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# Unusual Cyclization of *N*-(1-Aryl-1-chloro-2,2,2-trifluoroethyl)-*N*'-(*p*-tolyl)-carbodiimides in the Presence of Triethylamine

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**Abstract**—1-Aryl-1-chloro-2,2,2-trifluoroethyl)-*N*'-(*p*-tolyl)carbodiimides treated with triethylamine undergo intramolecular cyclization into 4-aryl-6-methyl-2-triethylammonio-4-trifluoromethyl-4-dihydroquinazolidines.

N,N-Disubstituted alkyl- or arylcarbodiimides cleanly take up primary and secondary amines affording tri- and tetrasubstituted guanidines [1,2]. The tertiary amines do not react with carbodiimides although a reaction of diphenylcarbodiimide with compounds containing a tertiary nitrogen, *N*-*n*-alkyloxaziridines, was described [3]. The reaction furnished hexahydro-1,3,5-triazines. Komatsu *et al*. [3] believed that the reaction either occurred through a nucleophilic attack of a nitrogen on the heterocumulene group to form zwitter-ion intermediates, or along [2+3]-cycloaddition path. It was assumed [4] that dimerization of N-sulfonylcarbodiimides catalyzed by pyridine is also accomplished through primary formation of zwitter-ion intermediates. We formerly established [5] that 1-chloroalkylcarbodiimides with alcohols and secondary amines furnished products of respectively carbodiimide and 2,4-diaza-1,3-diene structure. In these conversions the triethylamine served as a hydrogen chloride acceptor. Here are reported results of a new direction we discovered in the reaction between 1-chloroalkylcarbodiimides with triethylamine that led to a nontrivial cyclization.

It was found that the storage for 48 h at room temperature of *N*-(1-aryl-1-chloro-2,2,2-trifluorolethyl)-*N*'-(*p*-tolyl)carbodiimides **Ia–Ic** with a double excess of triethylamine gave rise to fused zwitter-ion structures containing exocyclic triethylammonium fragments: 4-aryl-6-methyl-4-trifluorolmethyl-2-triethylammonio-3,4-dihydroquinazolidines **IIa–Ic**. The comparison of the data obtained with results published in [5] suggests that in the absence of a proton-donor nucleophile its function may be preformed by the triethylamine that attacks the highly electrophilic carbon atom of the heterocumulene group providing imtermediates of A type.The bond between a chlorine and an α-carbon in the latter is strongly polarized, and therefore these intermediates may exist in equilibrium with a diazadiene form B.The presence of a triethylammonium moiety considerably increases the electrophilicity both of the α-carbon intermediate A and the carbon atom in the N-ethylidene fragment in intermediate B. As a result a ring closure at the *ortho*-position of the N-tolyl moiety becomes possible. This cyclization pattern is consistent with a diazadiene scheme we formerly have advanced for the fusion of *N*-alkyl-idene-*N*'-arylureas into quinazolone derivatives [6].

The structure of zwitter-ion heterocyclic systems **IIa–IIc** was proved by spectral studies. The appearance in the $^1$H NMR spectra of doublets belonging to $H^8$ (6.54–6.61 ppm) and $H^7$ (6.80–6.82 ppm) protons (in compound **IIc** the doublet of $H^7$ overlapped with the doublet of the *ortho*-protons of the anisyl substituents), and also a singlet from the proton $H^5$ proved that the fusion occurred at the *ortho*-position of the N-tolyl substituents. The ring structure of the reaction products is also consistent with the $^{13}$C NMR spectra where the $sp^3$-hybridized carbon $C^4$ appears in the region 70.59–70.85 ppm as a quartet due to coupling with the fluorine nuclei of the exocyclic trifluorolmethyl group [7]. The resonance of the $CF_3$ group in the $^{19}$F NMR spectra is observed in the region 73.51–73.66 ppm characteristic of its signal in the 4-trifluoro-lmethyl-2-quinazolones [6].

In the mass spectra of compounds **IIa–IIc** appear molecular ion peaks $[M]^+$ of relative intensity 15–20%. Their fragmentation under the electron impact occurs with ejection of $CF_3$ group followed by aromatization of the heterocyclic system and formation of ammonium ions (Φ) with peak intensity 100%. Then a rearrangement takes place in the triethylammonium ion with hydrogen migration to a nitrogen atom, ethylene elimination, and formation

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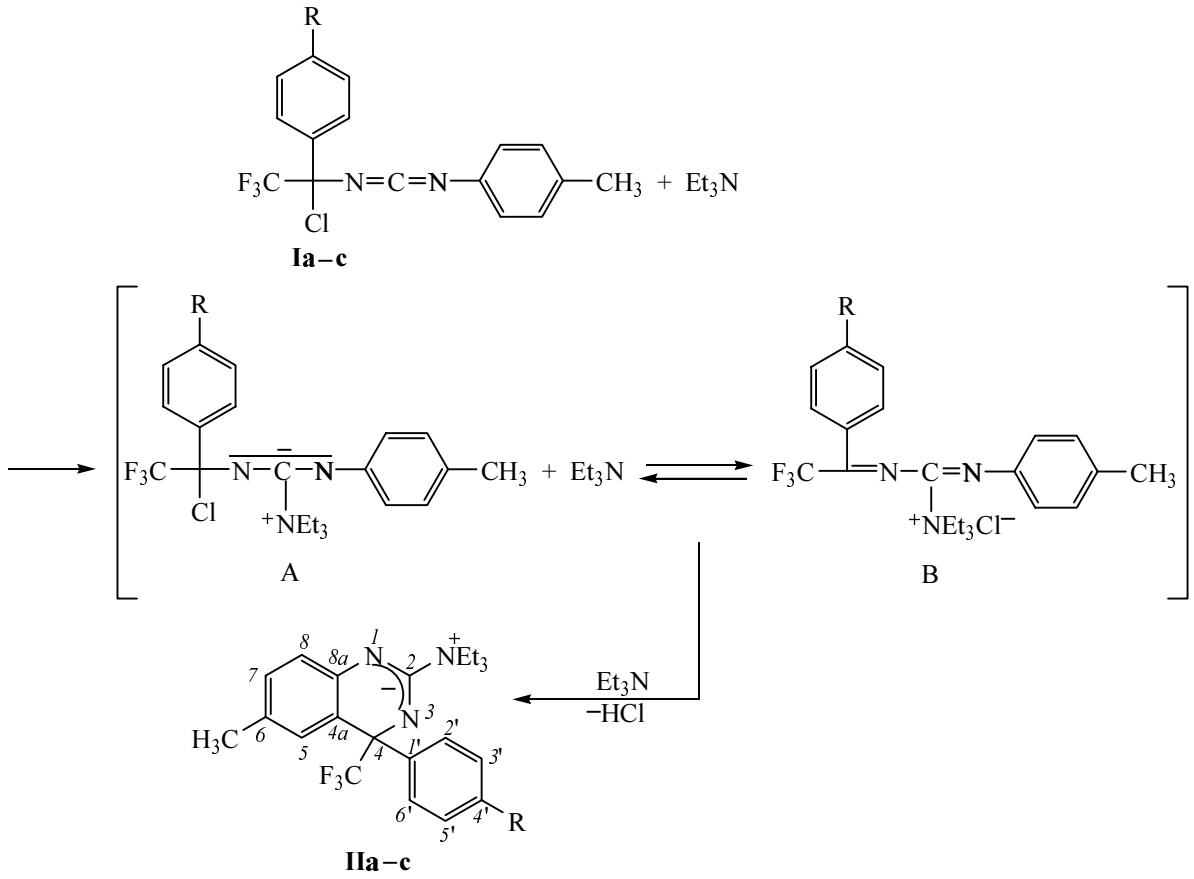
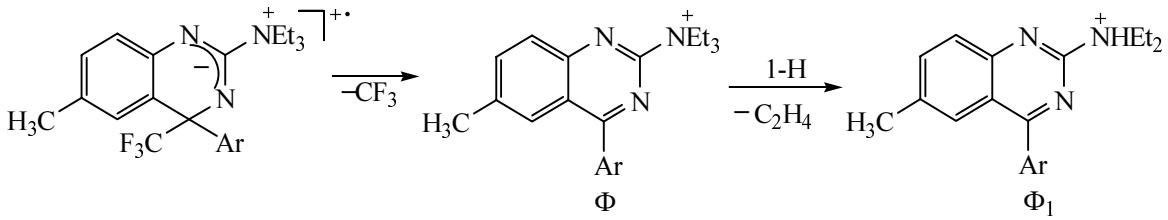



**I, II**, R = H (**a**), $CH_3$ (**b**), $CH_3O$ (**c**).




of ions ($\Phi_1$) with the peak intensity 54–76%. The latter most probably suffer decom-position along the patterns characteristic of amines and quinazolines fragmentation [8].

The spatial arrangement of compound **IIb*** determined by X-ray diffraction analysis is shown on the figure.

The central bicyclic system $N^1N^2C^{1-8}$ is approximately planar: deviation of atoms from rms plane do not exceed 0.13 Å, the dihedral angle between the rings $N^1N^2C^{1-4}$ and $C^{4-8}$ is 173.0°. By steric reasons the benzene ring $C^{17-22}$ is located virtually orthogonal to the central plane, and the corresponding dihedral angle amounts to 87.3°. A repulsion exists between spatially close atoms $C^{16}$ and $C^{22}$ [ the distance between them 2.968(5) Å is considerably shorter than the double van der Waals radius of carbon atom, 3.40 Å ]. The considerable leveling of bond lengths $C^1$–$N^1$ 1.282(5) Å and $C^1$–$N^2$ 1.301(5) Å indicates the negative charge delocalization in the moiety $N^1$–$C^1$–$N^2$ (the standard length of an ordinary N($sp^2$)–C($sp^2$) bond is 1.45 Å, of a double bond 1.27 A [9]). Therewith the endocyclic bond angle at $C^1$ atom is increased by 21.3(3) and 25.1(1)° compared to the bond angles at atoms $N^1$ and $N^2$. The significant elongation of the exocyclic bond $C^1$–$N^3$ to 1.554(4) Å also should be mentioned. The atom $N^3$ has nearly ideal tetrahedral coordination (the deviations of bond angles from the ideal value do not exceed 2.6°).

* Numeration of atoms does not correspond to that used in description of NMR spectra.

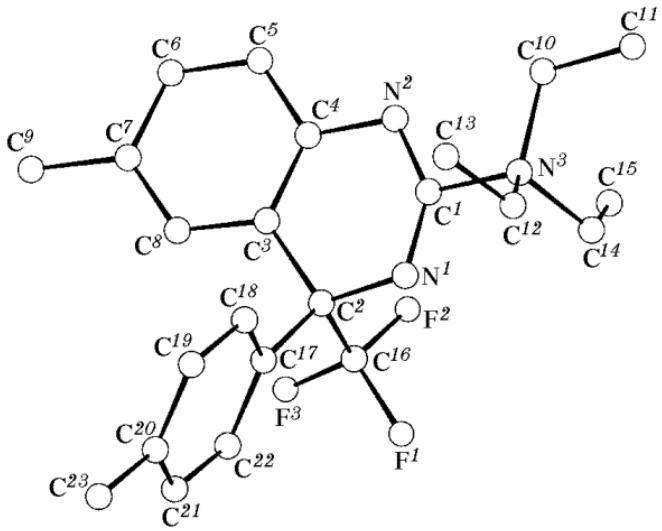
## EXPERIMENTAL

X-ray diffraction study on a single crystal of compound **IIb**, crystal habit 0.12×0.37×0.49 mm, was performed at room temperature on a four-circle diffractometer Enraf-Nonius CAD-4 (Mo$K_a$ irradiation, ratio of scanning rates 2θ/ω = 1.2, $\theta_{max}$ 26°, sphere segment ≤ *h* ≤ 11, 0 ≤ *k* ≤ 25, –13 ≤ *l* ≤ 13). Overall number of reflections obtained 4546, among them 4155 independent reflections ($R_{int}$ 0.020). Crystals of compound **IIb** monoclinic, *a* 9.522(3), *b* 20.871(6), *c* 10.749(3) Å, β 97.87(2)°, *V* 2107(1) Å$^3$, *M* 403.5, *Z* 4, $d_{calc}$ 1.27 g/cm$^3$, μ 0.89 cm$^{-1}$, *F*(000) 856.25, space group $P2_1/n$. The structure was solved by the direct method and refined with the use of least-squares procedure in a full-matrix anisotropic approximation applying software package CRYSTALS [10]. In the refinement were used 1745 reflections with $I > 3\sigma(I)$ (262 parameters refined, 6.7 reflections per parameter). All hydrogen atoms were revealed from the difference synthesis of the electron density and included in refining with the fixed position and thermal parameters. The accounting for absorption in the crystal was performed by means of azimuthal scanning [11]. The weight Chebyshev scheme was used in refining [12] with the following five parameters: 0.86, 0.23, 0.71, –0.02, and 0.21. The final values of divergence factors are R 0.051 and $R_W$ 0.054, GOF 1.159. The residual electron density from the difference is 0.20 and –0.32 *e*/Å$^3$. The coordinates of nonhydrogen atoms are listed in the table. The total set of crystallographic data in deposited into the Cambridge Structural Database (registered No. 185715 ).

NMR spectra were registered on spectrometer Varian-Gemini at operating frequencies 300 ($^1$H), 75.5 ($^{13}$C), and 188.28 MHz ($^{19}$F), internal references TMS ($^1$H, $^{13}$C), $CF_3Cl$ ($^{19}$F). Mass spectra were registered on MKh-1321 instrument with direct admission of the sample into the ion source, accelerating voltage for the ionizing ions 70 eV, ionizing chamber temperature 150°C.

1-Chloroalkylcarbodiimides **Ia–Ic** were prepared by procedure [13].

**4-Aryl-6-methyl-4-trifluorolmethyl-2-triethylammonio-3,4-dihydroquinazolinides IIa–c.** To a solution of 0.0015 mol of carbodiimide **Ia–c** in 5 ml of benzene was added within 10 min at stirring a solution of 0.417 ml (0.003 mol) of triethylamine in 5 ml of benzene. The reaction mixture was left standing for 48 h at room temperature, the precipitate formed was filtered off, washed with water (2 ×15 ml), and dried. The filtrate was evaporated, to the residue was added 2 ml of actonitrile, and the mixture was heated till dissolution. The precipitate formed on cooling was combined with the first portion of solid and recrystallized from dioxane.




Molecular structure of 6-methyl-4-(*p*-tolyl)-4-tri-fluorolmethyl-2-triethylammonio-3,4-dihydroquinazolidine **IIb** (hydrogen atoms not shown). Main bond lengths (Å ) and bond angles (deg): $N^1$–$C^1$ 1.282(5), $N^1$–$C^2$ 1.479(4), $N^2$–$C^1$ 1.301(5), $N^2$–$C^4$ 1.407(5), $N^3$–$C^1$ 1.554(4), average $N^3$–C(Et) 1.509(5), $C^2$–$C^3$ 1.533(5), $C^3$–$C^4$ 1.385(5); $C^1N^1C^2$ 115.4(3), $C^1N^2C^4$ 111.6(3), $N^1C^1N^2$ 136.7(3), $N^1C^1N^3$ 110.8(3), $N^2C^1N^3$ 112.5(3), $N^1C^2C^3$ 112.6(3), $C^2C^3C^4$ 118.6(3), $N^2C^4C^3$ 123.3(3).

**Compound (IIa).** Yield 34%, mp 210–211°C (decomp.). $^1$H NMR spectrum [$(CD_3)_2SO$–$CCl_4$, 2 : 1], δ, ppm: 1.11 t (9H, $CH_2$–$\underline{CH_3}$, *J* 7.1 Hz), 2.15 s (3H, $CH_3$), 3.56 q (6H, $\underline{CH_2}$–$CH_3$, *J* 7.1 Hz), 6.61 d (1H, $H^8$, *J* 8.0 Hz), 6.66 s (1H, $H^5$), 6.82 d (1H, $H^7$, *J* 8.0 Hz), 7.10–7.30 m (3H, $H^{3',4',5'}$), 7.45 d (2H, $H^{2',6'}$, *J* 7.7 Hz). $^{13}$C NMR spectrum ($CF_3COOD$), δ, ppm: 8.62 ($CH_2$–$\underline{CH_3}$), 21.39 (6-$CH_3$), 55.98 ($\underline{CH_2}$–$CH_3$), 70.85 ($C^4$, $^2J_{C-F}$ 28.6 Hz), 119.86 ($C^{4a}$), 121.58 ($C^8$), 127.26 ($CF_3$, $^1J_{C-F}$ 284.7 Hz), 129.75, 133.13 ($C^5$, $C^7$), 130.47 ($C^{3'}$, $C^{5'}$), 131.06 ($C^{2'}$, $C^{6'}$, $C^{4'}$), 135.27 ($C^{8a}$), 140.258 ($C^6$), 141.03 ($C^{1'}$), 146.01 ($C^2$). $^{19}$F NMR spectrum [$(CD_3)_2SO$–$CCl_4$, 2:1], δ, ppm: –73.51. Mass spectrum, *m/z* ($I_{rel}$, %): 389(20) $M^+$, 320(100) Φ, 292(65) $Φ_1$, 276(10), 262(21), 248(11), 219(9), 131(6), 86(7), 77(18). Found, %: C 67.51; H 6.78; F 14.39; N 10.97. $C_{22}H_{26}F_3N_3$. Calculated, %: C 67.87; H 6.68; F 14.65; N 10.80.

**Compound (IIb).** Yield 35%, mp 206–207°C (decomp.). $^1$H NMR spectrum [$(CD_3)_2SO$–$CCl_4$, 2:1], δ, ppm: 1.12 t (9H, $CH_2$–$\underline{CH_3}$, *J* 7.2 Hz), 2.15 s (3H, 6-$CH_3$), 2.30 s (3H, 4'-$CH_3$), 3.56 q (6H, $\underline{CH_2}$–$CH_3$, *J* 7.2 Hz), 6.54 d (1H, $H^8$, *J* 8.0 Hz), 6.63 s (1H, $H^5$), 6.80 d (1H, $H^7$, *J* 8.0 Hz), 7.06 d (2H, $H^{3',5'}$, *J* 8.0 Hz),

Coordinates of nonhydrogen atoms and equivalent isotropic thermal parameters $U_{eq}$ ($A^2$) in **IIb** structure

| Atom | *x* | *y* | *z* | $U_{eq}$ |
|---|---|---|---|---|
| $F^1$ | 0.5664(2) | 0.10703(12) | 0.2712(2) | 0.0616 |
| $F^2$ | 0.6376(3) | 0.19124(11) | 0.1823(2) | 0.0688 |
| $F^3$ | 0.7535(3) | 0.15666(11) | 0.3547(2) | 0.0633 |
| $N^1$ | 0.6769(3) | 0.08155(15) | 0.0488(3) | 0.0435 |
| $N^2$ | 0.7948(3) | 0.15448(15) | –0.0758(3) | 0.0469 |
| $N^3$ | 0.5884(3) | 0.09720(14) | –0.1633(3) | 0.0438 |
| $C^1$ | 0.7006(4) | 0.11343(17) | –0.0484(3) | 0.0404 |
| $C^2$ | 0.7718(4) | 0.09651(17) | 0.1661(3) | 0.0419 |
| $C^3$ | 0.9025(4) | 0.13532(16) | 0.1424(4) | 0.0403 |
| $C^4$ | 0.9028(4) | 0.16396(17) | 0.0260(4) | 0.0426 |
| $C^5$ | 1.0192(4) | 0.20179(19) | 0.0067(4) | 0.0513 |
| $C^6$ | 1.1338(4) | 0.2087(2) | 0.1014(5) | 0.0566 |
| $C^7$ | 1.1357(4) | 0.17840(19) | 0.2165(4) | 0.0517 |
| $C^8$ | 1.0193(4) | 0.14166(18) | 0.2344(4) | 0.0480 |
| $C^9$ | 1.2611(4) | 0.1855(2) | 0.3188(5) | 0.0679 |
| $C^{10}$ | 0.6238(4) | 0.1287(2) | –0.2810(4) | 0.0567 |
| $C^{11}$ | 0.5192(5) | 0.1156(3) | –0.3985(4) | 0.0803 |
| $C^{12}$ | 0.5812(4) | 0.02520(19) | –0.1781(4) | 0.0557 |
| $C^{13}$ | 0.7139(6) | –0.0059(2) | –0.2085(5) | 0.0820 |
| $C^{14}$ | 0.4450(4) | 0.1190(2) | –0.1333(4) | 0.0573 |
| $C^{15}$ | 0.4320(5) | 0.1905(3) | –0.1209(5) | 0.0796 |
| $C^{16}$ | 0.6822(4) | 0.13725(19) | 0.2428(4) | 0.0522 |
| $C^{17}$ | 0.8179(4) | 0.03264(17) | 0.2311(4) | 0.0411 |
| $C^{18}$ | 0.8780(4) | –0.0118(2) | 0.1593(4) | 0.0530 |
| $C^{19}$ | 0.9261(5) | –0.07087(19) | 0.2084(4) | 0.0586 |
| $C^{20}$ | 0.9164(4) | –0.0869(2) | 0.3310(4) | 0.0546 |
| $C^{21}$ | 0.8569(5) | –0.0427(2) | 0.4022(4) | 0.0610 |
| $C^{22}$ | 0.8081(5) | 0.01648(19) | 0.3543(4) | 0.0550 |
| $C^{23}$ | 0.9672(6) | –0.1517(2) | 0.3817(5) | 0.0825 |

7.29 d (2H, $H^{2',6'}$, *J* 8.0 Hz). $^{13}C$ NMR spectrum ($CF_3COOD$), δ, ppm: 8.66 ($CH_2$–$\underline{C}H_3$), 21.26 (4'-$CH_3$), 21.39 (6-$CH_3$), 56.02 ($\underline{C}H_2$–$CH_3$), 70.74 ($C^4$, $^2J_{C-F}$ 29.1 Hz), 120.34 ($C^{4a}$), 122.71 ($C^8$), 127.32 ($CF_3$, $^1J_{C-F}$ 285.2 Hz), 129.76 ($C^{3'}$, $C^{5'}$), 131.16 ($C^{2'}$, $C^{5'}$), 131.18, 133.13 ($C^5$, $C^7$), 135.59 ($C^{8a}$), 137.99 ($C^{1'}$), 140.37 ($C^6$), 142.06 ($C^{4'}$), 146.00 ($C^2$). $^{19}F$ NMR spectrum [$(CD_3)_2SO$–$CCl_4$, 2:1], δ, ppm: –73.69. Mass spectrum, *m/z* ($I_{rel}$, %): 403(15) $M^+$, 334(100) Φ, 306(54) $Φ_1$, 290(16), 276(18), 262(10), 233(7), 139(7), 91(13). Found, %: C 68.30; H 7.04; F 14.37; N 10.19. $C_{23}H_{28}F_3N_3$. Calculated, %: C 68.49; H 6.95; F 14.14; N 10.42.

**Compound (IIc).** Yield 34%, mp 200–201°C (decomp.). $^1H$ NMR spectrum [$(CD_3)_2SO$–$CCl_4$, 2:1], δ, ppm: 1.10 t (9H, $CH_2$–$\underline{C}H_3$, *J* 7.1 Hz), 2.15 s (3H, 6-$CH_3$), 3.54 q (6H, $\underline{C}H_2$–$CH_3$, *J* 7.1 Hz), 3.73 s (3H, 4'-$OCH_3$) 6.57 d (1H, $H^8$, *J* 8.0 Hz), 6.65 s (1H, $H^5$), 6.74–6.80 m (3H, $H^{2',6'}$ + $H^7$), 7.30 d (2H, $H^{3',5'}$, *J* 7.9 Hz). $^{13}C$ NMR spectrum ($CF_3COOD$), δ, ppm: 8.65 ($CH_2$–$\underline{C}H_3$), 21.41 (6-$CH_3$), 55.96 ($\underline{C}H_2$–$CH_3$), 57.40 (4'-$OCH_3$), 70.59 ($C^4$, $^2J_{C-F}$ 31.5 Hz), 116.33 ($C^{3'}$, $C^{5'}$), 119.59 ($C^{4a}$), 121.87 ($C^8$), 127.20 ($CF_3$, $^1J_{C-F}$ 286.1 Hz), 130.92, 133.22 ($C^5$, $C^7$), 131.59 ($C^{2'}$, $C^{6'}$), 135.17 ($C^{8a}$), 135.19 ($C^{1'}$), 140.25 ($C^6$), 146.17 ($C^2$), 160.43 ($C^{4'}$). $^{19}F$ NMR spectrum [$(CD_3)_2SO$–$CCl_4$, 2:1], δ, ppm: –73.66. Mass spectrum, *m/z* ($I_{rel}$, %): 419(19) $M^+$, 350(100) Φ, 322(76) $Φ_1$, 304(8), 292(19), 278(16), 249(10), 210(9), 175(8), 147(14), 77(7). Found, %: C 65.52; H 6.75; F 13.86; N 9.72. $C_{23}H_{28}F_3N_3O$. Calculated, %: C 65.87; H 6.68; F 13.60; N 10.02.

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