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Reaction of Carbodiimides with Trifluoromethanesulfonic Acid

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Abstract—Carbodiimides RN=C=NR (R = *i*-Pr, *c*-C_6H_{11}, Ph) react with trifluoromethanesulfonic acid with successive formation of *O*-triflyl isoureas RNHC(OTf)=NR, the isomeric *N*-triflyl ureas RN(Tf)C(O)NHR, and symmetrically substituted ureas RNHC(O)NHR. Carbodiimide $Me_3SiN{=}C{=}NSiMe_3$ in the reaction with TfOH undergoes desilylation to afford ester $CF_3SO_2OSiMe_3$ and unsubstituted carbodiimide (cyanamide), which gives the products of di- and trimerization and urea.

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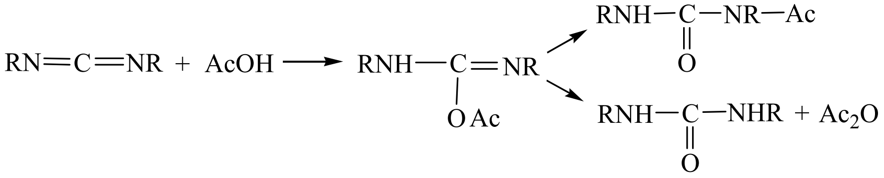
Carbodiimides RN=C=NR are highly electrophilic compounds, which actively react with various proton donors to form either the adducts or the products of their dehydration being converted to ureas $(RNH)_2CO$. In particular, carboxylic acids react with carbodiimides with the initial formation of acylimidocarbamates (*O*-acylisoureas), which further either rearrange to *N*-acylureas or react with the second molecule of the acid to give the corresponding urea and the acid anhydride [1, 2].



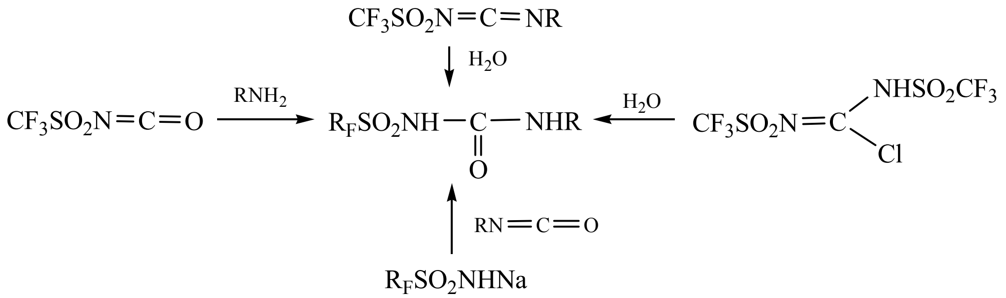
(1)

The structure of *N*-acylurea was proved, in particular, by XRD analysis for the adduct of polyfluorocarboxylic acid $C_6F_{13}(CH_2)_9COOH$ with dicyclohexyl carbodiimide [3].

Unlike the reaction with carboxylic acids, in the reaction with sulfonic acids carbodiimides act only as dehydrating reagents resulting in the formation of ureas and sulfonic acid anhydrides in good yields [1]. There are no data in the literature on the formation of intermediate *O*-alkyl(aryl)sulfonyl isoureas or *N*-alkyl (aryl)sulfonyl ureas, including the recent monograph [4].

At the same time, *N*-sulfonyl ureas show high biological and herbicidal activity [5]. As to perfluoroalkanesulfonyl ureas, several methods of their preparation are known. The first one was the reaction of trifluoromethylsulfonyl isocyanate with aniline [6] and other amines [7, 8]. The second method is the hydrolysis of *N*-trifluoromethylsulfonylcarbodiimides (*N*-triflylcarbodiimides) $CF_3SO_2N{=}C{=}NR$ (R = H, $SiMe_3$). The latter are obtained by the reaction of trifluoromethanesulfonic anhydride with bis(trimethylsilyl)carbodiimide [9], or by the aza-Curtius rearrangement in the reaction of *N*-(triflyl)carboxyimidoyl chloride with sodium azide [8], or by the rearrangement of *O*-trimethylsilyl- and *O*-tosylsubstituted triflylimides of arenehydroxamic acids [10]. The third methos is the hydrolysis of *N,N'*-bis(triflyl)carbamoyl chloride [11]. Finally, as the most available method for the synthesis of perfluoroalkylsulfonyl ureas, the reaction of sodium salts of perfluoroalkanesulfonamides with isocyanates in yields from 49 to 84% was claimed [5].

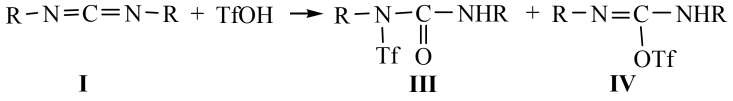
As follows from Eqs. (2), all these methods suggest the involvement in the process of different derivatives of triflamide $CF_3SO_2NH_2$ or its analogs. With this in mind and aiming at the elucidation of the possibility of



(2)

formation of *O*-triflyl isoureas and(or) *N*-triflyl ureas similar to *O*-acyl isoureas and *N*-acyl ureas shown in Scheme (1) as well as elaboration of the method of preparation of *N*-triflyl ureas based on the most accessible triflate starting materials, we have studied the reaction of carbodiimides RN=C=NR (**I**) [R = *i*-Pr (**a**), *c*-C_6H_{11} (**b**), Ph (**c**), Me_3Si (**d**)] and cyanamide H_2NCN (**II**) with trifluoromethanesulfonic acid (TfOH).

Carbodiimides **Ia–Ic** exothermically react with TfOH in methylene chloride solution at room temperature according to reaction (3) with the formation of high-melting solid products representing the mixtures of the isomeric adducts, *N*-triflyl ureas (**III**) and *O*-triflyl isoureas (**IV**), which were identified by IR spectroscopy.



$$\underset{\textbf{I}}{R{-}N{=}C{=}N{-}R} + TfOH \rightarrow \underset{\textbf{III}}{R{-}\underset{Tf}{N}{-}\underset{O}{\overset{}{C}}{-}NHR} + \underset{\textbf{IV}}{R{-}N{=}\underset{OTf}{C}{-}NHR} \quad (3)$$

In the IR spectra of *N*-triflyl ureas (**IIIa, IIIb**) in KBr the ν(C=O) stretching vibrations band at 1694 cm^{-1} is present, which coincides with the ν(C=O) band in compounds $R_FSO_2NHC(O)NHR$ [5, 6]. The band has a low-frequency shoulder at 1678 (**IIIa**) or 1667 cm^{-1} **IIIb**, which, on the basis of the literature data [12] was assigned to the stretching vibrations ν(C=N) in *O*-triflyl ureas (**IV**). In the IR spectra of the products the stretching vibration bands ν(NH) at 3370 (**IIIa**) or 3440 cm^{-1} **IIIb** and the bending vibrations δ(NH) at 1537 and 1282 cm^{-1} (**IIIa**) or 1527 and 1264 cm^{-1} (**IIIb**) are also present.

On addition of TfOH to the solution of diphenylcarbodiimide **Ic** in methylene chloride the solution instantly turns bright-yellow. For the reaction products **IIIc** and **IVc** the corresponding bands in the IR spectra are notably shifted to low frequencies and appear at 1674 (**IIIc**) and 1637 cm^{-1} (**IVc**). The observed ν(C=O) and ν(C=N) frequency values for compounds **IIIa–IIIc** and **IVa–IVc** are substantially higher than the ν(C=O) frequencies in the symmetrically substituted ureas RNH–C(O)–NHR (**V**), equal to 1629, 1626 and 1612 cm^{-1} for R = *i*-Pr, *c*-C_6H_{11} and Ph, respectively. This is indicative of a larger double-bonding character of the C=N and C=O bonds in compounds **III** and **IV** as compared to the C=O bond in compounds **V** due to strong electron-withdrawing effect of the triflyl group decreasing the polarization of this bond.

The IR monitoring of the reaction was performed by the example of the reaction with carbodiimide **Ib**. In the spectrum of the precipitate separated in a small amount from the reaction mixture, the major band is ν (C=O) band of product **IIIb** (see Fig. 1a). In the spectrum of the main product obtained after evaporation of the filtrate, the ν(C=N) band of product **IVb** and ν(C=O) bands of products **IIIb** and **Vb** with close peak intensities are present (see Fig. 1b). Finally, after the treatment of this product with water, practically only the low frequency band belonging to urea **Vb** remains (see Fig. 1c). All this points to the order of transformations **I** → **IV** → **III** → **V**, which is similar to that described in review [2] for the reaction of carbodiimides with carboxylic acids. According to these data, the formation of *N*-acyl ureas is favored by the higher temperature and the duration of the process [2]. We observed the same temperature dependence for the reaction of carbodiimides **Ia, Ib** with TfOH. When carrying out the reaction of compound **Ia** with TfOH at –30 to –40°C for 2 days, the precipitate was not formed even on the next day, and the IR spectrum after removal of the solvent contains the ν(C=O) band of **IIIa** only as a shoulder on the high-frequency wing of the ν(C=N) band of **IVa**.

It is known that in low polar solvents like CH_2Cl_2, isoureas from carbodiimides and carboxylic acids are formed instantly and in the absence of a nucleophile or base they can exist during several hours [13]. In our case, isourea **IVb** stabilized by the triflyl substituent undergoes rearrangement to compound **IIIb** and hydrolysis to urea **Vb** only upon boiling in water.

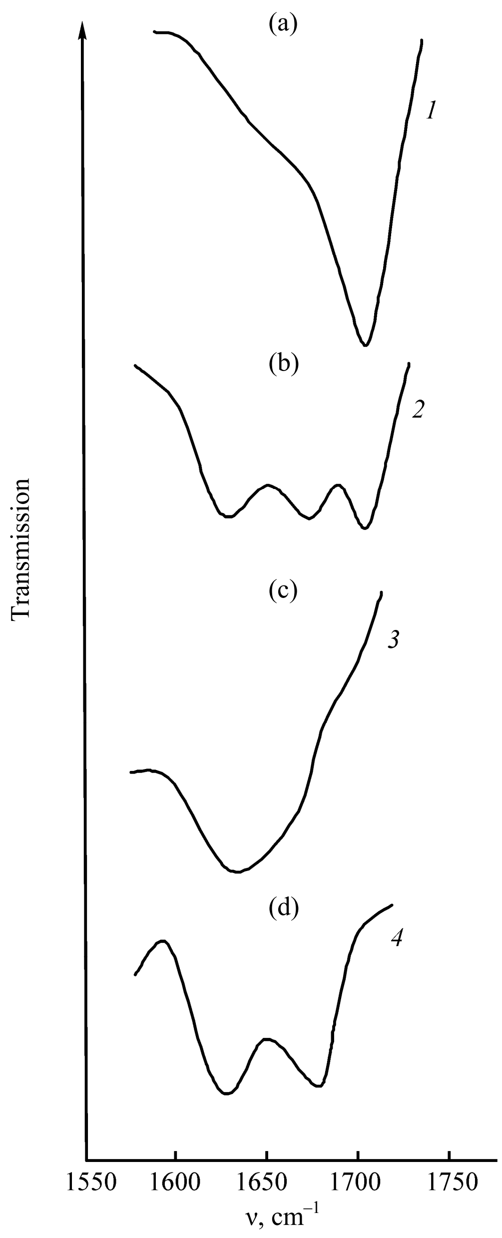
For the synthesis of *N*-acyl ureas not only the reaction with carboxylic acids but the transfer of the acyl group from their ammonium salts to carbodiimides is employed [3]. However, this technique cannot be applied to the triflate salts: the triethyl amine or pyridine triflates do not react with carbodiimide **Ib** even upon prolonged reflux in $CHCl_3$.

^1H and ^{13}C NMR spectra of the products of the reaction of trifluoromethanesulfonic acid with carbodiimides **Ia–Ic** are complicated not only due to overlapping of the signals of the two isomeric forms **III** and **IV**, but also due to nonequivalence of substituents R. Note that such nonequivalence was observed even in the formally symmetrical isoelectronic analogs of *O*-triflyl ureas (**IV**), *N*-triflyl guanidines $(RNH)_2C=NTf$ [14, 15].

Reaction of carbodiimide **Id** with one equivalent of TfOH proceeds with the formation of the products of exchange of one trimethylsilyl group with the triflyl group, *N*-triflyl-*N*'-trimethylsilylcarbodiimide **VI** and silanol **VII**. Close analog of reaction (4) is the desilylation of carbodiimide **Id** under the action of trifluoroacetic anhydride or trifluoroacetyl chloride [16].

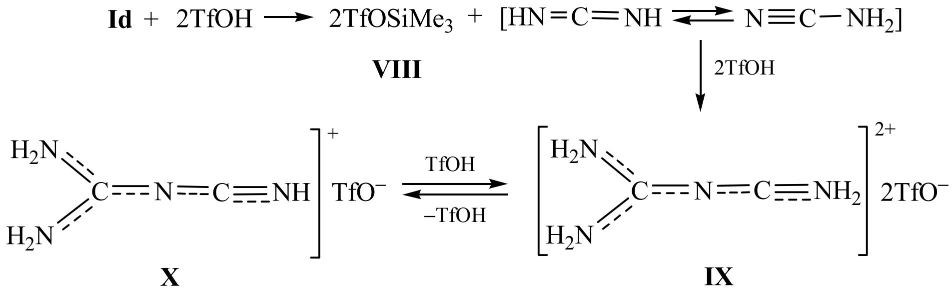
$$\underset{\textbf{Id}}{Me_3Si{-}N{=}C{=}N{-}SiMe_3} + TfOH \longrightarrow \underset{\textbf{VI}}{TfN{=}C{=}N{-}SiMe_3} + \underset{\textbf{VII}}{Me_3SiOH} \tag{4}$$

This is indicated by the shift of the ν(N=C=N) band from the value of 2203 cm^{-1} characteristic of compound **Id** to 2230 cm^{-1} coinciding with the literature data for compound (VI) [9]. The only signal in the ^{19}F NMR spectrum of the product of reaction (4) (–79.3 ppm) also coincides with that known for compound **VI** (–79.5 ppm) [8]. Compound **VI** is presented in the carbodiimide form, although the possibility of the carbodiimide–cyanamide isomerization was studied [17, 18]. The formed trimethylsilanol **VII** is converted into hexamethyldisiloxane, as proved by the presence of the intense ν(SiOSi) band at 1056 cm^{-1} in the IR spectrum, and a signal at 7.7 ppm in the ^{29}Si NMR spectrum that is in the region typical for siloxanes. The product of the reaction is a liquid that solidified upon storage. The IR spectrum has broadened bands in the range 3190–3360, 2220–2230, and 1550–1660 cm^{-1}, which become wider and merge in time. Apparently, this is the result of the processes of dimerization and trimerization typical for trifluoromethylsulfonyl carbodiimides [4] as well as of hydrolysis resulting in *N*-sulfonyl-substituted ureas [19].



IR spectra of the products of TfOH reaction with carbodiimides in the range 1550–1750 cm^{-1}. (a) The initial precipitate from the reaction with carbodiimide **Ib**; (b) he precipitate after removal of solvent; (c) after treatment with water; and (d) product of the reaction with carbodiimide **Ia** at –30 to –40°C.

Reaction of carbodiimide **Id** with two equivalents of TfOH leads to a complete desilylation and a formation of trimethylsilyl trifluoromethanesulfonate $CF_3SO_2OSiMe_3$ **VIII**, as is unequivocally proved by a large downfield chemical shift of the ^{29}Si NMR signal equal to 43.2 ppm (δ_{Si} 43.5 ppm [20]).



(5)

The formed carbodiimide existing in equilibrium with the more stable cyanamide tautomer is converted into the dimer, which can exist either as a double salt **IX** or as the mono-salt **X**, as was shown earlier [21]. From the data of elemental analysis, the product of the reaction is mono-salt **X** containing about 20% of salt **IX**. The presence of a wide ν(NH) band in the IR spectrum with several maxima in the range 3230–3430 cm^{-1} is consistent with the formation of salts **IX, X**.

According to reaction (5), the reaction of trifluoromethanesulfonic acid with cyanamide **II** must be similar to its reaction with carbodiimide **Id** in the 2:1 ratio. Indeed, the reaction proceeds with the complete conversion of cyanamide and the formation of double salt **IX** and mono-salt **X**, as well as of urea, the product of hydrolysis of cyanamide.

Therefore, in the reaction of carbodiimides with TfOH we did not observe the formation of the product of dehydration, trifluoromethanesulfonic anhydride with the characteristic ^{19}F NMR signal at –73.6 ppm. In the ^{19}F NMR spectrum of the product of reaction with carbodiimide **Ib** one signal at –78.4 ppm is observed, which is characteristic of substituted amides TfNHR. This is consistent with the order of transformations **I** → **IV** → **III** → **V** found by IR monitoring, and with the described in the literature O→N migration of acyl group in the reaction of carbodiimide **Ib** with carboxylic acids [2].

EXPERIMENTAL

IR spectra were recorded on a Bruker Vertex 70 instrument in KBr and in solutions in CCl_4, $CHCl_3$, and CH_2Cl_2. NMR spectra were registered on a Bruker DPX-400 spectrometer with working frequencies 400 (^1H), 100 (^{13}C), 376 (^{19}F), and 80 MHz (^{29}Si) in CD_3CN (if not stated otherwise). As an internal standard the signals of residual protons (for ^1H spectra) or carbon atoms (for ^{13}C spectra) of the solvent were used, the chemical shifts are given relative to TMS (^1H, ^{13}C, ^{29}Si) and CCl_3F (^{19}F).

N,N-Diisopropylcarbodiimide, *N,N*-dicyclohexylcarbodiimide, and *N,N*-bis(trimethylsilyl)carbodiimide were commercial reagents used without further purification. *N,N*-Diphenylcarbodiimide was prepared from *N,N'*-diphenylurea by the known procedure [22].

***N*-Trifluoromethylsulfonyl-*N,N'*-diisopropyl urea (IIIa).** To the suspension of 0.25 g (2.0 mmol) of carbodiimide **Ia** in 5 ml of CH_2Cl_2 0.30 g (2.0 mmol, 18 ml) of TfOH was added at vigorous stirring and cooling with cold water, the reaction mixture was stirred for 4 h at room temperature and left overnight. The precipitate formed was filtered off and dried in a vacuum. Yield 0.39 g (71%), mp 78°C. IR spectrum (KBr), ν, cm^{-1}: 3372, 2991, 1698, 1662, 1538, 1283, 1241, 1178, 1033, 637. ^1H NMR spectrum, δ, ppm: 5.73 br.s (1H, NH), 3.80–3.70 m (2H, NCH), 1.22 d (12H, CH_3, *J* 6.4 Hz). ^{13}C NMR spectrum, δ_C, ppm: 153.08 (C=O), 120.36 q (CF_3, $^1J_{CF}$ 322.0 Hz), 45.31, 45.15 (NCH), 22.50, 22.47 (CH_3). ^{19}F NMR spectrum: δ_F –79.08 ppm. Found, %: C 34.56; H 5.81; N 10.33; S 11.48. $C_8H_{15}F_3N_2O_3S$. Calculated, %: C 34.78; H 5.47; N 10.14; S 11.61.

***N*-Trifluoromethylsulfonyl-*N,N'*-dicyclohexyl urea (IIIb).** To the suspension of 0.413 g (2.0 mmol) of carbodiimide **Ib** in 5 ml of CH_2Cl_2 0.30 g (2.0 mmol, 18 ml) of TfOH was added at vigorous stirring and cooling with cold water, the reaction mixture was stirred for 6 h at room temperature and left overnight. The precipitate formed was filtered off and dried in a vacuum. Yield of product **IIIb** with the isomeric **IVb** 0.27 g (39%), mp 127°C. IR spectrum (KBr), ν, cm^{-1}: 3440, 3042, 2948, 2866, 1695, 1353, 1283, 1238, 1162, 1030, 636, 516. ^{1}H NMR spectrum, δ, ppm: 7.38 d (1H, NH, J 7.2 Hz), 3.80–3.70 m (0.5H, C$\underline{H}$NTf), 3.70–3.50 m (1.5H, C$\underline{H}$NH), 1.87–1.07 m (20H, CH_2). ^{13}C NMR spectrum, δ_C, ppm: 154.16 and 153.99 (C=O), 121.64 q (CF_3, J 319.8 Hz), 58.75 (TfNC), 51.71 (CNH), 33.61, 32.43, 32.10, 26.31, 26.18, 26.02, 25.84, 25.65, 25.41. ^{19}F NMR spectrum: δ_F –78.78 ppm. Found, %: C 45.91; H 6.50; F 15.92; N 7.77; S 8.84. $C_{14}H_{23}F_3N_2O_3S$. Calculated, %: C 47.18; H 6.50; F 15.99; N 7.86; S 9.00.

***N*-Trifluoromethylsulfonyl-*N,N'*-diphenyl urea (IIIc).** To the suspension of 0.39 g (2.0 mmol) of carbodiimide **Ic** in 3 ml of CH_2Cl_2 0.30 g (2.0 mmol, 18 ml) of TfOH was added at vigorous stirring and cooling with cold water, the reaction mixture was stirred for 3 h at room temperature and left overnight. Yield of product **IIIc** after evaporation of solvent 0.69 g (100%), yellow crystals, mp 120°C. IR spectrum (KBr), ν, cm^{-1}: 3432, 1674, 1637, 1612, 1587, 1492, 1285, 1242, 1227, 1172, 1030, 756, 691, 636. ^{1}H NMR spectrum, δ, ppm: 10.52 br.s (1H, NH), 8.15–7.00 m (10H, Ph). ^{13}C NMR spectrum, δ_C, ppm: 149.91 (C=O), 140.57, 135.42, 131.96, 131.80, 130.06, 128.77, 127.19, 125.43. ^{19}F NMR spectrum: δ_F –79.32 ppm. Found, %: C 48.39; H 3.11; N 7.47; S 8.84. $C_{14}H_{11}F_3N_2O_3S$. Calculated, %: C 48.84; H 3.22; F 16.55; N 8.14; S 9.31.

Reaction of bis(trimethylsilyl)carbodiimide (Id) with TfOH. *a*. To 0.37 g (2.0 mmol) of carbodiimide **Id** in 5 ml of CH_2Cl_2 with stirring and cooling with cold water 0.30 g (2.0 mmol, 0.18 ml) of TfOH was added, the mixture was stirred for 2 h and left overnight. After removal of the solvent 0.4 g of white viscous residue was obtained, which solidified upon storage. IR spectrum (film), ν, cm^{-1}: 2962, 2230, 1658, 1555, 1388, 1259, 1224, 1172, 1041, 846, 768, 640, 519. ^{13}C NMR spectrum (DMSO-d_6), δ_C: 156.89 ppm. ^{19}F and ^{29}Si NMR spectra see in the text.

b. To 0.37 g (2.0 mmol) of carbodiimide **Id** in 5 ml of CH_2Cl_2 0.60 g (4.0 mmol, 0.36 ml) of TfOH was added at stirring and cooling with cold water, the reaction mixture was stirred for 2.5 h and left overbight. The formed fine-dispersed precipitate was filtered off, dried, washed with hot ethyl acetate, and dried to obtain 0.36 g of white fine-dispersed powder, mp 202–204°C. IR spectrum (KBr), ν, cm^{-1}: 3429, 3385, 3348, 3242, 1735, 1696, 1592, 1278, 1244, 1228, 1171, 1031, 640, 518. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 8.0 br.s (2H, NH), 7.1 br.s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 155.74, 154.70, 120.92 q (CF_3, $^{1}J_{CF}$ 321.6 Hz). ^{19}F NMR spectrum: δ_F –77.85 ppm. Found, %: C 14.63; H 2.10; F 25.63; N 21.72; S 12.07. Calculated for the **IX**:**X** = 4:1 mixture of salts, %: C 14.81; H 2.03; F 25.40; N 22.06; S 14.29.

Reaction of cyanamide (II) with TfOH was carried out as above described for the reaction of **Id** with one equivalent of TfOH (*b*). Conversion of cyanamide 100%. IR specrum (KBr), ν, cm^{-1}: 3422, 3364, 3227, 1734, 1696, 1590, 1280, 1251, 1173, 1028, 640, 518. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 7.97 br.s (2H, NH), 7.1 br.s (1H, NH). ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 162.98, 161.87, 155.77, 154.68, 120.94 q (CF_3, $^{1}J_{CF}$ 321.9 Hz). ^{19}F NMR spectrum: δ_F –77.84 ppm.

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