# Reactions of α-difluoro azides with olefins

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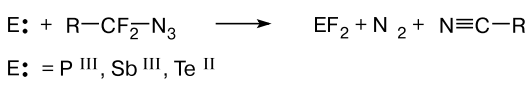
Reactions of α-difluoro azides with olefins result in oxidative fluoroamination or amination of the C=C bond.

**Key words:** α-difluoro azides, olefins, cycloaddition, fluoroamination.

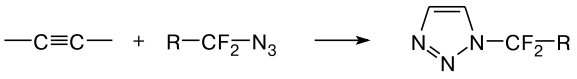
α-Difluoro azides (*i.e.*, compounds with the fragment $N_3—CF_2—$) were first obtained and studied by Knunyants *et al.*[1—3] These stable (at least up to 200 °C) organic azides are highly reactive. Their most interesting property is that they are oxidative fluorinating reagents for a wide range of organic compounds containing heteroelements[4—6] (Scheme 1).

**Scheme 1**



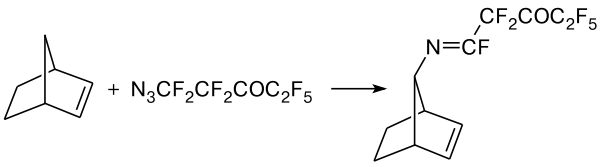

Reactions of α-difluoro azides with mono- and disubstituted acetylenes in high yields afford triazoles fluorinated in the side chain[7] (Scheme 2).

**Scheme 2**



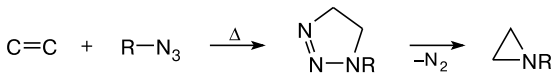

Earlier,[8] it has been found that α-difluoro azides are inert to 2,3-dimethylbutadiene but react with norbornene to give amination products (Scheme 3).

**Scheme 3**




Reactions of nonfluorinated azides with C=C-containing compounds are understood fairly well: they usually involve [3+2] cycloaddition followed by elimination of molecular nitrogen from intermediate 1,2,3-triazoline[9] (Scheme 4).

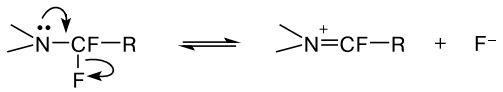
**Scheme 4**




This reaction is often used for the synthesis of aziridines.

It is easy to see that aziridines obtained from α-difluoro azides possess an interesting structural feature, *viz.*, the presence of the α-fluoro amine fragment $—\overset{|}{N}—CF_2$, in which the C—F bond is known[10,11] to be very labile (Scheme 5).

**Scheme 5**




Under favorable conditions, this would lead to intramolecular nucleophilic substitution affording a new C—F bond (Scheme 6).

It can be seen in Scheme 6 that nucleophilic substitution at one C—N bond in the aziridine produces a 2-fluoro amine derivative, while the substitution at two bonds yields 1,2-difluoride; these processes are equivalent to oxidative aminofluorination and difluorination of olefins, respectively.

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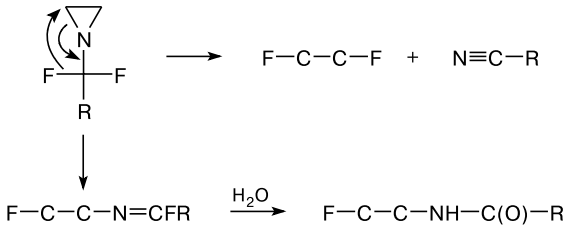
**Scheme 6**



Several α-difluoro azides have been documented.[1–3,12–14] We obtained two typical representatives of this family of reagents: 2-hydroperfluoropropyl azide (**I**) and methyl 3-azidotetrafluoropropionate (**II**).

$CF_3$—CHF—$CF_2$—$N_3$ $N_3$—$CF_2$—$CF_2$—COOMe

**I** **II**

It turned out that azides **I** and **II** indeed react with olefins, the reaction rate largely depending on the structure of the latter. Norbornenes react with azides most readily (even at room temperature or under slight heating). For instance, substituted benzonorbornadiene **1** reacts with azides **I** and **II** to give fluorinated amides **2a**,**b** as the sole products (Scheme 7).

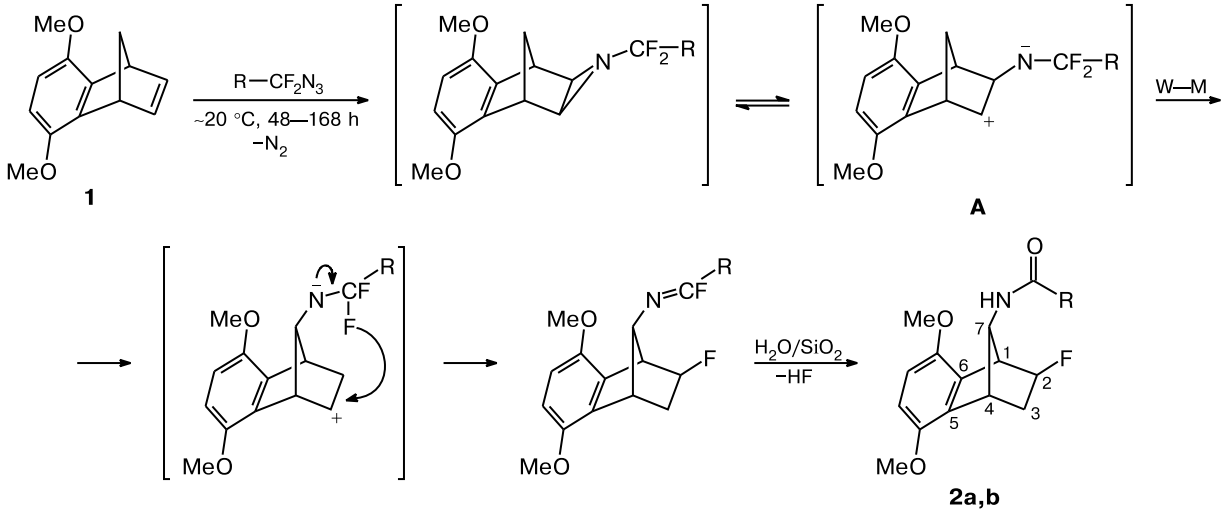
The formation of only rearranged fluorinated amides suggests the presence of considerable amounts of the "open" aziridine form (**A**), the opening being undoubtedly facilitated by the strong electronegative polyfluorinated substituent at the N atom. The final products are obtained by hydrolysis of labile intermediate imidoyl fluorides (detected in the reaction mixture by $^{19}F$ NMR spectroscopy prior to the hydrolysis).

The signal assignments in the spectrum of compound **2b** were confirmed by COSY and NOESY experiments. To confirm the 2-*exo*-7-*syn*-configuration, the signal of H(7) should unambiguously be assigned, separately from H(1) and H(4). The COSY spectrum shows cross peaks for H(1) and H(4) coupled with H(2) and H(3), the latter two being unambiguously assigned from the 1D spectrum; such cross peaks for H(7) are absent. The NOESY experiment revealed no coupling between H(7), H(2), and H(3); instead, the spectrum contains cross peaks of the signals of NH and one of the components H(3) (not H(2)), which provides convincing evidence for the *exo-syn*-configuration of the F atom and the NH group. This is additionally confirmed by the cross peak for H(7) and the OMe group attached to the benzene ring, as well as by $J_{F(2)-HN}$ = 7.5 Hz in the $^{19}F$ {HN} NMR spectrum.

The *syn*-configuration of the amide group with respect to the F atom suggests the *exo*-attack of the azide on the C=C bond of norbornene and, accordingly, the *exo*-structure of the intermediate aziridine.

The formation of amido fluorides **2a,b** is of considerable interest because fluorinated amines (notably fluorinated amino acids) are widely known as physiologically active compounds.[15] Currently existing routes to similar structures involve many steps and much labor. The first (to the best of our knowledge) direct synthesis[16] of compounds like **2a,b** from olefins and $XeF_2$ in the presence of acetonitrile afforded the target amido fluorides in low yields within complex mixtures of products. Alternative methods involve reactions of olefins with N—F compounds in acetonitrile[17] and electrochemical fluoroamination of olefins in acetonitrile—$Et_3N \cdot 3HF$.[18,19]

**Scheme 7**

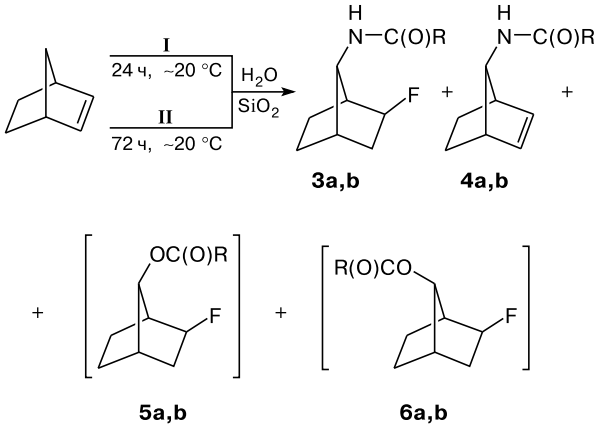


W—M stands for the Wagner—Meerwein rearrangement

**2:** R = $CHFCF_3$ (**a**), $CF_2COOMe$ (**b**); the yields are 40 (**a**) and 34% (**b**)

Norbornene reacts with azides **I** and **II** to give more complex mixtures of products than in the case of benzonorbornadiene **1**. However, the character of the reaction (oxidative fluorination) is generally retained (Scheme 8).

**Scheme 8**




| | **3** : **4** : **5** : **6** | Yield (%) |
|---|---|---|
| **a** (R = $CF_3CHF$) | 3 : 3 : 3 : 1 | 92 |
| **b** (R = $MeOCOCF_2$) | 4 : 4 : 5 : 1 | 89 |

It follows from Scheme 8 that all four products result from the oxidation of a norbornene molecule: aminofluorination (**3**), oxyfluorination (**5** and **6**), and oxidative amination (*i.e.*, formal replacement of the C—H bond in norbornene by a C—N bond) (**4**).

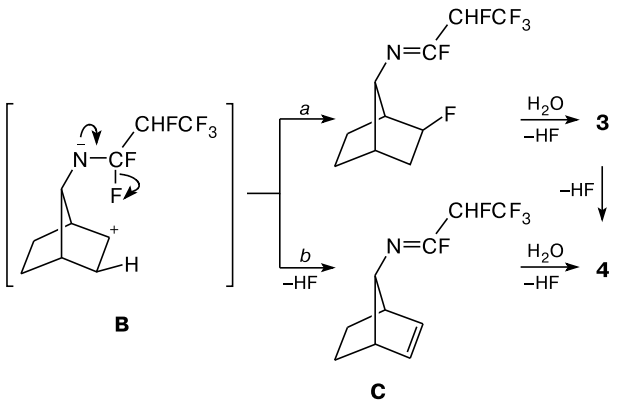
The structure of fluoro amide **3b** was determined using COSY and NOESY experiments. The absence of coupling between the H(2) and *endo*-H(6) atoms in the COSY spectrum, which is yet revealed by NOESY, suggests the *endo*-configuration of the H(2) proton (and, accordingly, the *exo*-configuration of the F atom). The observed spin-spin coupling between H(7) and H(2) (so-called *W* constant) in the COSY spectrum without a coupling between H(7) and *endo*-H(5) and *endo*-H(6) is unambiguous evidence for the *anti*-configuration of H(7) and, consequently, the *syn*-configuration of the substituent.

The *syn*-configuration of the substituent in amide **4b** was determined using the NOESY experiment. The spectrum reveals a coupling between the H(7) and *exo*-H(5) and H(6) protons, showing no couplings between H(7) and the olefinic protons or between the NH proton and *exo*-H(5) and H(6). This is sufficient proof for the *anti*-configuration of the H(7) proton.

The structure of ester **5b** was also identified using COSY and NOESY experiments. As with amide **3b**, the absence of spin-spin couplings of H(2) with *endo*-H(5) and H(6) in the COSY spectrum, which is revealed by NOESY, suggests the *exo*-configuration of the F atom. The presence of the couplings of H(7) with H(2) and *endo*-H(3) in the COSY spectrum without such couplings between H(7) and *endo*-H(5) and H(6) is evidence for the *syn*-configuration of the substituent.

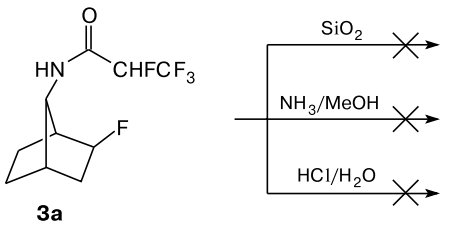
The formation of unsaturated amide **4** can be attributed to either *in situ* dehydrofluorination of fluoride **3** (pathway *a*) or a parallel reaction (pathway *b*) involving a transformation of intermediate cation **B** into unsaturated imidoyl fluoride **C** followed by its hydrolysis to the final amide **4** (Scheme 9).

**Scheme 9**




Pathway *b* seems to be more plausible for the formation of unsaturated amide **4**. This assumption is corroborated by the high chemical resistance of fluoro amide **3a** to hydrolysis on silica gel as well as to acid and basic hydrolysis (Scheme 10).

**Scheme 10**




Explanations should be given for the formation of oxygen-containing products **5** and **6**. We noticed several facts.

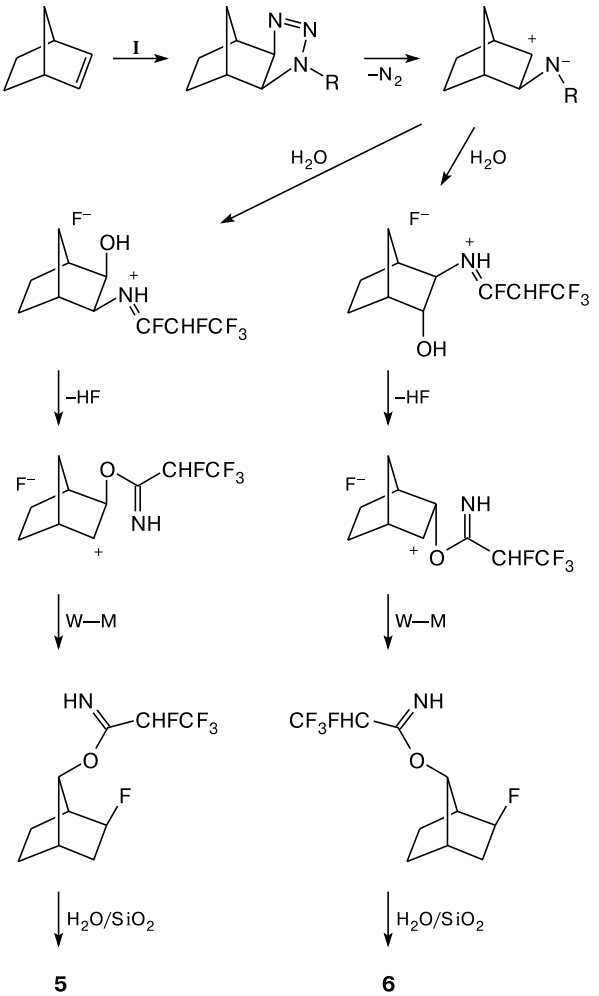
1. When the reactions of norbornene with azides **I** and **II** are carried out in dry $CH_2Cl_2$, the amounts and ratio of esters **5** and **6** are always nearly the same, regardless of the material of the ware (glass, quartz, or Teflon) in which the reaction mixtures are kept prior to hydrolysis.

2. When the reaction is carried out in a Teflon NMR tube, the $^{19}F$ NMR spectrum exhibits a signal of the acid fluoride R—CF(=NX) (δ 22, br.d) and, in low concentration, a signal of the fragment N—$CF_2$ (AB system) that does not relate to the starting azide. Both the signals disappear rapidly after the reaction mixture has been transferred to a glass tube.

3. When the reaction is carried out in a Teflon vessel, the reaction mixture produces a voluminous precipitate that disappears after the reaction mixture has been transferred to a glass tube. We failed to isolate the precipitate because it is easily prone to hydrolysis.

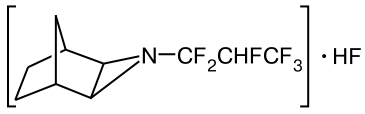
We suggest the following explanation to the observed phenomena. The reaction mixture always contains a considerable amount of HF liberated in the formation of unsaturated amide **4**. When in contact with glass or quartz ware, HF produces water (Si—OH + HF → SiF + $H_2O$) and hence hydrolysis takes place (Scheme 11).

**Scheme 11**

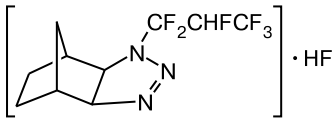



R = $CF_2CHFCF_3$

In Teflon ware, HF reacts with intermediate triazoline or aziridine to give hydrofluoride **III** insoluble in $CH_2Cl_2$ (white precipitate; low-concentration $^{19}F$ NMR spectrum shows a signal of the fragment N—$CF_2$). When treated with water or when in contact with glass, hydrofluoride **III** undergoes hydrolysis.



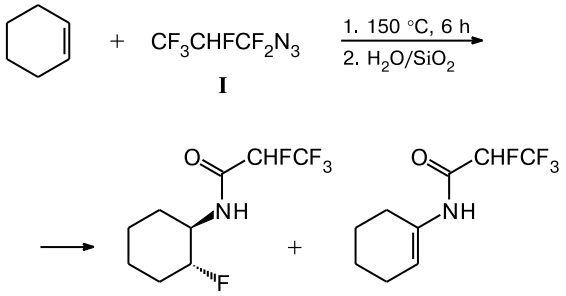

or




**III**

Little research has been concerned with reactions of α-difluoro azides with unstrained olefins.[8] Our present study was intended to fill the gap. We found that azide **I** reacts with cyclohexene under substantially harsher conditions than with norbornenes, though the reaction follows a similar pattern involving oxidative aminofluorination and oxidative amination of the olefin (Scheme 12).

**Scheme 12**

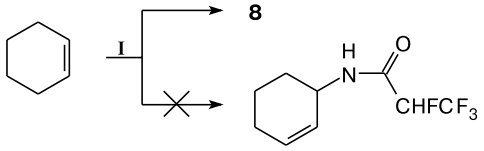



The yield of **7** + **8** is 50%; **7** : **8** = 1 : 1.

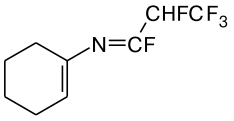
We assume that the substituents in product **7** are *trans* to each other ($^3J_{H-H}$ = 10.5 Hz). Compound **8** is formed as two conformers because of hindered rotation about the amide C—N bond.

It should be noted that compound **8** is structurally an acylated enamine rather than an allylic amide (Scheme 13).

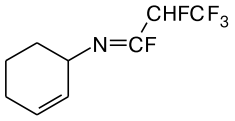
**Scheme 13**




Apparently, this is due to the fact that enamine imidoyl fluoride intermediate (**IV**) is more stable than allylic one (**V**) because of the conjugation between the double bonds C=C and C=N.



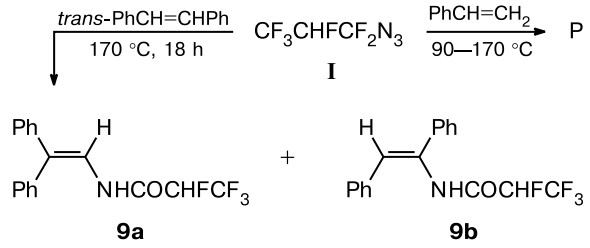
**IV**



**V**

We also studied reactions of azide **I** with some phenyl-containing olefins and found that styrene polymerizes under the reaction conditions, while *trans*-stilbene yields a mixture of two isomeric acylated enamines **9a,b** (Scheme 14).

**Scheme 14**

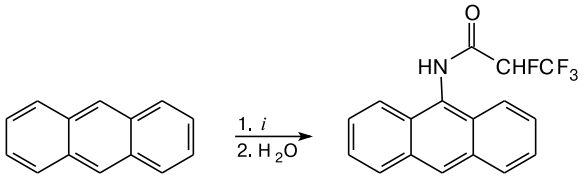


P stands for a polymer
The yield of **9a** + **9b** is 53%; **9a** : **9b** = 5 : 1.

The formation of rearranged enamine **9a** as the major product does not contradict the mechanism proposed to explain the formation of products **2a** and **2b** from norbornadiene **1**: the phenyl group can undergo 1,2-migration in a carbocation formed at one of the reaction steps.

A study of reactions of some aromatic compounds with azide **I** revealed that phenol, anisole, and naphthalene remain inert even at 200 °C. However, anthracene slowly reacts with azide **I** at elevated temperature to give *N*-acylated 9-aminoanthracene **10** as the sole product, though its conversion over 20 h is only 20% (Scheme 15).

**Scheme 15**



*i*. **I**, 180 °C, 20 h.

One can assume that the reaction pattern is similar to that observed for normal olefins (Scheme 16).

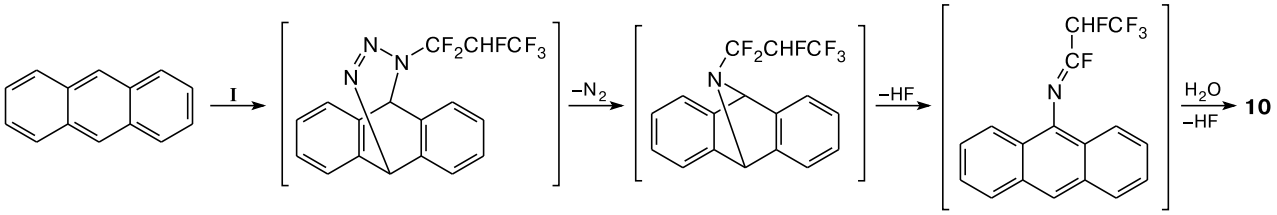
## Experimental

$^1$H, $^{13}$C, and $^{19}$F NMR spectra were recorded on a Bruker DPX-200 spectrometer (200, 50.8, and 188 MHz, respectively) with $Me_4Si$ and $CF_3COOH$ as the external standards. Correlation spectra (COSY and NOESY) were recorded on a Bruker AM-500 spectrometer. Mass spectra were measured on a Finnigan 4021 mass spectrometer. IR spectra were recorded on a Bruker IFS-113v spectrometer. Azides **I** (see Ref. 4) and **II** (see Ref. 12) were prepared as described earlier. Solvents were purified and dried in standard ways.

**Reaction of azide I with benzonorborna-2,5-diene (1).** A solution of 3′,6′-dimethoxybenzonorborna-2,5-diene (**1**) (300 mg, 1.56 mmol) and azide **I** (0.8 g, 4.1 mmol) in dry $CH_2Cl_2$ (5 mL) was stirred at ~20 °C for 6 h. The reaction mixture was poured into moist acetonitrile (30 mL) containing silica (5 g) and stirred for 2 h. The solution was filtered and the precipitate was washed with acetonitrile. The solvent was removed and the residue was chromatographed on silica (gradient elution with light petroleum—ethyl acetate (10 : 1 → 3 : 1)). The yield of fluoro amide **2a** as a 1 : 1 mixture of diastereomers was 0.22 g (40%), yellow oil. $^1$H NMR ($CDCl_3$), δ: 2.06 (m, 2 H, AB part of the ABMX system, $CH(3)_2$); 3.75 (two s (diastereoisomerism with the signals spaced at 14 Hz), 3 H, $OCH_3$); 3.78 (two s (diastereoisomerism with the signals spaced at 8 Hz), 3 H, $OCH_3$); 3.84 (m, 2 H, H(1), H(4)); 4.30 two d (diastereoisomerism with the signals spaced at 8 Hz), 1 H, H(7), $^3J_{H-H}$ = 7.6 Hz); 4.93 (asymmetric dm, 1 H, H(2), M part of the ABMX system, $^2J_{H-F}$ = 56 Hz); 5.08 (two dq (diastereoisomerism with the signals spaced at 3.5 Hz), 1 H, $CHFCF_3$, $^2J_{H-F}$ = 46 Hz, $^3J_{H-F}$= 6.4 Hz); 6.60 (2 H, AB (the signals are spaced at 2 Hz), H(4′), H(5′), $^3J_{H-H}$ = = 8.7 Hz); 7.4 (br.d, 1 H, NH). $^{19}$F NMR, δ: 1.08 (m, 3 F, $C\underline{F}_3CHF$); –95.23 (m, 1 F, F(2)); –125.3 (dm, 1 F, $CH\underline{F}CF_3$, $^2J_{H-F}$ = 46 Hz). The $^{19}F\{^1H\}$ NMR spectrum with complete proton decoupling reveals $J_{F(2)-CF3}$ = 2.6 Hz; along with the absence of the coupling $J_{F(2)-CFH}$, this indicates the 2-*exo*-7-*syn*-configuration of the substituents in the norbornyl ring. Found (%): C, 52.94; H, 4.60; N, 3.73. $C_{16}H_{16}F_5NO_3$. Calculated (%): C, 52.61; H, 4.41; N, 3.83. MS (EI, 70 eV), *m*/*z* ($I_{rel}$ (%)): 365 [$M^+$] (70), 345 [M – HF]$^+$ (100), 330 [M – HF – Me]$^+$ (65).

**Reaction of azide II with benzonorbornadiene 1.** A solution of compound **1** (600 mg, 3.1 mmol) and azide **II** (1.4 g, 7 mmol) in dry $CH_2Cl_2$ (10 mL) was stirred at ~20 °C for seven days. Then moist acetonitrile (10 mL) and silica (5 g) were added and the reaction mixture was stirred for an additional 2 h and filtered. The filtrate was concentrated and the residue was chromato-

**Scheme 16**



graphed on silica (gradient elution with light petroleum—ethyl acetate (10 : 1 → 3 : 1)). This workup gave fluoro amide **2b** (0.38 g, 34%) as yellowish crystals with m.p. 96 °C. $^1$H NMR, δ: 2.06 (m, 2 H, AB part of the ABMX system, H(3)); 3.76 (s, 3 H, OMe); 3.79 (s, 3 H, OMe); 3.88 (m, 2 H, H(1), H(4)); 3.95 (s, 3 H, COOMe); 4.27 (d, 1 H, H(7), $^3J_{H-H}$ = 7.8 Hz); 4.95 (asymmetric dm, 1 H, M part of the ABMX system, H(2), $^2J_{H-F}$ = 56 Hz); 6.65 (2 H, AB (the signals are spaced at 2 Hz), H(4′), H(5′), $^3J_{H-H}$ = 8.7 Hz); 7.48 (br.t, 1 H, NH). $^{19}$F NMR ($CDCl_3$), δ: −34.8 (F(2), AB, $CF_2$, $^2J_{F-F}$ = 269 Hz); −94.5 (m, 1 F, F(2)). $^{13}$C NMR, δ: 33.6 (d, C(3), $^2J_{C-F}$ = 20 Hz); 42.5 (C(4); 47.5 (d, C(1), $^2J_{C-F}$ = 22 Hz); 53.6 (C(7)); 55.5, 55.6 ($MeO_{Ar}$); 63.8 (COOMe); 95.8 (d, C(2), $^1J_{C-F}$ = 184 Hz); 106.8 (t, $CF_2$, $^1J_{C-F}$ = 286 Hz); 109.5, 110.7 ($CH_{Ar}$); 126.2 (d, C(6), $^3J_{C-F}$ = = 11 Hz); 134.5 (C(5)); 147.3, 148.3 ($COMe_{Ar}$); 159.8 (t, CONH, $^2J_{C-F}$ = 27 Hz); 161.2 (t, COOMe, $^2J_{C-F}$ = 31 Hz). IR ($CH_2Cl_2$), ν/cm$^{-1}$: 3434 (N—H); 3002, 2958, 2912, 2838 (C—H); 1786, 1769 sh (O=COMe); 1711 (HNC=O); 1533 (N—H); 1502, 1464, 1441 (C=C); 1200, 1148, 1084 (C—F). Found (%): C, 55.12; H, 5.07; N, 3.65. $C_{17}H_{18}F_3NO_5$. Calculated (%): C, 54.69; H, 4.86; N, 3.75. MS (EI, 70 eV), *m/z* ($I_{rel}$ (%)): 373 [M$^+$] (2), 353 [M − HF]$^+$ (50), 189 [M − $NHCOCF_2COOCH_3$ − − $OCH_3$ − H]$^+$ (50), 176 [M − $NHCOCF_2COOCH_3$ − $CH_3$] (100).

**Reaction of azide I with norbornene.** A solution of norbornene (3.1 g, 33 mmol) and azide **I** (7.6 g, 40 mmol) in dry $CH_2Cl_2$ (20 mL) was stirred at ~20 °C for 24 h (until nitrogen ceased to evolve). Then moist acetonitrile (15 mL) and silica (10 g) were added and stirring was continued for an additional 2 h. The reaction mixture was filtered, concentrated, and distilled *in vacuo*, while collecting a fraction with b.p. 50—70 °C (20 Pa). The total yield of products **3**—**6** was 92%. Their ratio was determined from the intensity ratio of the signals for F(2) and $CF_3$ in the $^{19}$F NMR spectra of the distilled reaction mixture. The products obtained were separated by column chromatography on silica (gradient elution with light petroleum—ethyl acetate (10 : 1 → 3 : 1)). The yields of fluoro amide **3a** and amide **4a** were 2.4 (29%) and 2.1 g (26%), respectively. Fluorinated esters **5a** and **6a** obtained in trace amounts undergo hydrolysis on silica; they were identified, and their configurations were determined, upon hydrolysis to the corresponding 2-fluoronorbornan-7-ols.

Fluoro amide **3a** (1 : 1 mixture of diastereomers), colorless oil. $^1$H NMR, δ: 1.0 (m, 2 H, *endo*-H(5), *endo*-H(6)); 1.58 (m, 2 H, *exo*-H(5), *exo*-H(6)); 1.82 (m, 2 H, $H(3)_2$); 2.34 (br.s, 2 H, H(1), H(4)); 3.96 (two d, 1 H (diastereoisomerism with the signals spaced at 5 Hz), H(7), $^3J_{H-H}$ = 6 Hz); 4.74 (asymmetric dm, 1 H, H(2)); 5.0 (two dq (diastereoisomerism with the signals spaced at 4.2 Hz), 1 H, $CHFCF_3$, $^2J_{H-F}$ = 46 Hz, $^3J_{H-F}$ = 6.8 Hz); 7.05 (br.s, 1 H, NH). $^{19}$F NMR, δ: 1.05 (two dd (diastereoisomerism with the signals spaced at 31 Hz), 3 F, $C\underline{F}_3CHF$, $^3J_{H-F}$ = = 6.8 Hz, $^3J_{F-F}$ = 11 Hz); −79.80 (m, 1 F, F(2)); −125.28 (m, 1 F, $CH\underline{F}CF_3$). MS (EI, 70 eV), *m/z* ($I_{rel}$ (%)): 257 [M$^+$] (5), 237 [M − HF]$^+$ (20), 136 [M − HF − $CF_3CHF$]$^+$ (15), 92 [$C_7H_8$]$^+$ (100). Found (%): C, 47.14; H, 4.86; N, 5.34. $C_{10}H_{12}F_5NO$. Calculated (%): C, 46.70; H, 4.70; N, 5.45. IR ($CH_2Cl_2$), ν/cm$^{-1}$: 3437 (N—H); 2988, 2980, 2926, 2885 (C—H); 1701 (HNC=O); 1537 (N—H); 1199, 1148, 1090 (C—F).

Amide **4a**, m.p. 57 °C. $^1$H NMR, δ: 1.0 (m, 2 H, *endo*-H(5), *endo*-H(6)); 1.78 (d, 2 H, *exo*-H(5), *exo*-H(6), $^3J_{H-H}$ = 7.8 Hz); 2.84 (br.s, 2 H, H(1), H(4)); 3.96 (d, 1 H, H(7), $^3J_{H-H}$ = 9 Hz); 5.0 (dq, 1 H, $CHFCF_3$, $^2J_{H-F}$ = 44 Hz, $^3J_{H-F}$ = 7 Hz); 6.02 (s, 2 H, H(2), H(3)); 6.55 (br.s, 1 H, NH). $^{19}$F NMR, δ: 1.18 (dd, 3 F, $C\underline{F}_3CHF$, $^3J_{H-F}$ = 7 Hz, $^3J_{F-F}$ = 11 Hz); −124.87 (dq, 1 F, $CH\underline{F}CF_3$, $^2J_{H-F}$ = 44 Hz, $^3J_{F-F}$ = 11 Hz). MS (EI, 70 eV), *m/z* ($I_{rel}$ (%)): 237 [M$^+$] (2), 202 [M − $C_2H_4$]$^+$ (2), 136 [M − $CF_3CHF$]$^+$ (10), 92 [$C_7H_8$]$^+$ (100). Found (%): C, 51.02; H, 4.85; N, 5.76. $C_{10}H_{11}F_4NO$. Calculated (%): C, 50.64; H, 4.67; N, 5.91. IR ($CH_2Cl_2$), ν/cm$^{-1}$: 3431 (N—H); 2982, 2949, 2878 (C—H); 1697 (C=O); 1533 (N—H); 1200, 1146, 1086 (C—F).

Ester **5a** (1 : 1 mixture of diastereomers), a highly hydrolyzable colorless oil. $^1$H NMR, δ: 1.13 (m, 2 H, *endo*-H(5), *endo*-H(6)); 1.68 (m, 2 H, *exo*-H(5), *exo*-H(6)); 1.96 (m, 2 H, $H(3)_2$); 2.48 (br.s, 1 H, H(4)); 2.75 (m, 1 H, H(1)); 4.71 (dm, 1 H, H(2), $^2J_{H-F}$ = 55 Hz); 4.88 (two s (diastereoisomerism with the signals spaced at 8 Hz), 1 H, H(7)); 5.07 (dq, 1 H, $CHFCF_3$, $^2J_{H-F}$ = = 45 Hz, $^3J_{H-F}$ = 6.8 Hz). $^{19}$F NMR, δ: 1.70 (two ddd (diastereoisomerism with the signals spaced at 21 Hz), 3 F, $C\underline{F}_3CHF$, $^3J_{H-F}$ = 6.3 Hz, $^3J_{F-F}$ = 12 Hz, $^9J_{F-F(2)}$ = 6.8 Hz in one stereoisomer and 2.7 Hz in the other); −86.60 (m, 1 F, F(2), in the $^{19}$F{$^1$H} NMR spectrum, the multiplet breaks down into two quartets at δ −85.73 ($^9J_{F-F(2)}$ = 2.7 Hz) and −85.98 ($^9J_{F-F(2)}$ = = 6.8 Hz)); −127.25 (m, 1 F, $CH\underline{F}CF_3$). Hydrolysis with ammonia in aqueous ethanol gave the corresponding alcohol 2-*exo*-fluoro-7-*syn*-hydroxybicyclo[2.2.1]heptane, m.p. 76 °C (*cf.* Ref. 20: m.p. 77—79 °C). $^1$H NMR, δ: 0.96 (m, 2 H, *endo*-H(5), *endo*-H(6)); 1.45 (m, H, *exo*-H(5)); 1.57 (m, 1 H, *exo*-H(6)); 1.83 (m, 1 H, *endo*-H(3)); 2.15 (m, 2 H, *exo*-H(3), H(4)); 2.34 (m, 1 H, H(1)); 3.2 (br.s, 1 H, OH); 3.95 (s, 1 H, H(7)); 4.65 (dd, 1 H, H(2), $^2J_{H-F}$ = 55 Hz, $^3J_{H-H}$ = 7 Hz). $^{19}$F NMR, δ: −81.15 (m). MS (EI, 70 eV), *m/z* ($I_{rel}$ (%)): 130 [M]$^+$ (traces), 110 [M − HF]$^+$ (50), 79 [M − $CF_2$ − H]$^+$ (100). $^1$H NMR (60 MHz), δ:[20] 0.8—2.5 (m, 8 H); 3.9 (s, 1 H); 4.6 (asymmetric dm, 1 H, $^2J_{H-F}$ = 57 Hz). MS, *m/z* ($I_{rel}$ (%)):[20] 130 [M]$^+$ (traces), 110 (35), 79 (100).

Ester **6a** was not isolated in the individual state because of its low yield and extremely easy hydrolysis. The signal for F(2) in the $^{19}$F NMR spectrum appeared at δ −83.38. Hydrolysis with ammonia in aqueous ethanol gave the corresponding alcohol 2-*exo*-fluoro-7-*anti*-hydroxybicyclo[2.2.1]heptane, m.p. 110—112 °C (*cf.* Ref. 20: m.p. 111—113 °C). $^1$H NMR, δ: 0.85—2.3 (m, 8 H); 3.55 (s, 1 H, OH); 4.21 (s, 1 H, H(7)); 4.47 (asymmetric dm, 1 H, H(2), $^2J_{H-F}$ = 57 Hz). $^{19}$F NMR, δ: −84.35 (m). MS (EI, 70 eV), *m/z* ($I_{rel}$ (%)): 130 [M]$^+$ (traces), 110 [M − HF]$^+$ (50), 79 [M − $CF_2$ − H]$^+$ (100). $^1$H NMR (60 MHz), δ:[20] 0.8—2.5 (m, 8 H); 3.5 (s, 1 H, OH); 4.2 (s, 1 H); 4.4 (asymmetric dm, 1 H, $^2J_{H-F}$ = = 57 Hz). MS, *m/z* ($I_{rel}$ (%)):[20] 130 [M]$^+$ (traces), 110 (17), 79 (100).

**Reaction of azide II with norbornene.** A solution of norbornene (1.7 g, 18 mmol) and azide **II** (4.2 g, 21 mmol) in dry $CH_2Cl_2$ (10 mL) was stirred at ~20 °C for three days (until nitrogen ceased to evolve). Then moist acetonitrile (15 mL) and silica (6 g) were added and the reaction mixture was stirred for an additional 2 h, filtered, and concentrated. The total yield of products **3b**—**6b** was 89%. Their ratio was determined from the intensity ratio of the signals for F(2) and $CF_2$ in the $^{19}$F NMR spectra of the reaction mixture. The products obtained were separated by column chromatography on silica (gradient elution with light petroleum—ethyl acetate (10 : 1 → 3 : 1)). The yields of fluoro amide **3b**, amide **4b**, and fluorinated ester **5b** were 1.5 (31%), 1.35 (29%), and 0.6 g (12%), respectively. A small amount of crude ester **6b** was obtained (esters **5b** and **6b** also undergo hydrolysis on silica; ester **3b** was identified, and its configuration was determined, upon hydrolysis to the corresponding 2-fluoronorbornan-7-ol).

Fluoro amide **3b**, colorless oil. $^1$H NMR (500 MHz), δ: 1.10 (m, 2 H, *endo*-H(5), *endo*-H(6)); 1.70 (m, 2 H, *exo*-H(5), *exo*-H(6)); 1.92 (m, 1 H, H(4)); 1.98 (m, 1 H, *endo*-H(3)); 2.48 (m, 2 H, H(1), *exo*-H(3)); 3.92 (s, 3 H, $OCH_3$); 4.00 (d, 1 H, H(7), $^3J_{H-H}$ = 8 Hz); 4.83 (asymmetric dd, 1 H, H(2), $^2J_{H-F}$ = = 55 Hz); 7.12 (br.s, 1 H, NH). $^{19}$F NMR (470 MHz), δ: −36.02 (2 F, AB (the signals spaced at 55 Hz), $CF_2$, $^2J_{F-F}$ = 267 Hz); −80.22 (m, 1 F, F(2)). MS (EI, 70 eV), *m/z* ($I_{rel}$ (%)): 265 $[M]^+$ (2), 245 $[M - HF]^+$ (20), 149 $[M - HF - CF_2COO]^+$ (30), 92 $[C_7H_8]^+$ (100). Found (%): C, 50.51; H, 5.43; N, 5.17. $C_{11}H_{14}F_3NO_3$. Calculated (%): C, 49.81; H, 5.32; N, 5.28. IR ($CH_2Cl_2$), ν/cm$^{-1}$: 3434 (N—H); 2976, 2961, 2928, 2883 (C—H); 1784, 1771 sh (O=COMe); 1709 (HNC=O); 1539 (N—H).

Amide **4b**, m.p. 41 °C. $^1$H NMR (500 MHz), δ: 0.98 (m, 2 H, AB, *endo*-H(5), *endo*-H(6)); 1.78 (2 H, AB, *exo*-H(5), *exo*-H(6), $^3J_{H-H}$ = 8 Hz); 2.83 (s, 2 H, H(1), H(4)); 3.86 (m, 4 H, $OCH_3$, H(7)); 6.00 (s, 2 H, H(2), H(3)); 6.70 (br.s, 1 H, NH). $^{19}$F NMR, δ: −35.7 (s). MS (EI, 70 eV), *m/z* ($I_{rel}$ (%)): 245 $[M]^+$ (6), 217 $[M - C_2H_4]^+$ (5), 154 $[NH_2COCF_2COOCH_3 + H]^+$ (80), 136 $[M - CF_2COMe]^+$ (40), 92 $[C_7H_8]^+$ (100). Found (%): C, 54.27; H, 5.52; N, 5.57. $C_{11}H_{13}F_2NO_3$. Calculated (%): C, 53.88; H, 5.34; N, 5.71. IR ($CH_2Cl_2$), ν/cm$^{-1}$: 3428 (N—H); 2988, 2947, 2880 (C—H); 1783, 1770 sh (O=COMe); 1704 (HNC=O); 1530 (N—H); 1167, 1098 (C—F).

Ester **5b**, a hydrolyzable colorless oil. $^1$H NMR (500 MHz), δ: 1.15 (m, 2 H, *endo*-H(5), *endo*-H(6)); 1.61 (m, 1 H, *exo*-H(5)); 1.73 (m, 1 H, *exo*-H(6)); 1.95 (m, 1 H, *endo*-H(3)); 2.10 (m, 1 H, *exo*-H(3)); 2.48 (br.s, 1 H, H(4)); 2.71 (m, 1 H, H(1)); 3.90 (s, 3 H, $OCH_3$); 4.69 (dd, 1 H, H(2), $^2J_{H-F}$ = 56 Hz, $^3J_{H-H}$ = 7.2 Hz); 4.85 (s, 1 H, H(7)). $^{19}$F NMR (470 MHz), δ: −35.9 (2 F, AB (the signals spaced at 16 Hz), $CF_2$, $^2J_{F-F}$ = = 275 Hz); −86.43 (m, 1 F, F(2)).

Ester **6b** was not isolated in the individual state because of its low yield and easy hydrolysis. $^{19}$F NMR, δ: −35.23 (s, 2 F, $CF_2$); −83.95 (m, 1 F, F(2)). Its structure was confirmed by hydrolysis to the documented[20] alcohol, which was obtained and identified as described above for ester **6a**.

**Reaction of cyclohexene with azide I.** A solution of cyclohexene (0.8 g, 10 mmol) and azide **I** (3 g, 15 mmol) in dry $CH_2Cl_2$ (10 mL) was heated in a steel tube at 150 °C for 6 h. The reaction mixture was cooled, poured into moist acetonitrile (20 mL) containing silica (5 g), and stirred for 1 h. Then it was filtered and concentrated and the residue was separated on silica (gradient elution with light petroleum—ethyl acetate (10 : 1 → 3 : 1)). The yields of fluoro amide **7** and cyclohexenyl amide **8** were 0.6 (25%) and 0.5 g (25%), respectively.

Fluoro amide **7**, colorless oil. $^1$H NMR, δ: 1.30—2.00 (m, 6 H, H(4), H(5), H(6)); 2.15 (m, 2 H, H(3)); 4.02 (m, 1 H, H(1)); 4.33 (dddd, 1 H, $^2J_{H-F}$ = 50.5 Hz, H(2), $^3J_{H(1a)-H(2a)}$ = 10.5 Hz, $^3J_{H(3a)-H(2a)}$ = 10.5 Hz, $^3J_{H(3e)-H(2a)}$ = 6.3 Hz); 5.08 (dq, 1 H, $CHFCF_3$, $^2J_{H-F}$ = 48 Hz, $^3J_{H-F}$ = 6.5 Hz); 6.5 (br.s, 1 H, NH). $^{19}$F NMR, δ: 1.54 (m, 3 F, $CF_3$); −101.4 (dm, 1 F, F(2), $^2J_{H-F}$ = = 50.5 Hz); −124.6 (m, 1 F, $CH\underline{F}CF_3$). IR ($CH_2Cl_2$), ν/cm$^{-1}$: 3419 (N—H); 2952, 2864 (C—H); 1704 (C=O); 1530 (N—H); 1450 (C—N); 1355 (CHF); 1201, 1148, 1093 (C—F). MS (EI, 70 eV), *m/z* ($I_{rel}$ (%)): 225 $[M - HF]^+$ (15), 184 $[C_3H_4NHCOCHFCF_3 + H]^+$ (100), 101 $[CF_3CHF]^+$ (40), 80 $[C_6H_8]^+$ (45). Found (%): C, 44.44; H, 5.05; N, 5.59. $C_9H_{12}F_5NO$. Calculated (%): C, 44.09; H, 4.93; N, 5.71.

Cyclohexenyl amide **8** (2 : 1 mixture of two conformers). $^1$H NMR, δ: 1.63—1.80 (m, 4 H, H(4), H(5)); 2.15—2.40 (m, 4 H, H(3), H(6)); 5.07 + 5.14 (dq, 1 H, $CHFCF_3$, $^2J_{H-F}$ = 48 Hz, $^3J_{H-F}$ = 6.6 Hz); 6.27 + 6.65 (dd, 1 H, H(2), $^3J_{H(3a)-H(2)}$ = 2 Hz, $^3J_{H(3e)-H(2)}$ = 4 Hz); 7.27 + 7.45 (br.s, 1 H, NH). $^{19}$F NMR, δ: 1.09 (m, 3 F, $CF_3$); −122.9, −125.6 (m, 1 F, $CH\underline{F}CF_3$). IR ($CH_2Cl_2$), ν/cm$^{-1}$: 3428 (N—H); 2964, 2870 (C—H); 1699 (C=O); 1538, 1524 (N—H); 1453, 1430 (C—N); 1353 (CHF); 1201, 1147, 1089 (C—F). MS (EI, 70 eV), *m/z* ($I_{rel}$ (%)): 225 $[M]^+$ (40), 197 $[M - C_2H_4]^+$ (25), 101 $[CF_3CHF]^+$ (25), 80 $[C_6H_8]^+$ (100).

**Reaction of *trans*-stilbene with azide I.** A solution of *trans*-stilbene (0.32 g, 1.88 mmol) and azide **I** (0.8 g, 4.1 mmol) in dry $CH_2Cl_2$ (5 mL) was heated in a steel tube at 170 °C for 18 h. The reaction mixture was chromatographed on silica with hexane—ethyl acetate (7 : 1) as an eluent. The yields of amides **9a** and **9b** were 0.25 g (44%) and 50 mg (9%), respectively.

Amide **9a**, colorless crystals, m.p. 84 °C. $^1$H NMR, δ: 5.45 (dq, 1 H, $CHFCF_3$, $^2J_{H-F}$ = 45 Hz, $^3J_{H-F}$ = 6.2 Hz); 7.20—7.62 (m, 11 H, Ph, CHNH); 8.30 (br.d, 1 H, NH, $^3J_{H-H}$ = 10 Hz). MS (EI, 70 eV), *m/z* ($I_{rel}$ (%)): 323 $[M]^+$ (100), 222 $[M - CF_3CHF]^+$ (10), 194 $[M - CF_3CHFCO]^+$ (70), 178 $[Ph_2C_2]^+$ (28). Found (%): C, 63.35; H, 4.42; N, 4.13. $C_{17}H_{13}F_4NO$. Calculated (%): C, 63.16; H, 4.05; N, 4.33. IR ($CH_2Cl_2$), ν/cm$^{-1}$: 3415 (N—H); 1711 (C=O); 1642 (C=C); 1510 (N—H); 1485, 1352 (CHF); 1201, 1147, 1090 (C—F).

Amide **9b**, colorless crystals, m.p. 101 °C. $^1$H NMR, δ: 5.65 (dq, 1 H, $CHFCF_3$, $^2J_{H-F}$ = 45 Hz, $^3J_{H-F}$ = 6.2 Hz); 6.96 (s, 1 H, PhCH); 7.30—7.70 (m, 10 H, Ph); 8.85 (br.s, 1 H, NH). MS (EI, 70 eV), *m/z* ($I_{rel}$ (%)) : 323 $[M]^+$ (70), 178 $[Ph_2C_2]^+$ (10). Found (%): C, 63.25; H, 4.36; N, 4.15. $C_{17}H_{13}F_4NO$. Calculated (%): C, 63.16; H, 4.05; N, 4.33. IR ($CH_2Cl_2$), ν/cm$^{-1}$: 3399 (N—H); 1717 (C=O); 1506 (N—H); 1448, 1354 (CHF); 1204, 1148, 1090 (C—F).

**Reaction of anthracene with azide I.** A mixture of anthracene (0.37 g, 2 mmol) and azide **I** (0.8 g, 4.1 mmol) in dry $CH_2Cl_2$ (5 mL) was heated in a steel tube (anthracene is poorly soluble in $CH_2Cl_2$ at room temperature) at 180 °C for 6 h. The reaction mixture was applied to silica (1 g) and chromatographed with hexane—ethyl acetate (10 : 1) as an eluent. The yield of amide **10** was 0.13 g (20%); the starting anthracene (0.26 g, 75%) was recovered.

Amide **10**, yellow crystals, m.p. 177 °C. $^1$H NMR, δ: 5.70 (dq, 1 H, $CHFCF_3$, $^2J_{H-F}$ = 45 Hz, $^3J_{H-F}$ = 6.2 Hz); 7.46—7.62 (m, 4 H, H(2), H(3), H(6), H(7)); 8.00—8.15 (m, 4 H, H(1), H(4), H(5), H(8)); 8.60 (s, 1 H, H(10)); 9.27 (br.s, 1 H, NH). $^{19}$F NMR, δ: 1.4 (m, 3 F, $CF_3$); −124.4 (m, 1 F, $CH\underline{F}CF_3$). MS (EI, 70 eV), *m/z* ($I_{rel}$ (%)): 321 $[M]^+$ (90), 220 $[M - CF_3CHF]^+$ (7), 192 $[M - CF_3CHFCO]^+$ (100). Found (%): C, 63.81; H, 3.79; N, 4.20. $C_{17}H_{11}F_4NO$. Calculated (%): C, 63.55; H, 3.45; N, 4.36.

## References


1. I. L. Knunyants, E. G. Bykhovskaya, *Dokl. Akad. Nauk SSSR*, 1960, **131**, 1338 [*Dokl. Chem.* (*Engl. Transl.*), 1960].
2. I. L. Knunyants, E. G. Bykhovskaya, *Zh. Vses. Khim. O-va im. D. I. Mendeleeva*, 1962, **7**, 585 [*Mendeleev Chem. J.* (*Engl. Transl.*), 1962, **7**].
3. Yu. V. Zeifman, V. V. Tyuleneva, A. P. Pleshkova, R. G. Kostyanovskii, I. L. Knunyants, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1975, 2732 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.* (*Engl. Transl.*), 1975, **24**].

4. S. A. Lermontov, I. I. Sukhojenko, A. V. Popov, A. N. Pushin, I. V. Martynov, N. S. Zefirov, P. J. Stang, *Heteroatom Chem.*, 1993, **4**, 579.
5. S. A. Lermontov, S. V. Shkavrov, A. S. Lermontov, V. O. Zavelsky, N. S. Zefirov, *J. Fluorine Chem.*, 1999, **94**, 43.
6. S. A. Lermontov, I. M. Rakov, S. V. Shkavrov, *Phosphorus, Sulfur, Silicon*, 1999, **149**, 75.
7. S. A. Lermontov, S. V. Shkavrov, A. N. Pushin, *J. Fluorine Chem.*, 2000, **105**, 141.
8. C. G. Krespan, *J. Org. Chem.*, 1986, **51**, 332.
9. F. D. Marsh, H. E. Simmons, *J. Am. Chem. Soc.*, 1965, **87**, 3529.
10. N. N. Yarovenko, M. A. Raksha, *Zh. Org. Khim.*, 1959, **29**, 2159 [*J. Org. Chem. USSR* (*Engl. Transl.*), 1959, **29**].
11. A. Takaoko, H. Iwakiri, N. Ishikawa, *Bull. Chem. Soc. Jpn*, **52**, 11, 3377.
12. C. G. Krespan, *J. Am. Chem. Soc.*, 1984, **106**, 5544.
13. C. G. Krespan, B. E. Smart, *J. Org. Chem.*, 1986, **51**, 320.
14. C. G. Krespan, *J. Org. Chem.*, 1986, **51**, 326.
15. R. H. Abeles, A. L. Maycock, *Acc. Chem. Res.*, 1978, **9**, 313.
16. R. A. Hildreth, M. L. Druelinger, S. A. Shackelford, *Tetrahedron Lett.*, 1982, **23**, 1059.
17. S. Stavber, T. S. Pecan, M. Papez, M. Zupan, *Chem. Commun.*, 1996, 2247.
18. E. Laurent, R. Tardivel, H. Benotmane, A. Bensadat, *Bull. Soc. Chim. Fr.*, 1990, **3**, 468.
19. W. Dmowski, T. Kozlovski, *Electrochim. Acta*, 1997, **42**, 513.
20. G. Gargaro, M. A. Loreto, L. Pellacani, P. A. Tardella, *J. Org. Chem.*, 1983, **48**, 2043.

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