = 483 (mass spectrometry).

Cyclohexylamide of Bis(trifluoromethyl)pyruvic Acid (VIIIb). a) One gram of dioxolane (VIb) was dissolved in 6 ml of ethanol, saturated with HCl. The mixture was allowed to stand at ~20° for 10 h, and then it was poured into water. Filtration gave 0.4 g (61%) of the (VIIIb) crystals with mp 111-115° (from hexane). Found: C 43.27; H 4.27; F 37.24; N 4.59%. $C_{11}H_{13}F_6NO_2$. Calculated: C 43.27; H 4.26; F 37.37; N 4.59%. Infrared spectrum (ν, cm^{-1}): 1540, 1680 (CONH), 1750 (C=O), 3340 (NH). ^{19}F NMR spectrum (in acetone): −14.6 [$(CF_3)_2CH$, doublet], J_{FH} 8.0 Hz. Mol. wt. of (VIIIb) = 305 (mass spectrometry). The filtrate was extracted with ether to give the ethyl ester of monohydrohexafluoroisobutyric acid (GLC).

b) To 0.26 g of dioxolane (VIb) in 10 ml of ether was added 4 drops of water. After three days we isolated from the mixture of 0.15 g (90.3%) of the (VIIIb) crystals with mp 111-115° (from hexane), which were identical with the crystals obtained in the preceding experiment. Monohydrohexafluoroisobutyric acid was detected (GLC and ^{19}F NMR data) in the filtrate.

N-Cyclohexylimidoyl Chloride of Bis(trifluoromethyl)pyruvic Acid (IX). With stirring, to 11.5 g of hexafluoroisobutyryl chloride at 0° was added 2.8 g of cyclohexyl isonitrile in drops. The mixture was kept at the same temperature overnight. We obtained 8 g (96.3%) of (IX) with bp 68° (3 mm). Found: C 40.83; H 3.77; F 35.33; Cl 10.93; N 4.16%. $C_{11}H_{12}F_6ClNO$. Calculated: C 40.86; H 3.74; F 35.29; Cl 10.83; N 4.33%. Infrared spectrum (ν, cm^{-1}): 1640 (C=N), 1745 (C=O). ^{19}F NMR spectrum: −14.3 [$(CF_3)_2CH$, doublet].

Hydrolysis of Imidolyl Chloride (IX). To 1.3 g of imidoyl chloride (IX) was added 4 ml of ethanol, saturated with HCl. After two days we filtered 0.98 g (80.3%) of crystals with mp 111-114°, which were identical with (VIIIb).

CONCLUSIONS

1. Bis(trifluoromethyl)ketene reacts with diazomethane and with isonitriles at its carbonyl group to give 1,3-dioxolanes.

2. The reaction of diazomethane with the β-lactone dimer of bis(trifluoromethyl)ketene was studied.

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