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Intramolecular cycloaddition of fluorinated 1,3,4-oxadiazoles to dienes

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Abstract

Cycloaddition reactions of fluorinated 1,3,4-oxadiazoles with conjugated and unconjugated dienes was studied. The reactions resulted in the formation of products of double cycloaddition (7-oxabicycloheptane type compounds), along with products of intramolecular cycloaddition (oxatricyclic and oxatetracyclic compounds). The structure of 4-(trifluoromethyl)-2-ethoxycarbonyl-1,6-dimethyl-3-oxatricyclo[2.2.1.$0^{2,6}$]heptane was confirmed by single crystal X-ray diffraction analysis.

Keywords: Fluorinated 1,3,4-oxadiazoles; Diene; [2 + 4]-Cycloaddition; [2 + 3]-Cycloaddition

1. Introduction

Previously [1–3], the cycloaddition of 1,3,4-oxadiazoles to alkenes was studied using 2,5-bis(trifluoromethyl)oxadiazole (**1a**) as an example. More recently, this reaction was extended to other oxa,diazoles, such as 2,5-bis(polyfluoroalkyl)-1,3,4-oxadiazoles (**1b–d**) [4–6], as well as 2,5-bis(methoxycarbonyl)-1,3,4-oxadiazole (**1e**) [3].

The first step of the process, involves [2 + 4]-cycloaddition with the formation of intermediate 2,3-diaza-7-oxabicyclo[2.2.1]hept-2-ene (**2**) intermediate (Scheme 1), which under reaction conditions (≥100 °C) undergoes retro [2 + 3]-cycloaddition with the elimination of nitrogen and the formation of carbonyl ylide (**3**, Scheme 1)—the most probable intermediate in this process, although the formation of a biradical and an oxirane intermediates was also considered [2,7].

The reactions are controlled by the LUMO of oxadiazoles and the HOMO of dienophiles. This statement agrees well with experimental data (low ionization potentials of fluorinated oxadiazoles [8]) and quantum-chemical calculation [6]. The donor properties of involved dienophiles also provide support for the inverted mechanism of oxadiazole cycloaddition; acceptor-type dienophiles (the derivatives of maleic acid, fumaric acid, acetylenedicarboxylic acid, etc.) do not enter cycloaddition. Steric factors also have considerable effect on cycloaddition—the yields of cycloadducts decrease going from ethylene to propylene, and isobutylene, despite substantial increase of electron density of double bond. Strained multiple bonds in cyclic alkenes are of crucial importance; and increase in the bond strain facilitates the occurrence of cycloaddition processes [4].

Donor 1,3,4-oxadiazoles are not prone to cycloaddition with the use of an endo-diene fragment. Thus, 2,5-dimethyl-1,3,4-oxadiazole reacts with perfluorobutyne-2 to form only condensed cycloadduct (**5**), which is the product of an initial ene reaction followed by the [4 + 2]-cycloaddition of perfluorobutyne-2 to the resulting exo-diene component (Scheme 2) [9].

Thus, the applicability of the double cycloaddition processes of 1,3,4-oxadiazoles with the participation of two alkene molecules to the synthesis of compounds from the 7-oxabicycloheptane series has been determined to date. The

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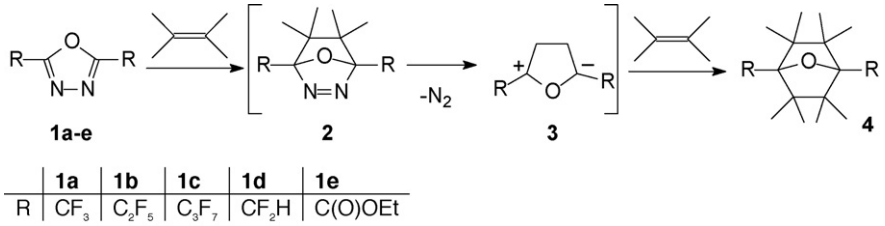


Scheme 1. Mechanism of reaction of fluorinated oxadiazoles with alkenes.

regioselectivity and stereoselectivity of the processes and the donor, acceptor, and steric requirements imposed on the formation of a transition state have been found.

Intramolecular cycloaddition reactions as the tool for synthesis of various cage compounds are of considerable interest. Zeitz and Gerninghans [10] were the first to study this 2-ethylsulfonyl-5-trifluoromethyl-1,3,4-oxadiazole (**1f**) in cycloaddition with cyclooctadiene-1,5. This reaction resulted in the formation of a tetracyclic compound (**6**) (Scheme 3). The cycloaddition reaction of 2,5-bis(trifluoromethyl)oxadiazole **1a** with 7-*tert*-butoxynorbornadiene resulted in the formation of oxabishomocubane (**7**) by the intramolecular cycloaddition mechanism [7], although norbornadiene reacted by different cycloaddition mechanism to form a cycloadduct (**8**) [2,4].

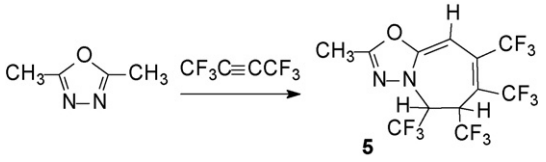
2. Results and discussion

In order to determine the scope and limitations of the intramolecular cycloaddition of fluorinated 1,3,4-oxadiazoles we studied bis(trifluoromethyl)-1,3,4-oxadiazole (**1a**) and 2,5-bis(perfluoropropyl)-1,3,4-oxadiazole (**1c**) in reaction with dienes. Both **1a** and **1b** [11,12], readily prepared using improved published procedure [6,8]. Unsymmetrical 2-trifluoromethyl-5-ethoxycarbonyl-1,3,4-oxadiazole (**1g**) and 2-trifluoromethyl-5-methoxycarbonyl-1,3,4-oxadiazole (**1h**) were prepared using standard procedure depicted by Scheme 4.

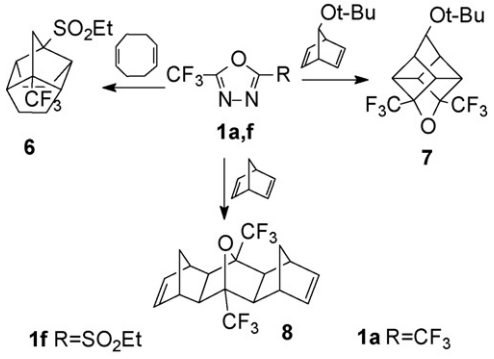
Butadiene-1,3,2,3-dimethylbutadiene-1,3 (representatives of acyclic dienes), along with unconjugated dienes containing heteroatoms (divinyl ether, divinyl sulfide, and diallyl ether), and other compounds with two multiple bonds were studied in cycloaddition reactions.

Oxadiazole **1a** reacted with butadiene under relatively mild conditions to form mixture of compounds **9** and **10** isolated in 25 and 24%, respectively. Because compound **10** is much more volatile than compound **9**, these products can be easily separated by fractional distillation. The mechanism of formation compounds **9** and **10** involves of a carbonyl ylide **9a** as common intermediate (Scheme 5). Compound **9** resulted from the interaction of **9a** with the second butadiene molecule, but oxatricycloheptane **10** forms as the result of intramolecular reaction.

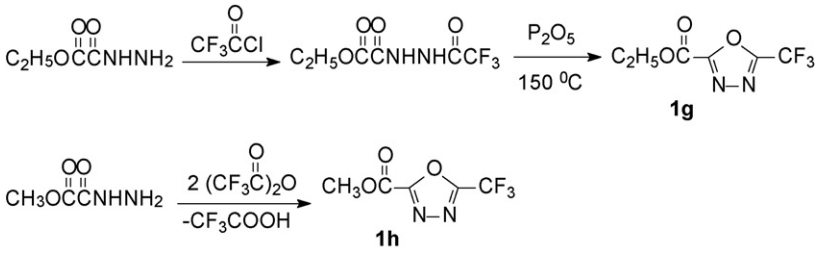
2,3-Dimethylbutadiene reacted with oxadiazole **1a** in a more complicated manner. In this case, we failed to isolate a double cycloaddition product. At the same time, an intramolecular cycloaddition product (**11**), as well as trifluoroacetamide (**12**) and 2-trifluoromethyl-4,5-dimethylpyridine (**13**), which unexpectedly resulted from this interaction, were isolated (Scheme 6). The formation of compounds **12** and **13** can be explained by an relative reactivity of 2,3-dimethylbutadiene, which is able to undergo [4 + 2]-cycloaddition to the C=N bond of oxadiazole



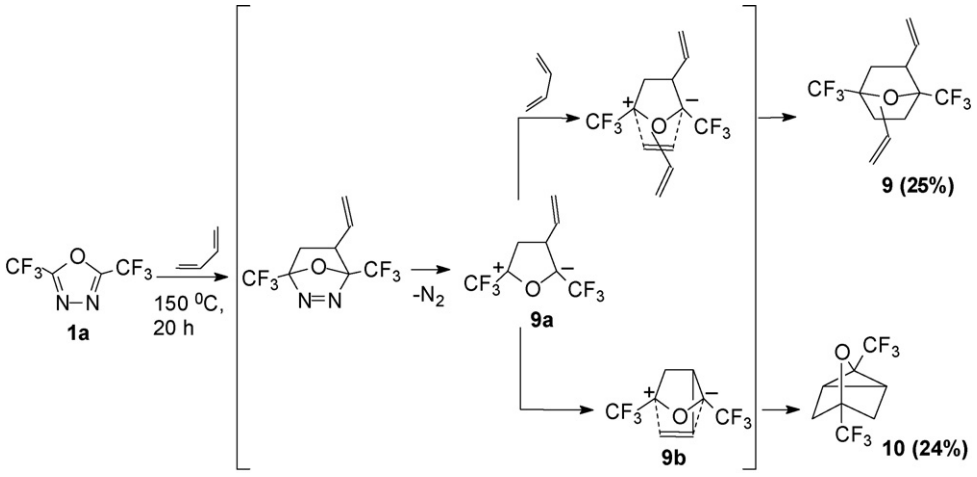
Scheme 2. Interaction of 2,5-dimethyl-1,3,4-oxadiazole with perfluorobutyne-2.



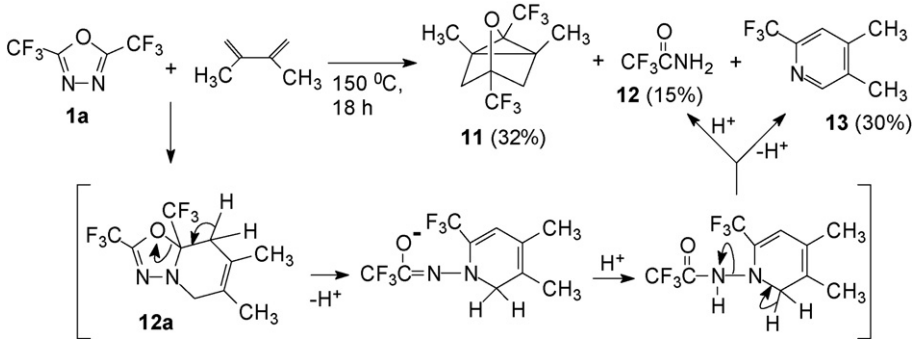
Scheme 3. Cycloaddition reactions of fluorinated oxadiazoles **1a** and **1f**.



Scheme 4. Synthesis of 2-trifluoromethyl-5-alkoxycarbonyl-1,3,4-oxadiazoles **1g** and **1h**.



Scheme 5. Interaction of oxadiazole **1a** with butadiene.



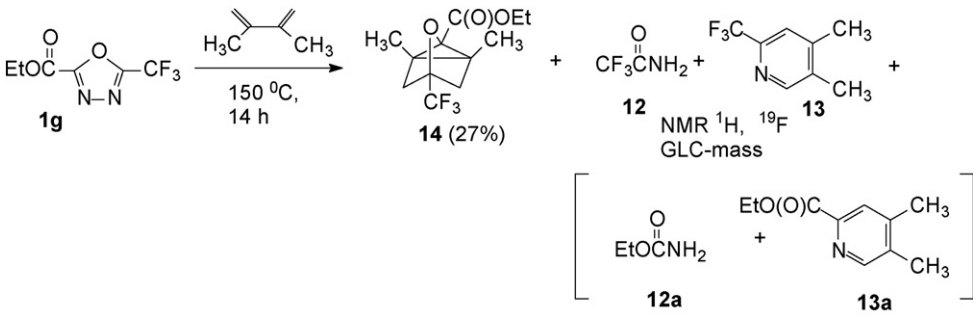
Scheme 6. Interaction of oxadiazole **1a** with 2,3-dimethylbutadiene.

1a forming an unstable cycloadduct (**12a**). Pyridine **13** resulted from the subsequent ionic transformations of cycloadduct **12a** involving ring opening of oxadiazoline and elimination of trifluoroacetamide **12** (Scheme 6).

Both processes occurred at comparable rates; it is likely that they are characteristic of the interaction of oxadiazoles with 2,3-dimethylbutadiene. This was supported by the reaction of oxadiazole **1g** with 2,3-dimethylbutadiene, which lead to a similar result: the formation of intramolecular cycloaddition product **14**, trifluoroacetamide **12**, and pyridine **13**, which were detected in reaction mixture by GC–MS and NMR spectroscopy. The intramolecular cycloaddition of compound **1g** is likely be a regiospecific, since the formation of only one isomer of oxatricycloheptane **14** was observed in this process (Scheme 7). However interaction is realized oppositely to charged distribution in molecules of **1g** and 2,3-dimethylbutadiene. As judged from the formation of compounds **12** and **13**, the [4 + 2]-cycloaddition of 2,3-dimethylbutadiene with oxadiazole **1g** occurred non-specifically. At the same time, urethane (**12a**) and 2-ethoxycarbonyl-4,5-dimethylpyridine (**13a**), which might be formed in this reaction, were not detected.

The structure of **14** was confirmed by single crystal X-ray diffraction (Fig. 1) and is in a good agreement with NMR data.

According to XRD **14** crystallize with two independent molecules, which are almost identical with small variation of ester group conformation. The bond lengths in **14** are close to



Scheme 7. Interaction of oxadiazole **1g** with 2,3-dimethylbutadiene.

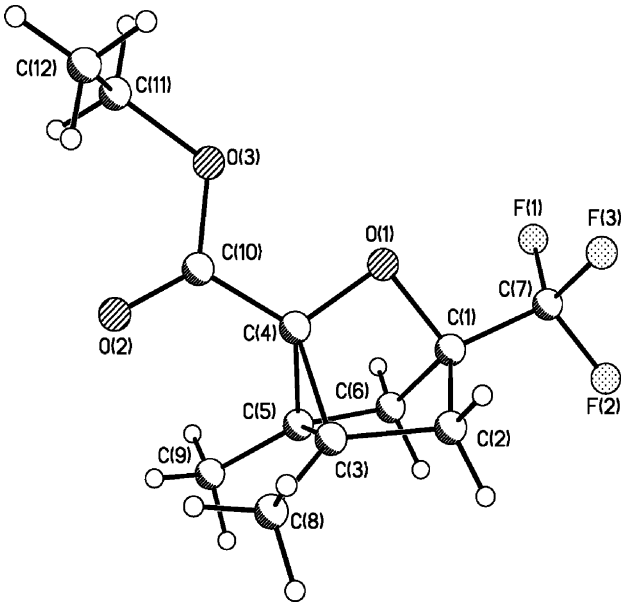
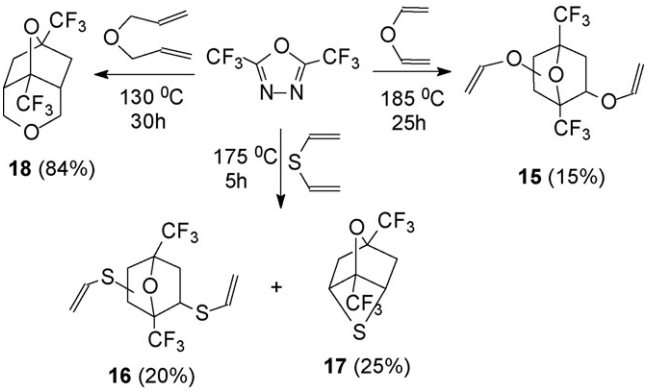


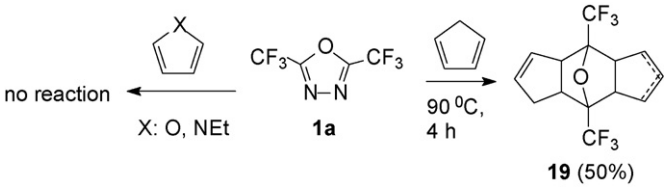
Fig. 1. The general view of one of the independent molecules **14**. The second position of the disordered ester group is omitted for clarity. Selected bond lengths (Å): O(1)–C(4) 1.422 (1), O(1)–C(1) 1.440 (2), O(2)–C(10) 1.204 (2), C(1)–C(2) 1.525 (2), C(1)–C(6) 1.527 (2), C(2)–C(3) 1.514 (2), C(3)–C(8) 1.4975 (19), C(3)–C(5) 1.5194 (19), C(3)–C(4) 1.5301 (18), C(4)–C(5) 1.5320 (19), C(5)–C(6) 1.518 (2) and angles (°): C(4)–O(1)–C(1) 98.00 (9), O(1)–C(1)–C(2) 103.57 (10), C(7)–C(1)–C(2) 118.09 (12), O(1)–C(1)–C(6) 103.50 (10), C(7)–C(1)–C(6) 118.05 (12), C(2)–C(1)–C(6) 102.96 (10), C(3)–C(2)–C(1) 95.75 (10), C(8)–C(3)–C(2) 121.26 (12), C(8)–C(3)–C(5) 124.98 (13), C(2)–C(3)–C(5) 106.47 (11), C(8)–C(3)–C(4) 125.09 (12), C(2)–C(3)–C(4) 102.93 (10), C(5)–C(3)–C(4) 60.31 (9), O(1)–C(4)–C(3) 108.77 (10), C(10)–C(4)–C(3) 125.66 (12), O(1)–C(4)–C(5) 108.60 (10), C(10)–C(4)–C(5) 124.06 (12), C(3)–C(4)–C(5) 59.50 (9), C(9)–C(5)–C(6) 121.64 (13), C(9)–C(5)–C(3) 124.47 (13), C(6)–C(5)–C(3) 106.82 (11), C(9)–C(5)–C(4) 124.63 (13), C(6)–C(5)–C(4) 103.01 (11), C(3)–C(5)–C(4) 60.19 (9), C(5)–C(6)–C(1) 95.41 (10).

expected. The conformation of five-membered rings O(1)C(1)C(2)C(3)C(4), O(1)C(1)C(6)C(5)C(4) and C(1)C(2)C(3)C(5)C(6) is envelope one with the deviation of C(1) atom by 0.76–0.80 Å. The C=O bond of ester group is characterized by antiperiplanar conformation with torsion angles O(2)C(10)C(4)O(1) in twin independent molecules vary in the range of 177.6–178.1°.

The interaction of oxadiazole **1a** with divinyl ether occurred only at high temperature leading product (**15**) isolated in a low yield. Divinyl sulfide reacted with oxadiazole **1a** under milder conditions to form compounds **16** and **17**. On the other hand, he reaction of oxadiazole **1a** with diallyl ether rapidly proceeds at 130 °C with high yield formation cycloadduct **18** (Scheme 8).



Scheme 8. Interactions of oxadiazole **1a** with divinyl ether, divinyl sulfide, and diallyl ether.



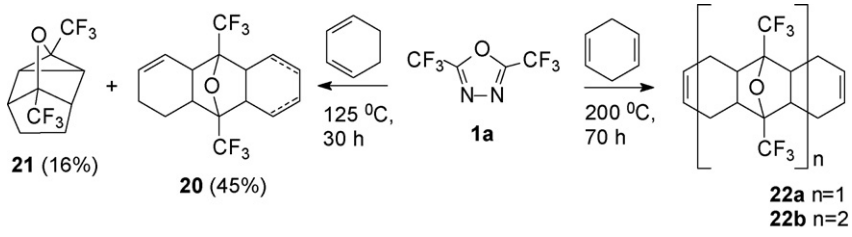
Scheme 9. Interactions of oxadiazoles **1a,c** with cyclopentadiene, furan, and *N*-ethylpyrrole.

Attempt to involve diallyl phthalate and diallyl acetal in reactions with oxadiazoles **1a,c** at elevated temperature (130–150 °C) resulted in the formation of polymer products only.

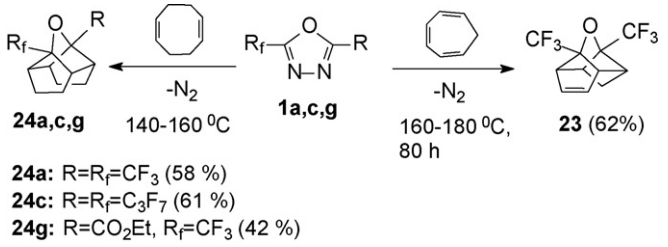
The interaction of cyclopentadiene with oxadiazole **1a** occurred under relatively mild conditions (90–100 °C, etc.), but resulted in the selective formation of cycloadduct (**19**) (Scheme 9) and the product of intramolecular cycloaddition was not detected, even when the reaction was carried out at a high degree of dilution. In reaction of furan or *N*-ethylpyrrole with oxadiazoles **1a,c** at temperatures higher than 200 °C only decomposition products were found.

Cyclohexadiene-1,3 reacted with oxadiazole **1a** at 125 °C forming mainly a cycloaddition product **20**, along with smaller amount of **21**. Cyclohexadiene-1,4 was essentially different from the above isomer; it reacted only at 200 °C to form a mixture of compounds **22a,b** (Scheme 10).

The reaction of oxadiazole **1a** with cycloheptatriene slowly occurred at elevated temperature, but surprisingly resulted in a moderate yield formation of an intramolecular cycloaddition product (**23**) (Scheme 11). After first distillation, tetracyclodecene **23** contained ~20% impurities of four unidentified isomers of the same molecular weight (GC–MS). Pure product



Scheme 10. Interactions of oxadiazole **1a** with cyclohexadiene-1,3 and cyclohexadiene-1,4.



Scheme 11. Interactions of fluorinated oxadiazoles with cycloheptatriene and cyclooctadiene-1,5.

23 was separated by repeated vacuum fractionation, and its structure was confirmed by NMR spectroscopy and single crystal X-ray diffraction analysis [13]. It should be also pointed out, that oxadiazole **1c** did not react with cycloheptatriene under analogous conditions.

The interaction of oxadiazoles **1a,c,g** with cyclooctadiene-1,5 resulted in exclusive formation of intramolecular cycloadducts; **24a,c,g**: 58, 61, and 42% yield, respectively (Scheme 11). Cycloaddition of oxadiazoles **1g** and **1a** occurred relatively fast (6 h at 140 °C; and 25 h at 150 °C, respectively), but the reaction of oxadiazole **1c** was slow even at 160 °C (80 h).

These differences in the reactivity of oxadiazoles **1a,c,g** are not explained by Frontier Orbital Method under consideration of the orbital characteristics of their molecules. The LUMO and HOMO energies calculated by the G 6-31* method are 2.53 and −12.33 eV (**1a**); 2.25 and −12.28 eV (**1c**); 1.98 and −11.76 eV (**1g**), respectively. Reactivity of oxadiazoles have to change as **1a** → **1c** → **1g**, but we observe another sequences: **1c** → **1a** → **1g**.

In conclusion, the cycloaddition of fluorinated 1,3,4-oxadiazoles to dienes offers interesting and relatively simple approach to the preparation of oxatricyclic and oxatetracyclic compounds. In general, we failed to find a direct relationship between the structures of parent dienes or oxadiazoles and the predominant formation of intramolecular cycloaddition or double cycloaddition products in of our experiments. It seemed likely the stereochemistry of approaching reactants, that is, the initial exo or endo addition of a multiple bond to an oxadiazole ring, was responsible for the resulting structure. At the same time, based on the experimental data available, we can conclude that the formation of intramolecular cycloaddition or double cycloaddition products is almost independent of process temperature; this is inconsistent with the effect of the stereozchemistry above. Moreover, the structure of flattened carbonyl ylide intermediate **9a**, which is formed in the reactions of acyclic dienes, suggests that the stereochemistry of initially approaching reactants does not play a crucial role because rapid conformational conversion into intermediate **9b** comes into play. It is likely that spatial correspondence in the resulting carbonyl ylide intermediate is a crucial stereochemical factor for the occurrence of intramolecular cycloaddition in the interaction of cyclic dienes.

3. Experimental

Commercial reagents and solvents used in the study were prepared according to known recommendations [14]. ^{1}H NMR spectra were recorded in $CDCl_3$ on a Bruker AC-300 spectrometer at 300.1 MHz. ^{19}F NMR spectra ($CDCl_3$) were recorded on "Bruker WP-200 SY" spectrometer at 188.31 MHz. ^{1}H ^{19}F NMR spectra were recorded in $CDCl_3$ on a Bruker DRX-500 spectrometer at 500.1 and 470.6 MHz for ^{1}H and ^{19}F, respectively; TMS and $CFCl_3$ was an internal standard for ^{1}H and ^{19}F, respectively. IR spectra recorded on a Hitachi 127-30 instrument (KBr or liquid film). The mass-spectra were recorded on an HP 5890 II Series gas chromatograph equipped with an HP 5972A MSD mass-selective detector. Melting points were determined in open capillaries and are uncorrected.

3.1. Crystallographic data

Crystals of **14** ($C_{12}H_{15}F_3O_3$, M = 264.24) are monoclinic, space group $P2_1/n$, at 100 K: a = 16.6738 (11), b = 12.0893 (8), c = 12.3106 (9) Å, β = 90.116 (6)°, V = 2481.5 (3) Å^3, Z = 8 (Z' = 2), d_{calc} = 1.415 g cm^{-3}, μ(Mo Kα) = 1.29 cm^{-1}, F(0 0 0) = 1104. Intensities of 19,028 reflections were measured with a Bruker SMART APEX2 CCD diffractometer [λ(Mo Kα) = 0.71072 Å, ω-scans, $2\theta < 58°$] and 6531 independent reflections [R_{int} = 0.0401] were used in further refinement. The structure was solved by direct method and refined by the full-matrix least-squares technique against F^2 in the anisotropic–isotropic approximation. The positions of hydrogen atoms were calculated geometrically. For **14** the refinement converged to wR2 = 0.1316 and GOF = 1.054 for all independent reflections (R1 = 0.0510 was calculated against F for 4353 observed reflections with $I > 2\sigma(I)$). All calculations were performed using SHELXTL PLUS 5.0.

The crystallographic data have been deposited with the Cambridge Crystallographic Data Center, CCDC 634037. Copies of this information may be obtained free of charge from: The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (Fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk or http://www.ccdc.cam.ac.uk).

3.2. 2-Trifluoromethyl-5-ethoxycarbonyl-1,3,4-oxadiazole (*1g*)

7.5 g (0.074 mol) of dry triethylamine was added with stirring to suspension of 10 g (0.075 mol) of $C_2H_5OC(O)$-$C(O)NHNH_2$ [15] in 150 ml of dry ether and then at −10 °C 12.0 g (0.09 mol) of trifluoroacetylchloride was slowly added as a gas over the reaction mixture (∼1 h). The reaction mixture was brought to room temperature, was hold for another 30 min, filtrated, the precipitate was washed 3× 30 ml of dry ether, the solvent was removed under vacuum and the residue 15.2 g (without additional cleaning) was mixed with 38.0 g (0.26 mol) of P_2O_5 and slowly heated the reaction mixture in vacuum (30 mmHg) up to 150–170 °C collecting liquid fractions. After consecutive distillation gave 8.42 g of oxadiazole **1g** (54%) with b.p. 88–90 °C (12 mmHg), n_D^{20} 1.3940. IR (KBr): ν 2990, 1740, 1620 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 1.45 (t, J = 7.0 Hz, 3H, –CH_3), 4.55 (q, J = 7.0 Hz, H, –CH_2); ^{19}F NMR ($CDCl_3$): δ −65.5 (s, CF_3); MS, 70 eV, m/z (%): 209 [$M-1$]$^+$ (2), 195 (4),

191 (4), 183 (45), 169 (6), 165 (40), 139 (12), 137 (43), 69 (100); Anal. Calcd. for $C_6H_5F_3N_2O_3$: C, 34.30; H, 2.40; N, 13.33. Found: C, 34.51; H, 2.49; N, 13.07.

3.3. 2-Trifluoromethyl-5-methoxycarbonyl-1,3,4-oxadiazole (**1h**)

5.0 g (0.024 mol) of anhydride of trifluoroacetic acid was added at 0 °C to 2.0 g (0.017 mol) of $CH_3OC(O)C(O)NHNH_2$ (see Section 3.2 [15]), then reaction mixture was slowly heated to boiling and hold while boiling for 2 h. Reaction mixture was brought to room temperature another 5.0 g (0.026 mol) of anhydride of trifluoroacetic acid and 0.2 g of dry pyridine was added and it was heated for another 3 h periodically (three times) cooling in order to add 0.1 g of pyridine. Mixture was fractioned twice in vacuum, after second distillation formed 1.2 g of oxadiazole **1h** (36%) with b.p. 80 °C (15 mmHg), n_D^{20} 1.3830. IR (KBr): ν 2995, 1750, 1630 cm^{-1}; ^1H NMR ($CDCl_3$): δ 4.10 (s, $-CH_3$); ^{19}F NMR ($CDCl_3$): δ −65.4 (s, CF_3); Anal. Calcd. for $C_5H_3F_3N_2O_3$: C, 30.61; H, 1.53; N, 14.29. Found: C, 30.70; H, 1.49; N, 14.17.

3.4. A general procedure for cycloaddition reactions of oxadiazoles. Preparation of compounds **9–24**

A mixture of oxadiazoles **1a,c,g** (0.019 mol) and a corresponding diene (0.019 mol) was heated in a sealed Pyrex tube and then fractionated or sublimed in a vacuum. IR-spectra of all cycloadducts exhibit a band at 2950–2980 cm^{-1} and the spectra of compounds **9**, **15**, **16**, **19**, **20**, **22**, **23** exhibit a low-intensity band at 1620–1650 cm^{-1}; in the spectra of compounds **14**, **24g** was present a high-intensity band at 1680–1700 cm^{-1}.

The reaction conditions and yields of compounds **9–21**, **23**, **24** are shown in Table 1.

3.4.1. 1,4-Bis(trifluoromethyl)-2,5(6)-divinyl-7-oxabicyclo[2.2.1]heptane (**9**) [13]

Mixture of three isomers: b.p. 82–84 °C (18 mmHg). ^1H NMR ($CDCl_3$): δ 1.7–2.5 (m, 4H, $2CH_2$), 2.8 and 3.3 (m, 2H, 2CH), 5.1, 5.3 and 5.6 (m, 6H, 6CH=); ^{19}F NMR ($CDCl_3$): δ −78.0 (s, CF_3), −76.5 (s, CF_3), −76.1 (s, CF_3), −72.8 (s, CF_3), −70.7 (s, CF_3); Anal. Calcd. for $C_{12}H_{12}F_6O$: C, 50.35; H, 4.20; N, 0.00. Found: C, 49.93; H, 4.05.

Table 1
Cycloaddition conditions and yield of compounds **9–24**

Entry	Compounds	Temperature (°C)	Time (h)	Yield[a] (%)
1	**9**, **10**	150	20	25 (**9**), 24 (**10**)
2	**11**, **12**, **13**	150	18	32 (**11**), 15 (**12**), 30 (**13**)
3	**14**	150	14	27 (**14**)
4	**15**	180–190	25	15 (**15**)
5	**16**, **17**	175	5	20 (**16**), 25 (**17**)
6	**18**	130	30	84 (**18**)
7	**19**	90	4	50 (**19**)
8	**20**, **21**	125	30	45 (**20**), 16 (**21**)
9	**22a,b**	200	70	–
10	**23**	160–180	80	62 (**23**)
11	**24a**	150	25	58 (**24a**)
12	**24c**	160	80	61 (**24c**)
13	**24g**	140	6	42 (**24g**)

[a] The ratio of addends was 1:1; the yields were calculated based on the amount of diene.

3.4.2. 2,4-Bis(trifluoromethyl)-3-oxatricyclo[2.2.1.$0^{2,6}$]heptane (**10**) [13]

B.p. 43 °C (18 mmHg) n_D^{20} 1.3565; ^1H NMR ($CDCl_3$): δ 1.7 (d, J_{AB} = 23.5 Hz, 2H, $2CH_2$), 1.8 (d, J_{AB} = 23.5 Hz, 2H, $2CH_2$), 2.15 (s, 2H, 2CH); ^{19}F NMR ($CDCl_3$): δ −69.6 (s, 3F, CF_3), −74.6 (s, 3F, CF_3); Anal. Calcd. for $C_8H_6F_6O$: C, 41.38; H, 2,59. Found: C, 41.55; H, 2.63.

3.4.3. 4-(Trifluoromethyl)-2-ethoxycarbonyl-1,6-dimethyl-3-oxatricyclo[2.2.1.$0^{2,6}$]heptane (**11**)

B.p. 60 °C (17 mmHg), n_D^{20} 1.3740; ^1H NMR ($CDCl_3$): δ 1.75 (br s, 6H, $2CH_3$), 1.7 (d, J_{AB} = 24.0 Hz, 2H, $2CH_2$), 1.8 (d, J_{AB} = 24.0 Hz, 2H, $2CH_2$); ^{19}F NMR ($CDCl_3$): δ −65.4 (s, 3F, CF_3), −75.3 (s, 3F, CF_3); Anal. Calcd. for $C_{10}H_{10}F_6O$: C, 46.15; H, 3.85. Found: C, 46.34; H, 4.03.

3.4.4. Trifluoracetamide (**12**)

B.p. 75 °C (17 mmHg), m.p. 75 °C, corresponding [16]; ^1H NMR (DMSO-d_6): δ 8.5 (br s, 1H, NH_2), 8.8 (br s, 1H, NH_2); ^{19}F NMR (DMSO-d_6): δ −75.4 (s, CF_3); Anal. Calcd. for $C_2H_2F_3NO$: C, 21.24; H, 1.77; N, 12.39. Found: C, 21.52; H, 1.92; N, 12.15.

3.4.5. 2-(Trifluoromethyl)-4,5-dimethylpyridine (**13**)

B.p. 85 °C (17 mmHg), n_D^{20} 1.4340; ^1H NMR ($CDCl_3$): δ 2.28 (s, 3H, CH_3), 2.35 (s, 3H, CH_3), 7.43 (s, 1H, Ar CH), 8.42 (s, 1H, Ar CH); ^{19}F NMR ($CDCl_3$): δ −68.0 (s, 3F, CF_3), −75.3 (s, 3F, CF_3); MS, 70 eV, *m/z* (%): 175 $[M]^+$ (2), 160 (3), 148 (34), 131 (5), 119 (100), 113 (2), 107 (60), 91 (46), 77 (25), 69 (7); Anal. Calcd. for $C_8H_8F_3N$: C, 54.86; H, 4.57; N, 8.00. Found: C, 52.31; H, 4.83; N, 8.19.

3.4.6. 4-(Trifluoromethyl)-2-ethoxycarbonyl-1,6-dimethyl-3-oxatricyclo[2.2.1.$0^{2,6}$]-heptane (**14**)

B.p. 78 °C (2 mmHg), m.p. 60–62 °C; ^1H NMR ($CDCl_3$): δ 1.30 (t, J = 7.0 Hz, 3H, CH_3), δ 1.40 (s, 6H, $2CH_3$), 1.82 (d, J_{AB} = 20.0 Hz, 2H, $2CH_2$), 1.94 (d, J_{BA} = 20.0 Hz, 2H, $2CH_2$), 4.32 (q, J = 7.0 Hz, 2H, CH_2O,); ^{19}F NMR ($CDCl_3$): −75.0 (s, CF_3); Anal. Calcd. for $C_{12}H_{15}F_3O_3$: C, 54.55; H, 5.68. Found: C, 54.81; H, 5.74.

3.4.7. 1,4-Bis(trifluoromethyl)-2-vinyloxy-5(6)-vinyloxy-7-oxabicyclo[2.2.1]heptane (**15**)

Mixture of three isomers: b.p. 98 °C (13 mmHg); ^1H NMR ($CDCl_3$): δ 1.5, 1.75, 2.02, 2.15, 2.50, 2.7, 3.1 (m, CH_2), 4.15, 4.2, 4.4, 4.55, 4.65 (m, CH), 5.1, 6.35 (m, CH=); ^{19}F NMR ($CDCl_3$): δ −78.4 (s, CF_3), −78.15 (s, CF_3), −76.4 (s, CF_3), −75.6 (s, CF_3), −72.85 (s, CF_3) −71.25 (s, CF_3); Anal. Calcd. for $C_{12}H_{12}F_6O_3$: C, 45.28; H, 3.77. Found: C, 45.57; H, 3.44.

*3.4.8. 1,4-Bis(trifluoromethyl)-2-vinylsulfanyl-5(6)-vinylsulfanyl-7-oxabicyclo[2.2.1]heptane (**16**)*

Mixture of two isomers: b.p. 88–90 °C (3 mmHg), n_D^{20} 1.4660; ^{1}H NMR ($CDCl_3$): δ 1.13–1.3, 1.5–1.75, 2.1–2.3, 2.4–2.6 (m, CH_2), 3.8–3.9, 4.1–4.2 (m, CH), 5.25–5.40, 6.2–6.5 (m, CH=); ^{19}F NMR ($CDCl_3$): δ −69.85 (s, CF_3), −73.96 (s, CF_3), −78.66 (s, CF_3); Anal. Calcd. for $C_{12}H_{12}F_6OS_2$: C, 41.14; H, 3.43. Found: C, 40.82; H, 3.20.

*3.4.9. 2,4-Bis(trifluoromethyl)-3-oxa-8-thiatetracyclo[3.3.0.0^{2,7}.0^{4,6}]octane (**17**)*

B.p. 64 °C (15 mmHg), m.p. 64 °C; ^{1}H NMR ($CDCl_3$): δ 2.55 (m, 4H, $2CH_2$), 3.85 (br d, J = 7.7 Hz, 2H, 2CH); ^{19}F NMR ($CDCl_3$): δ −75.5 (s, 3F, CF_3), −78.5 (s, 3F, CF_3); Anal. Calcd. for $C_8H_6F_6OS$: C, 36.36; H, 2.27. Found: C, 36.94; H, 2.53.

*3.4.10. 6,8-Bis(trifluoromethyl)-3,7-dioxatetracyclo[4.4.0.0^{5,9}.0^{8,10}]decane (**18**)*

B.p. 81 °C (13 mmHg), m.p. 76 °C; ^{1}H NMR ($CDCl_3$): δ 2.0 (dd, J_{XA} = 16.0 Hz, J_{XB} = 5.0 Hz, 2H, 2CH), 2.4 (dd, J_{AB} = 18.5 Hz, J_{AX} = 16.0 Hz, 2H, $2CH_2$), 2.55 (dd, J_{BA} = 18.5 Hz, J_{BX} = 5.0 Hz, 2H, $2CH_2$), 3.6 (dd, $J_{A'B'}$ = 20.5 Hz, 2H, $2CH_2$), 3.9 (dd, 2H, $2CH_2$, $J_{B'A'}$ = 20.5 Hz); ^{19}F NMR ($CDCl_3$): δ −79.38 (s, 3F, CF_3), −82.10 (s, 3F, CF_3); Anal. Calcd. for $C_{10}H_{10}F_6O_2$: C, 43.48; H, 3.62. Found: C, 43.81; H, 3.83.

*3.4.11. 1,7-Bis(trifluoromethyl)-13-oxatetracyclo[5.5.1.0^{2,6}.0^{8,12}]trideca-3,9(10)-diene (**19**)*

Mixture of two isomers: b.p. 118–120 °C (13 mmHg), n_D^{20} 1.4520; ^{1}H NMR ($CDCl_3$): δ 2.4–2.5, 2.8, 2.85, 3.2–3.4, 3.7–3.9 (m, CH_2, CH), 5.5–5.6, 5.8 (m, CH=); ^{19}F NMR ($CDCl_3$): δ −70.1 (s, CF_3), −71.47 (s, CF_3), −71.85 (s, CF_3) −72.85 (s, CF_3); Anal. Calcd. for $C_{14}H_{12}F_6O$: C, 54.19; H, 3.87. Found: C, 53.82; H, 3.45.

*3.4.12. 1,8-Bis(trifluoromethyl)-15-oxatetracyclo[6.6.1.0^{2,7}.0^{9,14}]pentadeca-3,10(12)-diene (**20**)*

Mixture of two isomers: b.p. 138 °C (13 mmHg), m.p. 38–41 °C. ^{1}H NMR ($CDCl_3$): δ 1.3, 1.55–2.3 (m, 8H, $4CH_2$), 2.75–3.10 (m, 4H, 4CH), 5.65–5.70, 6.0–6.2 (m, 4H, 4CH=); ^{19}F NMR ($CDCl_3$): δ −70.58 (s, CF_3), −70.91 (s, CF_3), −71.36 (s, CF_3), −71.54 (s, CF_3); Anal. Calcd. for $C_{16}H_{16}F_6O$: C, 56.80; H, 4.73. Found: C, 57.11; H, 4.98.

*3.4.13. 4,6-Bis(trifluoromethyl)-5-oxatetracyclo[4.3.0.0^{2,4}.0^{3,7}]nonane (**21**)*

B.p. 71 °C (14 mmHg), m.p. 73 °C; ^{1}H NMR ($CDCl_3$): δ 1.94 (br d, 2H, $2CH_2$, J_{AB} = 12.5 Hz), 2.00 (d, 2H, $2CH_2$, J_{BA} = 12.5 Hz), 2.05 (br s, 2H, 2CH), 2.51 (br s, 2H, 2CH); ^{19}F NMR ($CDCl_3$): δ −69.38 (s, 3F, CF_3), −72.05 (s, 3F, CF_3); MS, 70 eV, *m/z* (%): 258 $[M]^+$ (25), 239 (7), 230 (8), 189 (25), 161 (100), 146 (7), 141 (75), 133 (25), 114 (15), 91 (45), 69 (52); Anal. Calcd. for $C_{10}H_8F_6O$: C, 46.51; H, 3.10. Found: C, 46.78; H, 3.44.

*3.4.14. 1,5,12,16-Tetrakis(trifluoromethyl)-23,24-dioxaheptacyclo[14.6.1.1^{5,12}.0^{2,15}.0^{4,13}.0^{6,11}.0^{17,22}]tetracosa-8,19-diene (**22a**) and 1,5,12,16,20,27-hexakis-(trifluoromethyl)-31,32,33-trioxadecacyclo-[14.14.1.1^{5,12}.1^{20,27}.0^{2,15}.0^{4,13}.0^{6,11}.0^{17,30}.0^{19,28}.0^{21,26}] tritriaconta-8,23-diene (**22b**) [13]*

Product **22a** was sublimated at 2 mmHg and 110 → 130 °C, m.p. 192–213 °C, contained ∼70% main compound with n = 1; ^{1}H NMR ($CDCl_3$) main compound: δ 1.6, 1.8, 2.0–2.3 (m, CH_2); 2.95 (br s, CH); 5.95 (s); 6.0 (br s); ^{19}F NMR ($CDCl_3$): δ −70.5 (br s, CF_3); MS, 70 eV, *m/z* (%): 338 $[M]^+$ (2), 266 (3), 256 (100), 215 (15), 197 (16), 185 (7), 159 (22), 141 (15), 127 (5), 109 (4), 91 (20), 79 (60), 69 (6), 67 (32).

Product **22b** was sublimed at 2 mmHg and 130 → 160 °C, m.p. 280–310 °C (decom.), contains main compound with n = 2, and n = 1, and n > 2; ^{1}H NMR ($CDCl_3$): δ 1.5, 1.7, 2.0, 2.3 (m, CH_2); 2.8–3.0 (m, CH); 5.9 (br s); 6.0 (m); ^{19}F NMR ($CDCl_3$): δ −71.0 (br s, CF_3); MS, 70 eV, *m/z* (%): 527 $[M - 69]^+$ (2), 515 $[M - 80 - 1]^+$ (3), 159 (6), 141 (4), 127 (3), 82 (100), 69 (2), 67 (25).

*3.4.15. 5,7-Bis(trifluoromethyl)-6-oxatetracyclo[5.3.0.0^{2,5}.0^{4,8}]dec-9-ene (**23**) [13]*

B.p. 77 °C (10 mmHg), m.p. 45–47 °C; ^{1}H NMR ($CDCl_3$): δ 1.35 (d, J = 12.1, 1H, CH_2); 2.15 (d.t, J = 12.1, J = 7.3, 1H, CH_2); 2.66 (dd, J = 7.3, J = 6.8, 2H, 2CH); 2.98 (br.d, 2H, 2CH, J = 6.8); 6.08 (br.s, 2H, CH=CH); ^{19}F NMR ($CDCl_3$): δ −75.4 (s, 3F, CF_3); −74.2 (s, 3F, CF_3); ^{13}C NMR ($CDCl_3$): δ 130.5 (s, C=); 130.5 (s, C=); 123.1 (q, J = 1077.5, CF_3); 122.8 (q, J = 1100.5, CF_3); 102.3 (q, J = 120.0, CCF_3); 91.9 (q, J = 120.0, CCF_3); 49.4 (s, CH); 41.1 (s, CH); 21.1 (s, CH_2). Anal. Calcd. for $C_{11}H_8F_6O$: C, 48.89; H, 2.96. Found: C, 48.55; H, 3.17.

*3.4.16. 6,8-Bis(trifluoromethyl)-7-oxatetracyclo[6.3.0.0^{2,6}.0^{5,9}]undecane (**24a**) [13]*

B.p. 101 °C (17 mmHg), m.p. 83–85 °C; ^{1}H NMR ($CDCl_3$): δ 1.85 (s, 8H, $4CH_2$); 2.53 (s, 4H, 4CH); ^{19}F NMR −75.1 (s, CF_3); Anal. Calcd. for $C_{12}H_{12}F_6O$: C, 50.35; H, 4.20. Found: C, 50.61; H, 4.63.

*3.4.17. 6,8-Bis(n-heptafluoropropyl)-7-oxatetracyclo[6.3.0.0^{2,6}.0^{5,9}]undecane(**24c**) [13]*

B.p. 78 °C (2 mmHg), m.p. 45 °C; ^{1}H NMR ($CDCl_3$): δ 1.85 (s, 8H, $4CH_2$); 2.65 (s, 4H, 4CH); ^{19}F NMR −81.0 (br s, 6F, $2CF_3$); −117.3 (br s, 4F, $2CF_2$); −125.6 (br s, 4F, $2CF_2$). Anal. Calcd. for $C_{16}H_{12}F_{14}O$: C, 39.51; H, 2.47. Found: C, 39.76; H, 2.25.

*3.4.18. 6-Trifluoromethyl-8-ethoxycarbonyl-7-oxatetracyclo[6.3.0.0^{2,6}.0^{5,9}]undecane (**24g**)*

B.p. 98 °C (1 mmHg), n_D^{20} 1.4630; ^{1}H NMR ($CDCl_3$): δ 1.3 (t, 3H, CH_3); 1.83 (br s, 8H, $4CH_2$), 2.45 (s, 4H, 4CH), 4.3 (q, 2H, CH_2O); ^{19}F NMR −74.84 (s, CF_3); Anal. Calcd. for $C_{14}H_{17}F_3O_3$: C, 57.93; H, 5.86. Found: C, 58.23; H, 5.51.

References

[1] N.V. Vasil'ev, Y.E. Lyashenko, A.F. Kolomietz, G.A. Sokolski, Khim. Geterotsikl. Soedin., SSSR (1987) 562–564 [N.V. Vasiliev, Y.E. Lyashenko, A.F. Kolomietz, G.A. Sokolski, Chem. Het. Com. (English Transl.) 23 (1987) 470–471].

[2] C. Seitz, H. Wassmuth, Chem.-Ztg. 112 (1988) 80–81.

[3] F. Thalhammer, V. Wallfahrer, J. Sauer, Tetrahedron Lett. 29 (1988) 3231–3234.

[4] N.V. Vasil'ev, Y.E. Lyashenko, M.V. Galahov, A.F. Kolomietz, A.F. Gontar, G.A. Sokolski, Khim. Geterotsikl. Soedin., SSSR (1990) 95–100 [N.V. Vasiliev, Y.E. Lyashenko, M.V. Galahov, A.F. Kolomietz, A.F. Gontar, G.A. Sokolski, Chem. Het. Com. (English Transl.) 26 (1990) 81–86].

[5] Y.E. Lyashenko, N.V. Vasil'ev, A.F. Gontar, G.A. Sokolski, SU Patent 1553533 (1990).

[6] N.V. Vasil'ev, Y.E. Lyashenko, A.E. Patalakha, G.A. Sokolski, J. Fluor. Chem. 65 (1993) 227–231.

[7] R.N. Warrener, G.M. Elsey, R.A. Russell, E.R.T. Tiekink, Tetrahedron Lett. 36 (1995) 5275–5278.

[8] A.V. Golovin, N.V. Vasil'ev, A.A. Rodin, A.F. Kolomietz, Y.V. Sinyakov, L.M. Reingand, Zh. Obsch. Khim. 59 (1989) 2698–2702 [J. Gen. Chem. USSR (English Transl.) 59 (1989) 2411–2415].

[9] V.M. Koshelev, A.N. Chehlov, N.V. Vasil'ev, A.F. Gontar, I.V. Martynov, Izv. Akad. Nauk SSSR, Ser. Khim. (1988) 744–748 [Bull. Acad. Sci. USSR, Div. Chem. Sci. 38 (1989) 671–675].

[10] G. Zeitz, C.H. Gerninghans, Pharmazie 49 (1994) 102–106.

[11] H.C. Brown, M.T. Cheng, L.J. Parcell, D. Pilipovich, J. Org. Chem. 26 (1961) 4407–4409.

[12] W.J. Chambers, D.D. Goffman, J. Org. Chem. 26 (1961) 4410–4412.

[13] Preliminary communication: N.V. Vasil'ev, D.V. Romanov, T.D. Truskanova, K.A. Lyssenko, G.V. Zatonsky, Mendeleev Commun. (2006) 186–188.

[14] A.J. Gordon, R.A. Ford, The Chemist's Companion, Wiley-Interscience Publication, New York/London/Sydney/Toronto, 1972.

[15] Th. Curtius, J. Prakt. Chem. (1915) 415–441.

[16] A.M. Lovelace, D.A. Rausch, M. Postelnek, Aliphatic Fluorine Compounds, Rein. Publ. Corp., New York, 1957.