Journal of Fluorine Chemistry 147 (2013) 22–30

Contents lists available at SciVerse ScienceDirect

Journal of Fluorine Chemistry

journal homepage: www.elsevier.com/locate/fluor

On the reactions of trialkyl(trifluorovinyl)silanes with isocyanates and isothiocyanates – Expected and surprising results

Natalia V. Kirij [a], Wieland Tyrra [**,b], Harald Scherer [c], Yurii L. Yagupolskii [a,*], Ingo Pantenburg [b], Dieter Naumann [b]

[a] Institute of Organic Chemistry, National Academy of Sciences of Ukraine, Murmanskaya 5, UA-02094 Kiev, Ukraine
[b] Institut für Anorganische Chemie, Universität zu Köln, Greinstraße 6, D-50939 Köln, Germany
[c] Institut für Anorganische und Analytische Chemie, Albert-Ludwigs-Universität Freiburg, Albertstraße 21, D-79104 Freiburg, Germany

ARTICLE INFO

Article history:
Received 18 October 2012
Received in revised form 8 January 2013
Accepted 12 January 2013
Available online 19 January 2013

Keywords:
Iso(thio)cyanates
Amides
β-Lactams
Synthons

ABSTRACT

Conditions for the addition of trialkyl(trifluorovinyl)silanes to the carbonyl- and thiocarbonyl function of commercially available isocyanates and isothiocyanates in the presence of tetramethylammonium fluoride (TMAF) to give corresponding amides of 2,3,3-trifluoroacrylic and 2,3,3-trifluorothioacrylic acids have been elaborated. The behaviour of the synthesized amides towards fluoride ions was studied. The syntheses of the amides of 2,3,3,3-tetrafluoropropionic and 2,3,3,3-tetrafluorothiopropionic acids and some unexpected cyclic products with the β-lactam structure are described. The molecular structures of the *c*-hexyl amide of 2,3,3,3-tetrafluoropropionic acid and two isomers of β-lactams deriving from the reaction of the *tert*-butyl amide of 2,3,3-trifluoroacrylic acid with a fluoride source have been elucidated by XRD measurements.

1. Introduction

2,3,3-Trifluoroacrylic acid and its derivatives are of great interest as synthons in organofluorine chemistry. However, the possibilities to use them are strictly limited due to the absence of convenient synthetic methods. The most simple, from a synthetic point of view, method to introduce a trifluorovinyl group into an organic molecule is via direct addition of this group to a carbonyl function. However, this approach can be successfully used solely to obtain perfluoroacrylic acid itself via reaction of lithium derivatives of some trifluoroethylenes with carbon dioxide [1]. In contrast, esters [2] and unsubstituted amides [3] of perfluoroacrylic acid were obtained in most cases from the corresponding derivatives of trifluoropropionic acid via halogen or hydrohalogenic acid elimination. Commonly, trifluoropropionic acid derivatives are not readily available, and their synthesis is a separate task. On the other hand, to our knowledge, synthesis and properties of substituted amides of perfluoroacrylic acid are not reported in the literature. Similarly, perfluorothioacrylic acid and its derivatives are not studied, and representatives of this class of compounds remain unknown until now. It is probable that such compounds as well as derivatives of perfluoroacrylic acid will be of great interest as synthons in organofluorine chemistry.

We demonstrated previously that trimethyl(trifluoromethyl)-silane in the presence of fluoride ions can conveniently be used to convert isocyanates and isothiocyanates into the corresponding trifluoroacetamides and trifluorothioacetamides [4].

In extension of our systematic studies on reactions of perfluorinated anions generated from the corresponding fluoroorgano silanes in the presence of fluoride ions with heterocumulenes of the type R–X = Y = Z, with X = N, S; Y = C, S; Z = O, S in different combinations, we now report on the reactions of isocyanates and isothiocyanates with trialkyl(trifluorovinyl)silanes ($Alk_3SiCF=CF_2$, Alk = Me, Et) in the presence of tetramethylammonium fluoride ($[Me_4N]F$) and the conversion of the synthesized amides of 2,3,3-trifluoroacrylic and 2,3,3-trifluorothioacrylic acids under the influence of fluoride ions.

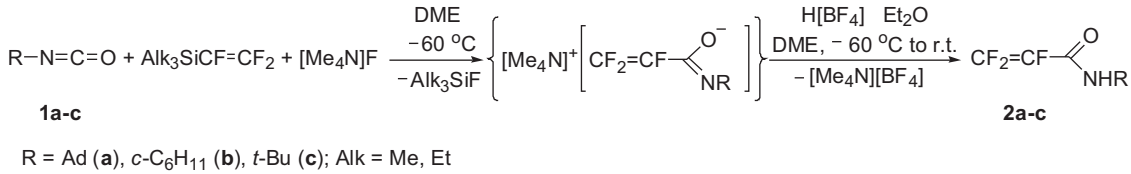
2. Results and discussion

We found that the reaction of equimolar quantities of the isocyanates **1a–c**, $Alk_3SiCF=CF_2$ (Alk = Me, Et) and $[Me_4N]F$ in dimethoxyethane (DME) at −60 °C proceeds selectively within 2 h; protolysis of the intermediates led to the formation of amides of trifluoroacrylic acid **2a–c** in 60–70% yields (Scheme 1).

Reaction intermediates in all cases were tetramethylammonium salts of the N-substituted amides of 2,3,3-trifluoroacrylic acid which were directly formed after mixing of the reagents. Upon

* Corresponding author. Tel.: +38 044 5590349; fax: +38 044 5732643.
** Co-corresponding author.
E-mail address: yagupolskii@ioch.kiev.ua (Y.L. Yagupolskii).

0022-1139/$ – see front matter © 2013 Elsevier B.V. All rights reserved.
http://dx.doi.org/10.1016/j.jfluchem.2013.01.011



Scheme 1. Synthesis of **2a–c**.

treatment of these salts with $H[BF_4]\cdot Et_2O$ at −60 °C, they were converted selectively into the corresponding amides. We observed no significant difference upon usage of trimethyl- and triethyl(trifluorovinyl)silanes.

Compounds **2a–c** were isolated as colourless stable solids and were characterized by ^{1}H, ^{19}F, ^{13}C NMR and mass spectra. Elemental analyses supported the compositions. It should be noted that the reaction of ethyl- and phenylisocyanate with the system $Alk_3SiCF{=}CF_2/F^-$ (Alk = Me, Et) under similar conditions proceeded less selectively and led to product mixtures. Unfortunately, we failed to isolate the pure amides, but their formation was monitored by ^{19}F NMR spectroscopy comparing the chemical shifts and couplings with those of the isolated products.

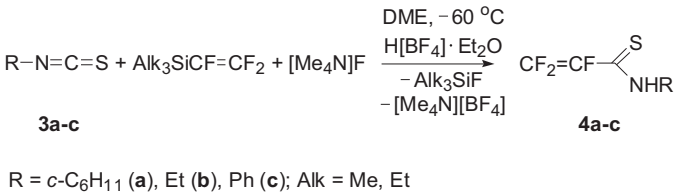
In order to extend this reaction to derivatives of 2,3,3-trifluorothioacrylic acid, we investigated the possibility of synthesising so far unknown amides of trifluorothioacrylic acid. The isothiocyanates **3a–c** react with the system $Alk_3SiCF{=}CF_2/F^-$, in a similar manner as described for **2a–c**, to yield the amides of trifluorothioacrylic acid **4a–c** (Scheme 2).

The thioamide **4a** was obtained using column chromatography in 50% yield as a yellow liquid. Its composition was elucidated by NMR spectroscopic methods, mass spectra and elemental analysis. The thioamides **4b** and **4c**, initially formed in 60–70% yields as monitored by ^{19}F NMR spectroscopic means (relative to 1,4-difluorobenzene) exhibited to be less stable. Upon attempted isolation of compound **4b** using column chromatography, a great amount of **4b** decomposed finally leading to 15% of the neat product which was identified by NMR spectroscopic techniques and supported by satisfactory elemental analyses; amide **4c** could not be isolated and is proposed solely on its characteristic ^{19}F NMR spectrum in comparison with those of **4a** and **b**. Compounds **4a,b** are stable in a dry argon atmosphere at −30 °C for several weeks exhibiting no visible decomposition, while in solution all thioamides completely decomposed within some days.

Earlier, we showed that trifluorovinyl containing alcohols react with fluoride anions via addition to the C=C double bond [5].

Next, we investigated the reactions of the amides of 2,3,3-trifluoroacrylic and 2,3,3-trifluorothioacrylic acids with tetramethylammonium fluoride. Compounds **2a,b** react with one equivalent of $[Me_4N]F$ in DME in a temperature range from −30 °C to room temperature to form the amides of 2,3,3,3-tetrafluoropropionic acid **5a,b** (Scheme 3).

It has to be pointed out that amides of 2,3,3-trifluoroacrylic acid **2a,b** can be used without prior isolation in a reaction with $[Me_4N]F$ opening an easy and convenient one-pot synthesis route to obtain of the amides **5a,b** in high yields (Scheme 4). A mechanistic explanation how the $[Me_4N]$-cation serves as a proton source cannot be given.



Scheme 2. Synthesis of **4a–c**.

Compounds **5a,b** were isolated as colourless stable solids in 62% and 65% yields, respectively, and were characterized by 1D and 2D NMR spectroscopic methods as well as EI mass spectra. Elemental analyses supported the compositions. Crystals of the amide **5b** suitable for XRD analysis were grown from pentane-hexane mixtures. The molecular structure of **5b** is depicted in Fig. 1. Crystallographic data are summarized in the experimental part. Selected bond lengths and angles are given in the caption of Fig. 1.

2.1. Description of the molecular structure of *5b*

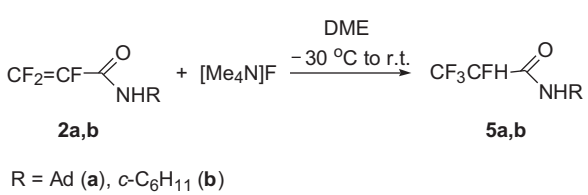
Compound **5b** crystallizes in the triclinic space group $P\bar{1}$ (no. 2) with two crystallographically independent molecules. All bond lengths and angles do not deviate from expectations for such a molecule. The carbon–oxygen distances of C13–O131 (123.3(3) pm) and C23–O231 (123.6(3) pm) clearly imply the character of a C=O double bond. Also the angles around C13 (N14) and C23 (N24) varying around 120 ± 5° describe a typical arrangement for an amide of a carboxylic acid.

In both independent molecules, the cyclohexyl groups reside in the chair conformation. In the packing, both molecules are connected to infinite chains along the crystallographic *a*-axis with alternating cyclohexyl groups exhibiting two intermolecular alternating graph set motifs C(4) [6] for hydrogen bridges following D–H (N14–H5) 82.5(22) pm; H···A (H5···O231) 208.9(24) pm; D···A (N14···O231) 288.2(9) pm; D–H···A 160.9(20)° and D–H (N24–H8) 79.6(25) pm; H···A (H8···O131) 213.9(23) pm; D···A (N24···O131) 289.7(15) pm; D–H···A 159.4(20)°.

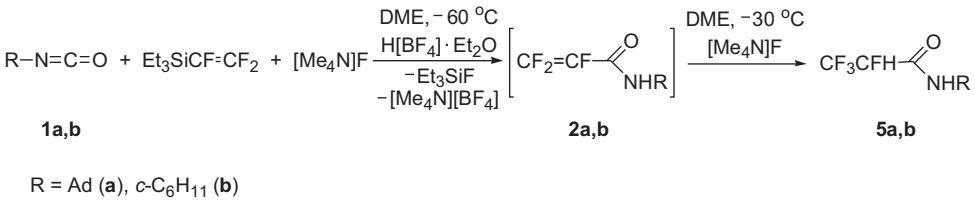
Surprisingly, the analogous reaction of the amide **2c** with tetramethylammonium fluoride afforded not only the expected amide of N-*tert*-butyl-2,3,3,3-tetrafluoropropanamide **5c** but the unexpected β-lactams **6** and **7** (Scheme 5).

The amount of tetramethylammonium fluoride was found to be critical for the products formation ratio. Thus, compound **2c** reacted with $[Me_4N]F$ in a molar ratio of 1:1 in DME in a temperature range between −30 °C to 20 °C to form the unprecedented mixture of the amide **5c** and the cyclic products **6** and **7** in a 9:1 ratio. Using a catalytic amount of tetramethylammonium fluoride caused lower amount of the amide **5c** (60%) but a concomitant increase of the formation of the products **6** and **7** (40%) (ratio approximately 3:2).

Most probably, attack of a fluoride ion at the double bond of **2c** initially affords the anion **8**. It should be noted that the trifluorovinyl group of compound **2c** is highly reactive toward nucleophiles. The nucleophilic addition of the anion **8** to the trifluorovinyl unit of **2c**, which leads to the formation of intermediates of type **A**, is accompanied by fluoride anion



Scheme 3. Synthesis of **5a,b**.



Scheme 4.

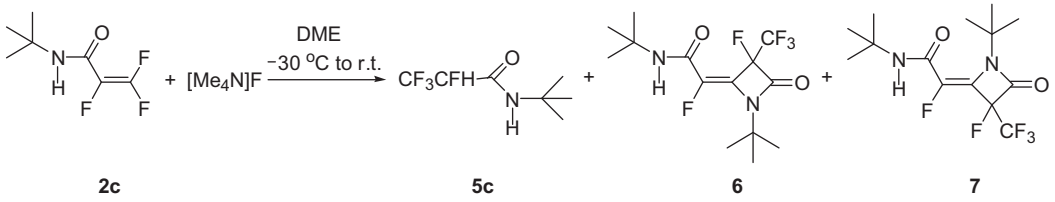
(intermediates of type **B**) and hydrofluoric acid elimination with formation of the products **6** and **7** (Scheme 6).

Compounds **5c**, **6** and **7** were isolated as colourless stable solids using column chromatography and were identified by NMR spectroscopic techniques, mass spectra and elemental analyses. Crystals suitable for X-ray analysis of **6** and **7** were grown from pentane solution and pentane-dimethoxyethane mixture, respectively. The molecular structures of **6** and **7** are depicted in Figs. 2 and 3. Crystallographic data are summarized in the experimental part. Selected bond lengths and angles are given in the caption of the corresponding Fig.

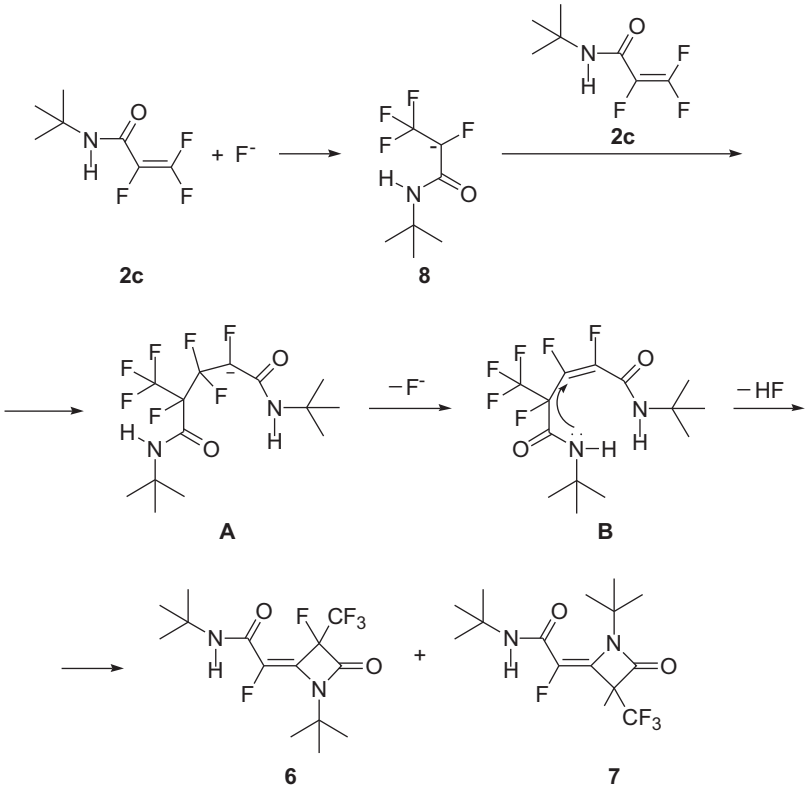
2.2. Comparative description of the molecular structures of **6** and **7**

Compound **6** crystallizes in the acentric orthorhombic space group $Pca2_1$ (no. 29), compound **7** in the monoclinic space group $P2_1/c$ (no. 14) both with 4 molecules per unit cell. Despite the fact of being stereoisomers, molecular structures of both do not deviate significantly from each other. Angular sums around the 4-membered ring are nearly identical together with bond lengths and angles (cp. captions to Figs. 2 and 3) and are in good agreement with the rare examples of structurally characterized compounds bearing an alkylidene azetidinone moiety [7–12]. The steric demand of both *tert*-butyl groups, when residing in the same direction as in isomer **7**, twists the amide moiety out of the plane, formed by the β-lactam and the unsaturated chain, by approximately 30°. In derivative **6**, coplanarity of the whole unit is evident as also observed in the molecular structure of 3-(1-hydroxyethyl)-4-[2-ethoxycarbonyl-(*Z*)-methylidene]-azetidin-2-one [8,9].

Identical structures in solution and in the solid state for both compounds have been established by NMR spectroscopic methods on the basis of 1D and 2D experiments (H,C{^{19}F} HSQC; H,C{^{19}F}



Scheme 5. Synthesis of **5c**, **6** and **7**.



Scheme 6. Probable mechanism for the formation of **6** and **7**.

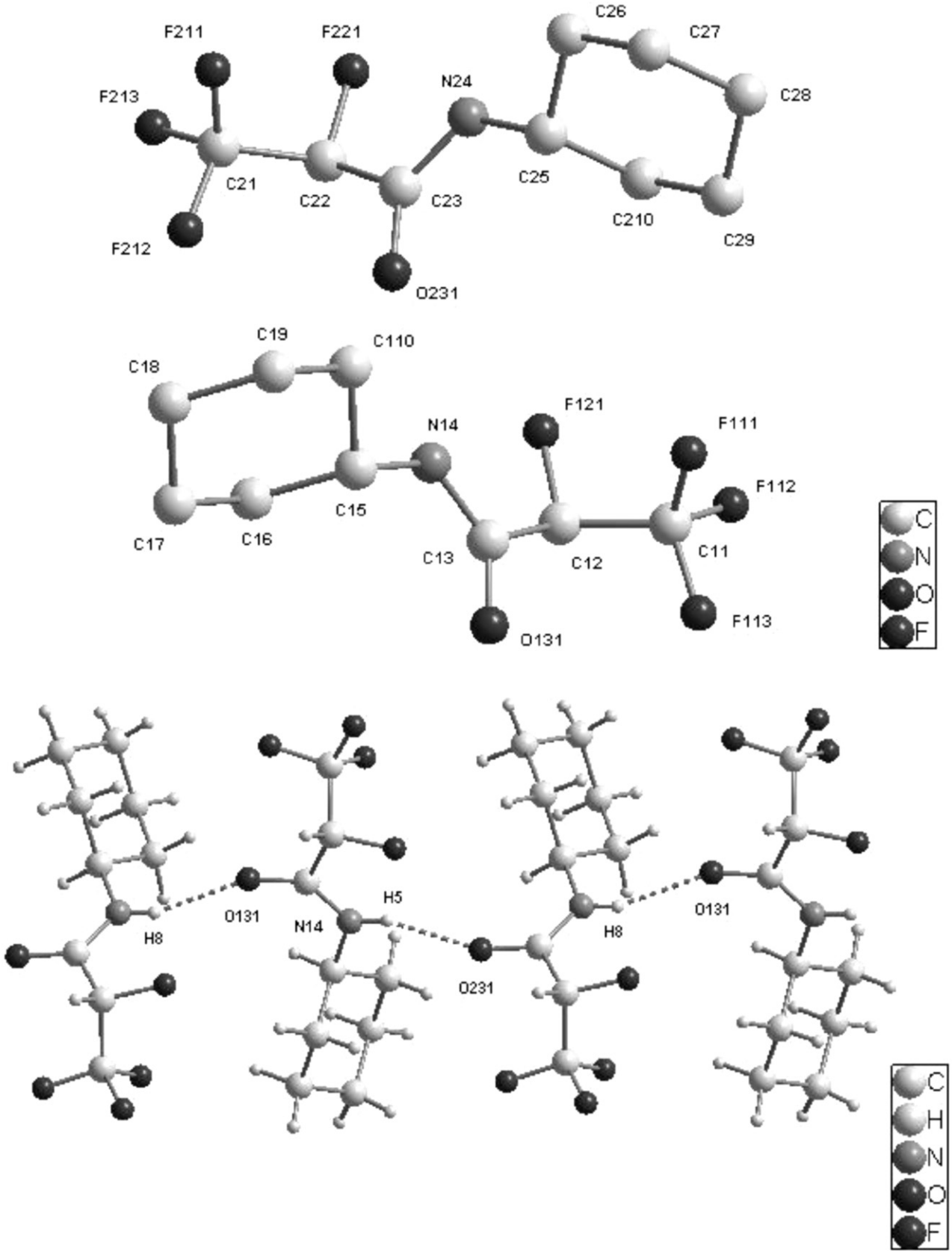


Fig. 1. Molecular structure of N-cyclohexyl-2,3,3,3-tetrafluoropropanamide (**5b**) with the corresponding numbering scheme depicted along the crystallographic *b*-axis (top); graph set motif C(4) (bottom). Selected bond lengths (pm) and angles (°): C13–O131 123.3(3); C15(ring)–N14 146.9(16); N14–C13 132.2(14), C13–C12 152.8(17); C12–C11 150.7(6); C15–N14–C13 122.74(16); N14–C13–C12 116.54(16); N14–C13–O131 123.37(15); O131–C13–C12 117.09(15); C23–O231 123.6(3); C25(ring)–N24 146.2(6); N24–C23 132.6(11); C23–C22 151.4(7); C22–C21 151.1(16); C25–N24–C23 122.92(16); N24–C23–C22 117.21(15); N24–C23–O231 125.58(15); O231–C23–C22 117.21(14).

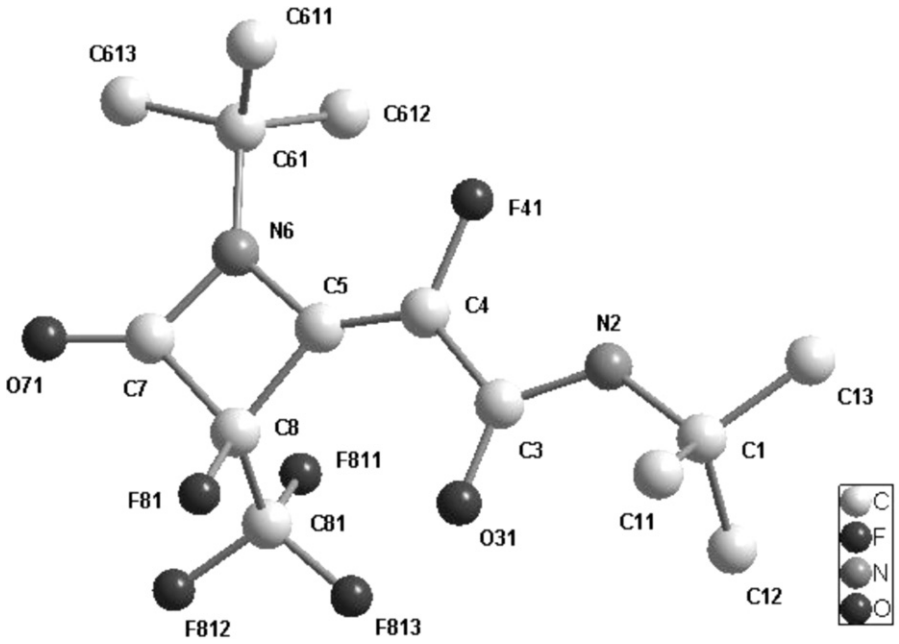


Fig. 2. Molecular structure of N-*tert*-butyl-2-[1-*tert*-butyl-3-fluoro-4-oxo-3-trifluoromethyl-azetidin-(2*Z*)-ylidene]-2-fluoro-acetamide (**6**) with the corresponding numbering scheme. Selected bond lengths (pm) and angles (°): C31–O31 121.8(6); C71–O71 122.2(6); C5–C4 130.7(6); C4–C3 149.4(7); C3–N2 132.9(6); N2–C1 149.3(6); ring; C5–C6 141.3(6); C7–C6 135.8(7); C7–N6–C5 93.5(5); N6–C5–C8 89.8(4); C5–C8–C7 83.9(4); C8–C7–C6 91.7(4); angular sum (4-membered ring) 359.3. Torsion angle C5–C4–C3–O31 −5.23(83).

HMBC; F,C{^{1}H} HSQC; F,C{^{1}H} HMBC; H,H NOESY; F,F COSY; F,F NOESY; F,H HOESY). Some specific features have to be mentioned. In the ^{19}F NMR spectrum of the *Z*-isomer (**6**), the signal of the CF_3 group is split into a doublet (−74.2, $^3J_{F,F}$ = 10.0 Hz), that of the adjacent fluorine atom (−173.9, $^3J_{F,F}$ = 10 Hz; $^4J_{F,F} \approx 1$ Hz) into a quartet of doublets due to the coupling with the olefinic fluorine atom which itself occurs as a broadened singlet (−139.6, $\Delta_{1/2} \approx 7$ Hz). The spatial vicinity of the olefinic fluorine atom and the *tert*-butyl group attached to the β-lactam (shortest d(F,H) ≈ 226 pm; shortest d(F,C) ≈ 306 pm in the solid state) together with the rigidity of alkylidene azetidinone kernel effect long-range ("through space") couplings of $^5J_{F,C}$ = 7 Hz and $^6J_{F,H}$ = 0.9 Hz. These phenomena are frequently observed for compounds showing similar spatial arrangements [13,14].

In the ^{19}F NMR spectrum of the *E*-isomer (**7**), signals of all fluorine groups are split into more or less complex multiplets.

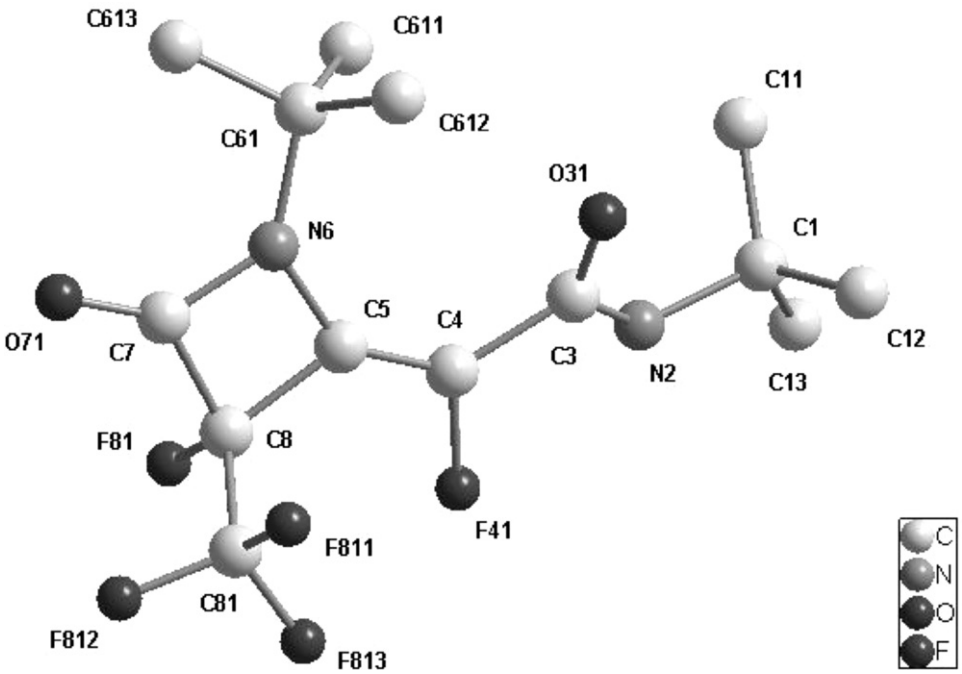
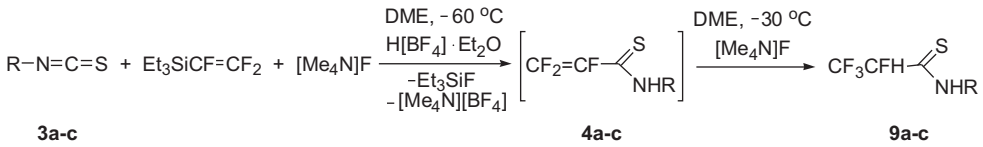


Fig. 3. Molecular structure of N-*tert*-butyl-2-[1-*tert*-butyl-3-fluoro-4-oxo-3-trifluoromethyl-azetidin-(2*E*)-ylidene]-2-fluoro-acetamide (**7**) with the corresponding numbering scheme. Selected bond lengths (pm) and angles (°): C31–O31 121.0(4); C71–O71 121.0(4); C5–C4 132.5(4); C4–C3 150.1(4); C3–N2 132.9(4); N2–C1 148.4(4); ring; C5–C6 142.5(4); C7–C6 138.4(4); C7–N6–C5 93.5(2); N6–C5–C8 90.8(2); C5–C8–C7 84.8(2); C8–C7–C6 91.0(2); angular sum (4-membered ring) 360.1. Torsion angle C5–C4–C3–O31 +28.26(56).



Scheme 7. Synthesis of **9a–c**.

While the fluorine atom directly bond to the β-lactam exhibits a quartet of doublets (−177.6, $^{3}J_{F,F}$ = 10.9 Hz; $^{4}J_{F,F}$ = 6.6 Hz) and the CF_3 group a doublet of doublets (−76.3, $^{3}J_{F,F}$ = 10.9 Hz; $^{5}J_{F,F}$ = 13.6 Hz (!!!)), the resonance of the olefinic fluorine atom (−143.4, $^{5}J_{F,F}$ = 13.6 Hz (!!!); $^{4}J_{F,F}$ = 6.6 Hz; $^{4}J_{F,H}$ = 4.5 Hz (!!!)) is split into a quartet of doublets of an additional doublet due to the coupling with the proton of the adjacent amino group. The exceptional large $^{5}J_{F,F}$ and $^{4}J_{F,H}$ couplings may again be attributed to the spatial vicinity of those nuclei. However, the NH resonance is observed only as a broadened singlet ($\Delta_{1/2} \approx 15$ Hz) in the ^{1}H NMR spectrum.

The β-lactam structure is of great interest as a fundamental and versatile building block in the design and synthesis of several biologically active compounds. It has widely been used to obtain fundamental antibacterial products (β-lactam antibiotics) [15], unusual peptide derivatives [16] and enzymatic inhibitors of different serine proteases [17]. It should be noted that fluorinated compounds **6** and **7** obtained in the course of research are of great practical interest. The procedure described above opens a convenient alternative route to cyclic products with the β-lactam motif directly accessible from relative inexpensive isocyanates as starting materials.

We further investigated the reaction of amides of the 2,3,3-trifluorothioacrylic acid and tetramethylammonium fluoride.

In a similar manner as described for the synthesis of **5a,b**, the unstable amides **4a–c**, obtained without prior isolation, reacted with one equivalent $[Me_4N]F$ in DME in the temperature range from −30 °C to room temperature to form the amides of the 2,3,3,3-tetrafluorothiopropionic acid **9a–c** (Scheme 7).

The thioamides **9a–c** were obtained as yellow liquids using column chromatography. Their compositions were elucidated by NMR spectroscopic methods, mass spectra and elemental analyses.

Taking into consideration the availability of the reagents we have used together with the good yields of the final products, the method presented opens an attractive alternative route to obtain amides of 2,3,3,3-tetrafluoropropionic and 2,3,3,3-tetrafluorothiopropionic acids which again may become sources of new and innovative synthetic procedures.

3. Conclusions

In summary, a new, convenient and efficient synthesis of amides of 2,3,3-trifluoroacrylic **2** and 2,3,3-trifluorothioacrylic acids **4** has been developed by means of the direct addition of the trifluorovinyl group – generated from trialkyl(trifluorovinyl)silanes in the presence of tetramethylammonium fluoride – to easily available or commercial substances such as organic isocyanates and isothiocyanates. The formation of compounds **2** and **4** opens an easy and convenient route to the synthesis of amides of 2,3,3,3-tetrafluoropropionic **5** and 2,3,3,3-tetrafluorothiopropionic **9** acids. It should also be noted that the reaction of **2c** and $[Me_4N]F$ proceeds to yield the fluorine containing β-lactams **6** and **7** which were fully characterized including the solid state structures.

4. Experimental

General: All reactions were carried out in a dry argon atmosphere by using Schlenk techniques. The following products were synthesized according to literature procedures: $Me_3SiCF{=}CF_2$ [1a], $Et_3SiCF{=}CF_2$ [1a], $[Me_4N]F$ [18]. All solvents were purified according to literature procedures [19]. ^{1}H, ^{13}C and ^{19}F NMR were recorded with Bruker AvanceII 300 and Avance 400 spectrometers. Chemical shifts are referenced relative to the external standards Me_4Si (^{1}H and ^{13}C) and CCl_3F (^{19}F). Mass spectra (EI; 20 eV) were obtained with a Finnigan MAT 95 spectrometer. Melting points were measured in one-end-open glass capillaries and are uncorrected. Column chromatography was carried out by using 60–240 mesh silica gel at atmospheric pressure. C, H, N and F analyses were performed with HEKAtech Euro EA 3000 and Analytikjena Spekol 1100 instruments.

Data collection for X-ray structure determination was performed on STOE IPDS I/II diffractometers using graphite-monochromated Mo–Kα radiation. The data were corrected for Lorentz and polarization effects. A numerical absorption correction based on crystal-shape optimisation was applied for all data [20]. The programs used in this work are Stoe's X-Area [21], including X-RED and X-Shape for data reduction and absorption correction [22], and the WinGX suite of programs [23], including SIR-92 [24] and SHELXL-97 [25] for structure solution and refinement. The hydrogen atoms were placed in idealized positions and constrained to ride on their parent atom. The last cycles of refinement included atomic positions for all the atoms, anisotropic thermal parameters for all the non-hydrogen atoms and isotropic thermal parameters for all of the hydrogen atoms. Crystallographic data for the structures have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. CCDC-873761 (**5b**), CCDC-873759 (**6**), and CCDC-873760 (**7**). Copies of the data can be obtained, free of charge, on application to CHGC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 1223 336033 or deposit@ccdc.cam.ac.uk).

4.1. General procedure for the synthesis of 2,3,3-trifluoroacrylamides *2*

To a solution of isocyanate **1** (5 mmol) in dimethoxyethane (DME) (25 mL) at −60 °C was added $R_3SiCF{=}CF_2$ (R = Me, Et) (6.25 mmol) and $[Me_4N]F$ (0.51 g, 5.5 mmol). The mixture was stirred for 2 h at −55 ± 5 °C and then $HBF_4{\cdot}Et_2O$ (0.81 g, 5 mmol) was added. The mixture formed was allowed to reach room temperature and stirred for 1 h. The solvent and all other volatile materials were evaporated in vacuo and the product was extracted into hexane. The precipitated $[Me_4N][BF_4]$ was filtered and the solvent was removed in vacuo. The amides **2** were purified by crystallization from pentane or by sublimation.

4.2. N-1-Adamantyl-2,3,3-trifluoroacrylamide (*2a*)

Yield 0.86 g (66%), white solid, mp 114–115 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 1.7 (broad s, 6H, Ad), 2.06 (broad s, 6H,

Ad), 2.11 (broad s, 3H, Ad), 5.75 (broad s, 1H, NH). ^{13}C (100.623 MHz, $CDCl_3$): δ 29.4 (3C, CH), 36.2 (3C, CH_2), 41.5 (3C, CH_2), 52.9 (C), 124.5 (ddd, $^1J_{C,F}$ = 248 Hz, $^2J_{C,F}$ = 32 Hz, $^2J_{C,F}$ = 18 Hz, =CF–), 156.0 (ddd, $^1J_{C,F}$ = 298 Hz, $^1J_{C,F}$ = 301 Hz, $^2J_{C,F}$ = 41 Hz, =CF_2), 156.5 (ddd, $^2J_{C,F}$ = 23 Hz, $^3J_{C,F}$ = 6.4 Hz, $^3J_{C,F}$ = 5.5 Hz, CO). ^{19}F (282.4 MHz, $CDCl_3$): δ −87.5 (dd, $^1J_{F,C}$ = 298 Hz, $^2J_{F,F}$ = 32 Hz, $^3J_{F,Fcis}$ = 35 Hz, =C*F*F), −100.8 (dd, $^1J_{F,C}$ = 301 Hz, $^2J_{F,F}$ = 32 Hz, $^3J_{F,Ftrans}$ = 113 Hz, =C*F*F), −181.1 (dd, $^1J_{F,C}$ = 248 Hz, $^3J_{F,Ftrans}$ = 113 Hz, $^3J_{F,Fcis}$ = 35 Hz, =CF–) ppm. MS (EI): *m*/*z* (%) = 259 (90) $[M]^+$. Anal. Calcd for $C_{13}F_3H_{16}NO$ (259.27): C 60.22, F 21.98, H 6.22, N 5.4. Found: C 60.14, F 21.91, H 6.17, N 5.34.

4.3. *N*-Cyclohexyl-2,3,3-trifluoroacrylamide (**2b**)

Yield 0.71 g (69%), white solid, mp 103–104 °C. ^1H NMR (300.13 MHz, $CDCl_3$): δ 1.28 (m, 5H, *c*-C_6H_{11}), 1.63 (m, 1H, *c*-C_6H_{11}), 1.72 (m, 2H, *c*-C_6H_{11}), 1.94 (m, 2H, *c*-C_6H_{11}), 3.85 (m, 1H, *c*-C_6H_{11}), 6.11 (broad s, 1H, NH). ^{13}C (100.623 MHz, $CDCl_3$): δ 25.0 (2C, CH_2), 25.6 (CH_2), 33.0 (2C, CH_2), 48.5 (CH), 124.7 (ddd, $^1J_{C,F}$ = 248 Hz, $^2J_{C,F}$ = 31 Hz, $^2J_{C,F}$ = 18 Hz, =CF–), 156.2 (ddd, $^1J_{C,F}$ = 297 Hz, $^1J_{C,F}$ = 301 Hz, $^2J_{C,F}$ = 42 Hz, =CF_2), 156.9 (ddd, $^2J_{C,F}$ = 22 Hz, $^3J_{C,F}$ = 6.5 Hz, $^3J_{C,F}$ = 5.4 Hz, CO). ^{19}F (282.4 MHz, $CDCl_3$): δ −87.7 (dd, $^1J_{F,C}$ = 297 Hz, $^2J_{F,F}$ = 32 Hz, $^3J_{F,Fcis}$ = 35 Hz, =C*F*F), −100.6 (dd, $^1J_{F,C}$ = 301 Hz, $^2J_{F,F}$ = 32 Hz, $^3J_{F,Ftrans}$ = 114 Hz, =C*F*F), −183.7 (dd, $^1J_{F,C}$ = 248 Hz, $^3J_{F,Ftrans}$ = 114 Hz, $^3J_{F,Fcis}$ = 35 Hz, =CF). MS (EI): *m*/*z* (%) = 207 (10) $[M]^+$, 126 (100) $[M-C_2F_3]^+$. Anal. Calcd for $C_9F_3H_{12}NO$ (207.2): C 52.17, F 27.51, H 5.84, N 6.76. Found: C 52.11, F 27.45, H 5.79, N 6.72.

4.4. *N*-tert-Butyl-2,3,3-trifluoroacrylamide (**2c**)

Yield 0.59 g (65%), white solid, mp 66–67 °C. ^1H NMR (300.13 MHz, $CDCl_3$): δ 1.43 (s, 9H, *tert*-Bu), 5.9 (broad s, 1H, NH). ^{13}C (100.623 MHz, $CDCl_3$): δ 28.7 (3C, CH_3), 52.2 (C), 124.6 (ddd, $^1J_{C,F}$ = 250 Hz, $^2J_{C,F}$ = 32 Hz, $^2J_{C,F}$ = 19 Hz, =CF), 155.9 (ddd, $^1J_{C,F}$ = 299 Hz, $^1J_{C,F}$ = 301 Hz, $^2J_{C,F}$ = 43 Hz, =CF_2), 156.8 (ddd, $^2J_{C,F}$ = 21 Hz, $^3J_{C,F}$ = 6.5 Hz, $^3J_{C,F}$ = 5.5 Hz, CO). ^{19}F (282.4 MHz, $CDCl_3$): δ −87.6 (dd, $^1J_{F,C}$ = 299 Hz, $^2J_{F,F}$ = 31 Hz, $^3J_{F,Fcis}$ = 35 Hz, =C*F*F), −100.7 (dd, $^1J_{F,C}$ = 301 Hz, $^2J_{F,F}$ = 31 Hz, $^3J_{F,Ftrans}$ = 114 Hz, =C*F*F), −181.5 (dd, $^1J_{F,C}$ = 250 Hz, $^3J_{F,Ftrans}$ = 114 Hz, $^3J_{F,Fcis}$ = 35 Hz, =CF–). MS (EI): *m*/*z* (%) = 181 (10) $[M]^+$, 166 (100) $[M-CH_3]^+$. Anal. Calcd for $C_7F_3H_{10}NO$ (181.16): C 46.41, F 31.46, H 5.56, N 7.73. Found: C 46.34, F 31.41, H 5.52, N 7.67.

4.5. General procedure for the synthesis of 2,3,3-trifluorothioacrylamides **4**

To a mixture of isothiocyanate **3** (5 mmol) and $[Me_4N]F$ (0.51 g, 5.5 mmol) in dimethoxyethane (DME) (30 mL) at −60 °C was added $Et_3SiCF=CF_2$ (1.23 g, 6.25 mmol) dropwise over a period of 30 min. The mixture was stirred for 90 min at −55 ± 5 °C and then $HBF_4{\cdot}Et_2O$ (0.81 g, 5 mmol) was added. The mixture formed was allowed to warm to the room temperature and stirred for 1 h. All volatile components were removed in vacuo and the product was extracted into hexane. The precipitated $[Me_4N][BF_4]$ was filtered and the solvent was evaporated in vacuo. The thioamides **4** were purified by silica gel column chromatography.

4.6. *N*-Cyclohexyl-2,3,3-trifluorothioacrylamide (**4a**)

Yield 0.55 g (49%), yellow liquid, R_f 0.15 (hexane/benzene 4:1). ^1H NMR (400.14 MHz, $CDCl_3$): δ 1.25 (m, 3H, *c*-C_6H_{11}), 1.38 (m, 2H, *c*-C_6H_{11}), 1.64 (m, 1H, *c*-C_6H_{11}), 1.73 (m, 2H, *c*-C_6H_{11}), 2.05 (m, 2H, *c*-C_6H_{11}), 4.44 (m, 1H, *c*-C_6H_{11}), 7.45 (broad s, 1H, NH). ^{13}C (100.623 MHz, $CDCl_3$): δ 24.9 (2C, CH_2), 25.7 (CH_2), 31.7 (2C, CH_2), 53.0 (CH), 128.8 (ddd, $^1J_{C,F}$ = 246 Hz, $^2J_{C,F}$ = 21.5 Hz, $^2J_{C,F}$ = 22.6 Hz, =CF), 156.6 (ddd, $^1J_{C,F}$ = 295 Hz, $^1J_{C,F}$ = 302 Hz, $^2J_{C,F}$ = 48 Hz, =CF_2), 179.4 (ddd, $^2J_{C,F}$ = 15 Hz, $^3J_{C,F}$ = 8.3 Hz, $^3J_{C,F}$ = 4.6 Hz, CS). ^{19}F (282.4 MHz, $CDCl_3$): δ −85.6 (dd, $^1J_{F,C}$ = 295 Hz, $^2J_{F,F}$ = 14 Hz, $^3J_{F,Fcis}$ = 35 Hz, =C*F*F), −95.9 (dd, $^1J_{F,C}$ = 302 Hz, $^2J_{F,F}$ = 14 Hz, $^3J_{F,Ftrans}$ = 116 Hz, =C*F*F), −171.8 (dd, $^1J_{F,C}$ = 246 Hz, $^3J_{F,Ftrans}$ = 116 Hz, $^3J_{F,Fcis}$ = 35 Hz, =CF–). MS (EI): *m*/*z* (%) = 223 (100) $[M]^+$. Anal. Calcd for $C_9F_3H_{12}NS$ (223.27): C 48.42, F 25.53, H 5.42, N 6.27. Found: C 48.33, F 25.48, H 5.39, N 6.22.

4.7. *N*-Ethyl-2,3,3-trifluorothioacrylamide (**4b**)

Yield 0.13 g (15%), yellow liquid, R_f 0.17 (hexane/diethyl ether 9:1). ^1H NMR (300.13 MHz, $CDCl_3$): δ 1.32 (t, $^3J_{H,H}$ = 7.2 Hz, 3H, CH_3), 3.76 (qd, $^3J_{H,H}$ = 7.2 Hz, $^3J_{H,H}$ = 5.2 Hz, 2H, CH_2), 7.72 (broad s, 1H, NH). ^{13}C (75.47 MHz, $CDCl_3$): δ 12.9 (CH_3CH_2), 39.6 (CH_3CH_2), 128.1 (=CF), 155.8 (=CF_2), 179.8 (CS). ^{19}F (282.4 MHz, $CDCl_3$): δ −85.2 (dd, $^1J_{F,C}$ = 297 Hz, $^2J_{F,F}$ = 15 Hz, $^3J_{F,Fcis}$ = 35 Hz, =C*F*F), −95.4 (dd, $^1J_{F,C}$ = 300 Hz, $^2J_{F,F}$ = 15 Hz, $^3J_{F,Ftrans}$ = 116 Hz, =C*F*F), −170.7 (dd, $^1J_{F,C}$ = 248 Hz, $^3J_{F,Ftrans}$ = 116 Hz, $^3J_{F,Fcis}$ = 35 Hz, =CF–). MS (EI): *m*/*z* (%) = 169 (100) $[M]^+$. Anal. Calcd for $C_5F_3H_6NS$ (169.18): C 35.50, F 33.69, H 3.57, N 8.28. Found: C 35.44, F 33.65, H 3.54, N 8.23.

4.8. *N*-Phenyl-2,3,3-trifluorothioacrylamide (**4c**)

^{19}F (282.4 MHz, DME): δ = −91.29 (dd, $^1J_{F,C}$ = 297 Hz, $^2J_{F,F}$ = 25 Hz, $^3J_{F,Fcis}$ = 35 Hz, =C*F*F), −99.73 (dd, $^1J_{F,C}$ = 301 Hz, $^2J_{F,F}$ = 25 Hz, $^3J_{F,Ftrans}$ = 117 Hz, =C*F*F), −167.98 (dd, $^1J_{F,C}$ = 249 Hz, $^3J_{F,Ftrans}$ = 117 Hz, $^3J_{F,Fcis}$ = 35 Hz, =CF–).

4.9. General procedure for the synthesis of 2,3,3,3-tetrafluoropropionamides **5**

Method A: To a solution of isocyanate **1** (5 mmol) in dimethoxyethane (DME) (25 mL) at −60 °C $R_3SiCF=CF_2$ (R = Me, Et) (6.25 mmol) and $[Me_4N]F$ (0.51 g, 5.5 mmol) was added. The mixture was stirred for 2 h at −55 ± 5 °C and then $HBF_4{\cdot}Et_2O$ (0.81 g, 5 mmol) was added. The reaction mixture was stirred for 30 min at −35 ± 5 °C and $[Me_4N]F$ (0.46 g, 5 mmol) was added. The mixture formed was stirred for 1 h at −35 ± 5 °C and then allowed to reach room temperature. All volatile components were removed in vacuo and the product was extracted into hexane. The precipitated $[Me_4N][BF_4]$ was filtered and the solvent was evaporated in vacuo. The amides **5** were purified by crystallization from pentane or sublimation.

4.10. *N*-1-Adamantyl-2,3,3,3-tetrafluoropropionamide (**5a**)

Yield 0.87 g (62%), white solid, mp 105 °C. ^1H NMR (300.13 MHz, $CDCl_3$): δ 1.71 (broad s, 6H, Ad), 2.05 (broad s, 6H, Ad), 2.13 (broad s, 3H, Ad), 5.02 (dq, $^2J_{H,F}$ = 46.9 Hz, $^3J_{H,F}$ = 6.5 Hz, 1H, CHF), 5.98 (broad s, 1H, NH). ^{13}C (75.47 MHz, $CDCl_3$): δ 29.4 (3C, CH), 36.1 (3C, CH_2), 41.2 (3C, CH_2), 53.1 (C), 85.4 (CFH), 120.8 (CF_3), 159.7 (CO). ^{19}F (282.4 MHz, $CDCl_3$): δ −76.1 (dd, $^1J_{F,C}$ = 282 Hz, $^3J_{F,F}$ = 10.9 Hz, $^3J_{F,H}$ = 6.5 Hz, CF_3), −198.5 (dqd, $^1J_{F,C}$ = 203 Hz, $^2J_{F,H}$ = 46.9 Hz, $^3J_{F,F}$ = 10.9 Hz, $^4J_{F,H}$ = 3.8 Hz, CFH). MS (EI): *m*/*z* (%) = 279 (90) $[M]^+$. Anal. Calcd for $C_{13}F_4H_{17}NO$ (279.28): C 55.91, F 27.21, H 6.14, N 5.02. Found: C 55.84, F 27.17, H 6.11, N 4.99.

4.11. *N*-Cyclohexyl-2,3,3,3-tetrafluoropropionamide (**5b**)

Yield 0.74 g (65%), white solid, mp 96 °C (lit. 89–90 °C [26]). ^1H NMR (400.13 MHz, $CDCl_3$): δ 1.25 (m, 5H, *c*-C_6H_{11}), 1.61 (m, 1H, *c*-C_6H_{11}), 1.69 (m, 2H, *c*-C_6H_{11}), 1.88 (m, 2H, *c*-C_6H_{11}), 3.81 (m, 1H, *c*-C_6H_{11}), 5.02 (dq, $^2J_{H,F}$ = 46.4 Hz, $^3J_{H,F}$ = 6.5 Hz, 1H, CHF), 6.43 (broad s, 1H, NH). ^{13}C (100.61 MHz, $CDCl_3$): δ 25.5 (d, $^6J_{C,F}$ = 3.7 Hz, 2C,

CH_2), 26.1 (CH_2), 33.4 (d, $^5J_{C,F}$ = 11.5 Hz, 2C, CH_2), 49.5 (CH), 86.2 (dq, $^1J_{C,F}$ = 203 Hz, $^2J_{C,F}$ = 33 Hz, CFH), 121.5 (qd, $^1J_{C,F}$ = 282 Hz, $^2J_{C,F}$ = 25 Hz, CF_3), 161.0 (d, $^2J_{C,F}$ = 19 Hz, CO). ^{19}F (376.4 MHz, $CDCl_3$): δ −76.2 (dd, $^1J_{F,C}$ = 282 Hz, $^3J_{F,F}$ = 10.8 Hz, $^3J_{F,H}$ = 6.5 Hz, CF_3), −201.9 (dqdd, $^1J_{F,C}$ = 203 Hz, $^2J_{F,H}$ = 46.4 Hz, $^3J_{F,F}$ = 10.8 Hz, $^4J_{F,H}$ = 2.6 Hz, $^6J_{F,H}$ = 1.3 Hz, CFH). MS (EI): m/z (%) = 227 (10) $[M]^+$, 146 (100) $[M-C_2F_3]^+$. Anal. Calcd for $C_9F_4H_{13}NO$ (227.21): C 47.58, F 33.45, H 5.77, N 6.16. Found: C 47.51, F 33.39, H 5.71, N 6.12.

Crystal data of **5b**: $C_4H_{13}F_4NO$, 227.20 g mol^{-1}. Diffractometer IPDS-II, Stoe Darmstadt; Mo–$K_{a-\alpha}$ (graphite monochromator, λ = 71.073 pm); T = 170(2) K; $2\theta_{max}$ = 59.5°; 0° ≤ ω ≤ 180°, φ = 0°, 0° ≤ ω ≤ 54°, φ = 90°, $\Delta\omega$ = 2°, 117 images; −13 ≤ h ≤ 13, −15 ≤ k ≤ 15, −15 ≤ l ≤ 15; ρ_{calc} = 1.401 g cm^{-3}; 13,636 measured reflections of which 5916 were symmetrically independent; R_{int} = 0.0279; F(000) = 472; μ = 0.137 mm^{-1}. Triclinic, $P\bar{1}$ (no. 2), a = 962.2(2), b = 1113.9(2), c = 1145.8(2) pm, α = 64.54(1), β = 76.32(1), γ = 82.70(1)°, V = 1076.8(3) 10^6 pm^3, Z = 4; R values: R_1/wR_2 for 3614 reflections with $[I_0 > 2\sigma(I_0)]$: 0.0500/0.1358, for all data: 0.0832/0.1614; S_{all} = 1.038.

4.12. *N*-tert-*Butyl-2,3,3,3-tetrafluoropropionamide (**5c**)*

Yield 0.61 g (61%), white solid, mp 55 °C. ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 1.43 (s, 9H, CH_3), 4.95 (dq, $^2J_{H,F}$ = 46.9 Hz, $^3J_{H,F}$ = 6.6 Hz, 1H, CHF), 6.13 (broad s, 1H, NH). ^{13}C (75.47 MHz, $CDCl_3$): δ 28.5 (3C, CH_3), 52.4 (C), 85.6 (CFH), 122.1 (CF_3), 160.0 (CO). ^{19}F (282.4 MHz, $CDCl_3$): δ −76.1 (dd, $^1J_{F,C}$ = 282 Hz, $^3J_{F,F}$ = 10.9 Hz, $^3J_{F,H}$ = 6.6 Hz, CF_3), −199.0 (dqd, $^1J_{F,C}$ = 204 Hz, $^2J_{F,H}$ = 46.9 Hz, $^3J_{F,F}$ = 10.9 Hz, $^4J_{F,H}$ = 3.7 Hz, CFH). MS (EI): m/z (%) = 201 (10) $[M]^+$, 186 (100) $[M-CH_3]^+$. Anal. Calcd for $C_7F_4H_{11}NO$ (201.17): C 41.79, F 37.78, H 5.51, N 6.96. Found: C 41.73, F 37.70, H 5.48, N 6.92.

Method B: To a solution of 2,3,3-trifluoroacrylamide **2** (5 mmol) in dimethoxyethane (DME) (15 mL) at −35 °C $[Me_4N]F$ (0.47 g, 5 mmol) was added. The mixture was stirred for 1 h at −35 ± 5 °C and then allowed to reach room temperature. All volatile components were removed in vacuo and the product was extracted into hexane. Insoluble impurities were filtered off and the solvent was evaporated in vacuo. The amides **5a** and **5b** were purified by crystallization from pentane to yield 0.91 g (65%) and 0.76 g (67%), correspondingly. The amide **5c** and cyclic products **6** and **7** were separated by silica gel column chromatography.

*N-tert-Butyl-2,3,3,3-tetrafluoropropionamide (**5c**)*: Yield 0.36 g (36%).

4.13. *N*-tert-*butyl-2-[1*-tert-*butyl-3-fluoro-4-oxo-3-trifluoromethyl-azetidin-(2Z)-ylidene]-2-fluoro-acetamide (**6**)*

Yield 0.38 g (22%), white solid, mp 141–142 °C, R_f 0.2 (hexane/diethyl ether 4:1). ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 1.43 (s, 9H, CH_3 (*t*-Bu) amide), 1.54 (d, $^6J_{H,F}$ = 0.9 Hz, 9H, CH_3 (*t*-Bu) lactam), 5.95 (broad s, $\Delta_{1/2} \approx$ 12 Hz, 1H, NH). ^{13}C (100.61 MHz, $CDCl_3$): δ 28.6 (3C, CH_3 (*t*-Bu) amide), 28.7 (d, $^5J_{F,C}$ = 7 Hz, 3C, CH_3 (*t*-Bu) lactam), 51.8 (C (*t*-Bu) amide), 58.4 (C (*t*-Bu) lactam), 97.8 (**C**F(CF_3)), 120.1 (CF_3), 124.3 (F**C** = **C** lactam), 133.9 (F**C** = C lactam), 157.0 (CO amide), 158.4 (CO lactam). ^{19}F (376.4 MHz, $CDCl_3$): δ −74.2 (d, $^1J_{F,C}$ = 284 Hz, $^3J_{F,F}$ = 10.0 Hz, CF_3), −139.0 (broad s, $\Delta_{1/2} \approx$ 7 Hz, $^1J_{F,C}$ = 267 Hz, **F**C = C), −173.9 (qd, $^1J_{F,C}$ = 247 Hz, $^3J_{F,F}$ = 10.0 Hz, $^4J_{F,F} \approx$ 1 Hz, C**F**(CF_3)). MS(EI): m/z (%) = 342 (15) $[M]^+$, 286 (55) $[M-C_4H_8]^+$, 230 (100) $[M-2C_4H_8]^+$. Anal. Calcd for $C_{14}F_5H_{19}N_2O_2$ (342.31): C 49.12, F 27.75, H 5.59, N 8.18. Found: C 49.03, F 27.69, H 5.54, N 8.14.

Crystal data of **6**: $C_{14}H_{19}F_5N_2O_2$, 342.31 g mol^{-1}. Diffractometer IPDS-I, Stoe Darmstadt; Mo–$K_{a-\alpha}$ (graphite monochromator, λ = 71.073 pm); T = 293(2) K; $2\theta_{max}$ = 56.3°; 0° ≤ φ ≤ 200°, $\Delta\varphi$ = 2°, 100 images; −14 ≤ h ≤ 14, −23 ≤ k ≤ 23, −11 ≤ l ≤ 10; ρ_{calc} = 1.290 g cm^{-3}; 12,401 measured reflections of which 3739 were symmetrically independent; R_{int} = 0.0955; F(000) = 712; μ = 0.121 mm^{-1}. Orthorhombic, $Pca2_1$ (no. 29), a = 1073.7(3), b = 1819.2(4), c = 902.6(2) pm, V = 1763.0(7) 10^6 pm^3, Z = 4; R values: R_1/wR_2 for 1223 reflections with $[I_0 > 2\sigma(I_0)]$: 0.0585/0.1074, for all data: 0.1862/0.1428; S_{all} = 0.824, Flackx = −0.1 (15).

4.14. *N*-tert-*butyl-2-[1*-tert-*butyl-3-fluoro-4-oxo-3-trifluoromethyl-azetidin-(2*E*)-ylidene]-2-fluoro-acetamide (**7**)*

Yield 0.26 g (15%), white solid, mp 83–84 °C, R_f 0.35 (hexane/diethyl ether 19:1). ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 1.44 (s, 9H, CH_3 (*t*-Bu) amide), 1.62 (s, 9H, CH_3 (*t*-Bu) lactam), 6.16 (broad s, $\Delta_{1/2} \approx$ 15 Hz, 1H, NH). ^{13}C (100.61 MHz, $CDCl_3$): δ 28.2 (3C, CH_3 (*t*-Bu) amide), 28.5 (s, 3C, CH_3 (*t*-Bu) lactam), 52.0 (C (*t*-Bu) amide), 60.6 (C (*t*-Bu) lactam), 97.5 (**C**F(CF_3)), 120.1 (CF_3), 127.0 (FC = **C** lactam), 134.8 (F**C** = C lactam), 157.4 (CO amide), 157.6 (CO lactam). ^{19}F (376.4 MHz, $CDCl_3$): δ −76.3 (dd, $^1J_{F,C}$ = 283 Hz, $^5J_{F,F}$ = 13.6 Hz, $^3J_{F,F}$ = 10.9 Hz, CF_3), −143.4 (qdd, $^1J_{F,C}$ = 245 Hz, $^5J_{F,F}$ = 13.6 Hz, $^4J_{F,F}$ = 6.6 Hz, $^4J_{F,H}$ = 4.5 Hz, **F**C = C), −177.6 (qd, $^1J_{F,C}$ = 242 Hz, $^3J_{F,F}$ = 10.9 Hz, $^4J_{F,F}$ = 6.6 Hz, C**F**(CF_3)). MS (EI): m/z (%) = 342 (10) $[M]^+$, 286 (40) $[M-C_4H_8]^+$, 230 (100) $[M-2C_4H_8]^+$. Anal. Calcd for $C_{14}F_5H_{19}N_2O_2$ (342.31): C 49.12, F 27.75, H 5.59, N 8.18. Found: C 49.01, F 27.70, H 5.52, N 8.13.

Crystal data of **7**: $C_{14}H_{19}F_5N_2O_2$, 342.31 g mol^{-1}. Diffractometer IPDS-I, Stoe Darmstadt; Mo–$K_{a-\alpha}$ (graphite monochromator, λ = 71.073 pm); T = 293(2) K; $2\theta_{max}$ = 56.3°; 0° ≤ φ ≤ 200°, $\Delta\varphi$ = 2°, 100 images; −15 ≤ h ≤ 15, −12 ≤ k ≤ 13, −18 ≤ l ≤ 18; ρ_{calc} = 1.348 g cm^{-3}; 14,258 measured reflections of which 3775 were symmetrically independent; R_{int} = 0.0613; F(000) = 712; μ = 0.127 mm^{-1}. Monoclinic, $P2_1/c$ (no. 14), a = 1179.6(3), b = 1079.3(2), c = 1377.2(4) pm, β = 105.91(2)°, V = 1686.4(7) 10^6 pm^3, Z = 4; R values: R_1/wR_2 for 1732 reflections with $[I_0 > 2\sigma(I_0)]$: 0.0623/0.1542, for all data: 0.1343/0.1842; S_{all} = 0.975.

4.15. *General procedure for the synthesis of 2,3,3,3-tetrafluorothiopropionamides **9***

To a mixture of isothiocyanate **3** (5 mmol) and $[Me_4N]F$ (0.51 g, 5.5 mmol) in dimethoxyethane (DME) (30 mL) at −60 °C, $Et_3SiCF=CF_2$ (1.23 g, 6.25 mmol) was added dropwise over a period of 30 min. The mixture was stirred for 90 min at −55 ± 5 °C and then $HBF_4{\cdot}Et_2O$ (0.81 g, 5 mmol) was added. The reaction mixture was stirred for 30 min at −35 ± 5 °C and $[Me_4N]F$ (0.47 g, 5 mmol) was added. The resulting mixture was stirred for 1 h at −35 ± 5 °C and then allowed to reach room temperature. All volatile components were removed in vacuo and the product was extracted into hexane. The precipitated $[Me_4N][BF_4]$ was filtered and the solvent was evaporated in vacuo. The thioamides **9** were purified by silica gel column chromatography.

4.16. *N-Cyclohexyl-2,3,3,3-tetrafluorothiopropionamide (**9a**)*

Yield 0.63 g (52%), liquid, bp 64–65 °C/0.04 Torr, R_f 0.4 (hexane/diethyl ether 19:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 1.36 (m, 5H, *c*-C_6H_{11}), 1.73 (m, 3H, *c*-C_6H_{11}), 2.08 (m, 2H, *c*-C_6H_{11}), 4.41 (m, 1H, *c*-C_6H_{11}), 5.46 (dq, $^2J_{H,F}$ = 46.9 Hz, $^3J_{H,F}$ = 5.5 Hz, 1H, CHF), 7.72 (broad s, 1H, NH). ^{13}C (100.47 MHz, $CDCl_3$): δ 24.4 (d, $^6J_{C,F}$ = 4 Hz, 2C, CH_2), 25.3 (CH_2), 31.0 (d, $^5J_{C,F}$ = 7 Hz, 2C, CH_2), 51.6 (CH), 90.9 (dq, $^1J_{C,F}$ = 209 Hz, $^2J_{C,F}$ = 32 Hz, CFH), 120.5 (qd, $^1J_{C,F}$ = 283 Hz, $^2J_{C,F}$ = 27 Hz, CF_3), 184.9 (d, $^2J_{C,F}$ = 14 Hz, CS). ^{19}F (282.4 MHz, $CDCl_3$): δ −75.8 (dd, $^1J_{F,C}$ = 283 Hz, $^3J_{F,F}$ = 10.9 Hz, $^3J_{F,H}$ = 5.5 Hz, CF_3), −187.9 (dqdd, $^1J_{F,C}$ = 209 Hz, $^2J_{F,H}$ = 46.9 Hz, $^3J_{F,F}$ = 10.9 Hz, $^4J_{F,H}$ = 5.6 Hz, $^6J_{F,H}$ = 1.6 Hz, CFH). MS (EI): m/z (%) = 243 (100) $[M]^+$. Anal. Calcd for $C_9F_4H_{13}NS$ (243.28): C 44.43, F 31.24, H 5.39, N 5.76. Found: C 44.33, F 31.15, H 5.32, N 5.70.

4.17. N-Ethyl-2,3,3,3-tetrafluorothiopropionamide (**9b**)

Yield 0.47 g (49%), liquid, bp 58 °C/10 Torr, R_f 0.15 (hexane/diethyl ether 19:1). ^{1}H NMR (400.13 MHz, $CDCl_3$): δ 1.33 (t, $^3J_{H,H}$ = 7.2 Hz, 3H, CH_3), 3.76 (qd, $^3J_{H,H}$ = 7.2 Hz, $^3J_{H,H}$ = 5.2 Hz, 2H, CH_2), 5.49 (dq, $^2J_{H,F}$ = 46.8 Hz, $^3J_{H,F}$ = 5.6 Hz, 1H, CHF), 7.86 (broad s, 1H, NH). ^{13}C (100.6 MHz, $CDCl_3$): δ 12.9 (CH_3), 34.5 (CH_2), 91.2 (dq, $^1J_{C,F}$ = 209 Hz, $^2J_{C,F}$ = 32 Hz, CFH), 120.6 (qd, $^1J_{C,F}$ = 283 Hz, $^2J_{C,F}$ = 27 Hz, CF_3), 186.5 (d, $^2J_{C,F}$ = 14 Hz, CS). ^{19}F (282.4 MHz, $CDCl_3$): δ −76.9 (dd, $^1J_{F,C}$ = 283 Hz, $^3J_{F,F}$ = 11 Hz, $^3J_{F,H}$ = 5.6 Hz, CF_3), −189.5 (dqdd, $^1J_{F,C}$ = 209 Hz, $^2J_{F,H}$ = 46.8 Hz, $^3J_{F,F}$ = 11 Hz, $^4J_{F,H}$ = 4.4 Hz, CFH). MS (EI): m/z (%) = 189 (100) $[M]^+$. Anal. Calcd for $C_5F_4H_7NS$ (189.19): C 31.74, F 40.17, H 3.73, N 7.40. Found: C 31.65, F 40.09, H 3.68, N 7.35.

4.18. N-Phenyl-2,3,3,3-tetrafluorothiopropionamide (**9c**)

Yield 0.70 g (59%), yellow solid, mp 58 °C, R_f 0.25 (hexane/diethyl ether 9:1). ^{1}H NMR (300.13 MHz, $CDCl_3$): δ 5.63 (dq, $^2J_{H,F}$ = 46.9 Hz, $^3J_{H,F}$ = 5.6 Hz, 1H, CHF), 7.36 (t, $^3J_{H,H}$ = 7.6 Hz, 1H, C_6H_5), 7.46 (t, $^3J_{H,H}$ = 7.6 Hz, 2H, C_6H_5), 7.77 (d, $^3J_{H,H}$ = 7.6 Hz, 2H, C_6H_5), 9.28 (broad s, 1H, NH). ^{13}C (100.6 MHz, $CDCl_3$): δ 91.9 (dq, $^1J_{C,F}$ = 211 Hz, $^2J_{C,F}$ = 32 Hz, CFH), 120.6 (qd, $^1J_{C,F}$ = 283 Hz, $^2J_{C,F}$ = 27 Hz, CF_3), 123.6 (2C, C_6H_5), 128.1 (C, C_6H_5), 129.5 (2C, C_6H_5), 137.0 (C, C_6H_5), 184.4 (d, $^2J_{C,F}$ = 14 Hz, CS) ^{19}F (282.4 MHz, $CDCl_3$): δ −75.6 (dd, $^1J_{F,C}$ = 283 Hz, $^3J_{F,F}$ = 11.2 Hz, $^3J_{F,H}$ = 5.6 Hz, CF_3), −184.9 (dqd, $^1J_{F,C}$ = 211 Hz, $^2J_{F,H}$ = 46.9 Hz, $^3J_{F,F}$ = 11.2 Hz, $^4J_{F,H}$ = 7.0 Hz, CFH). MS (EI): m/z (%) = 237 (100) $[M]^+$. Anal. Calcd for $C_9F_4H_7NS$ (237.23): C 45.57, F 32.04, H 2.97, N 5.90. Found: C 45.49, F 31.97, H 2.93, N 5.84.

Acknowledgements

The generous financial support of this work by the DFG (grant 436 UKR 113) is gratefully acknowledged. We are indebted to Dr. Alexander B. Rozhenko (Kiev) for recording a great number of the ^{13}C NMR spectra and Dr. Hendrik T. M. Fischer (Köln) for selecting and mounting single crystals of compounds **6** and **7**.

References

[1] (a) J. Burdon, P.L. Coe, I.B. Haslock, R.L. Powell, Chem. Commun. (1) (1996) 49–50;
(b) F.G. Drakesmith, R.D. Richardson, O.J. Stewart, P. Tarrant, J. Org. Chem. 33 (1968) 286–291;
(c) I.L. Knunyants, R.N. Sterlin, R.D. Yatsenko, L.N. Pinkina, Russ. Chem. Bull. 7 (1958) 1297–1299;
(d) R.N. Sterlin, L.N. Pinkina, I.L. Knunyants, L.F. Nezgavorov, Khim. Nauka i Prom. 4 (1959) 809–810, C.A. (1960) 10837.
[2] (a) T. Nguyen, C. Wakselman, Synth. Commun. 20 (1990) 97–99;
(b) A.Ya. Yakubovich, S.M. Rozenshtein, J. Gen. Chem. USSR 31 (1961) 1995–2000;
(c) O. Paleta, A. Posta, Z. Novotna, Coll. Czech. Chem. Commun. 33 (1968) 2970–2982;
(d) D.C. England, L. Solomon, C.G. Krespan, J. Fluorine Chem. 3 (1973) 63–89.
[3] (a) J.D. LaZerte, D.A. Rausch, R.J. Koshar, J.D. Park, W.H. Pearlson, J.R. Lacher, J. Am. Chem. Soc. 78 (1956) 5639–5641;
(b) J.L. Rendall, St. Paul, W.H. Pearlson, Minnesota mining and manufacturing company. Patent: US2795601 (1957).
[4] N.V. Kirij, Yu.L. Yagupolskii, N.V. Petukh, W. Tyrra, D. Naumann, Tetrahedron Lett. 42 (2001) 8181–8183.
[5] N.V. Kirij, D.A. Dontsova, N.V. Pavlenko, Yu.L. Yagupolskii, H. Scherer, W. Tyrra, D. Naumann, Eur. J. Org. Chem. (2008) 2267–2272.
[6] J. Bernstein, R.E. Davis, L. Shimoni, N.-L. Chang, Angew. Chem., Int. Ed. Engl. 34 (1995) 1555–1573.
[7] N. Marubayashi, T. Ogawa, T. Kuroita, T. Hamasaki, I. Ueda, Tetrahedron Lett. 33 (1992) 4585–4588.
[8] G. Cainelli, P. Galetti, M. Gazzano, D. Giacomini, A. Quintavalla, Tetrahedron Lett. 43 (2002) 233–235.
[9] G. Cainelli, D. Giacomini, P. Galetti, A. Quintavalla, Eur. J. Org. Chem. (2003) 1765–1774.
[10] Y. Cheng, L.-Q. Cheng, J. Org. Chem. 72 (2007) 2625–2630.
[11] Y.-Y. Yang, W.-G. Shou, D. Hong, Y.-G. Wang, J. Org. Chem. 73 (2008) 3574–3577.
[12] P. Galetti, A. Quintavalla, C. Ventrici, D. Giacomini, Eur. J. Org. Chem. (2009) 4541–4547.
[13] J.W. Lyga, R.N. Henrie II, G.A. Meier, R.W. Creekmore, R.M. Patera, Magn. Reson. Chem. 31 (1993) 323–328.
[14] L.C. So, C.-C. Liu, M.C.W. Chan, J.C.Y. Lo, K.-H. Sze, N. Zhu, Chem. Eur. J. 18 (2012) 565–573.
[15] (a) T. Kumagai, S. Tamai, T. Abe, M. Hikida, Curr. Med. Chem. Anti Infect. Agents 1 (2002) 1–14;
(b) D. Kuhn, P. Imming, C. Imming, D. Dettmering, D. Dix, Pharm. Ztg 144 (1999) 3405ff http://www.pharmazeutische-zeitung.de/index.php?id=titel_43_1999.
[16] (a) M. Suffiness, Taxol, Science and Applications, CRC Press, Boca Raton, FL, 1995;
(b) I. Ojima, M. Zhao, T. Yamato, K. Nakahashi, M. Yamashita, R. Abe, J. Org. Chem. 56 (1991) 5263–5277.
[17] M.I. Konaklieva, Curr. Med. Chem. Anti Infect. Agents 1 (2002) 215–238.
[18] A.A. Kolomeitsev, F.U. Seifert, G.-V. Röchenthaler, J. Fluorine Chem. 71 (1995) 47–49.
[19] D.D. Perrin, W.L.F. Armarego, D.R. Perrin, Purification of Laboratory Chemicals, second ed., Pergamon, Oxford, 1980.
[20] X-Shape 1.06, Crystal Optimisation for Numerical Absorption Correction (C) 1999 STOE & Cie GmbH Darmstadt.
[21] X-Area 1.16, Stoe & Cie GmbH Darmstadt, 2003.
[22] X-RED 1.22, Stoe Data Reduction Program (C) 2001 Stoe & Cie GmbH Darmstadt.
[23] L.J. Farrugia, J. Appl. Crystallogr. 32 (1999) 837.
[24] A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, J. Appl. Crystallogr. 26 (1993) 343.
[25] G.M. Sheldrick, SHELXL-97. Programs for Crystal Structure Analysis, University of Göttingen, 1997.
[26] R.E. Banks, D. Berry, M.J. McGlinchey, G.J. Moore, J. Chem. Soc. (C) (8) (1970) 1017–1023.