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A facile stereoselective synthesis of 2-perfluoroalkyl-3a,4,5,6-tetrahydroimidazo[1,5-*b*]isoxazoles

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ABSTRACT

Methyl 2-perfluoroalkynoates 2 reacted readily with cyclic nitrones 1 *via* 1,3-dipolar cycloaddition at room temperature to give 2-perfluoroalkyl-3a,4,5,6-tetrahydroimidazo[1,5-*b*]isoxazoles **3** in good to excellent yields with high diastereoselectivity and regioselectivity.

1. Introduction

Fluorinated heterocycles represent an interesting class of fluorinated compounds that have found their wide application as agrochemicals, pharmaceuticals, and in the field of new material science [1]. Consequently, much attention has been addressed to develop new methodologies for the synthesis of these target structures by synthetic chemists the world over [2]. The 1,3-dipolar cycloaddition reactions of nitrones with a variety of alkynes or olefins, within the building-block strategy, has received particular attention for the synthesis of a variety of isoxazole derivatives, which can be transformed into numerous attractive building-block molecules for organic synthesis [3–5].

Though perfluoro-2-alkynoates exhibit high reactivity and exclusive regioselectivity in most cases of the cycloadditions [2c,6], there are merely scattered examples of 1,3-diploar cycloaddition using them as dipolarphiles. Herein, we wish to report the results of our studies on the 1,3-dipolar cycloaddition of perfluoro-2-akynoates with cyclic nitrones, which provide a new efficient and convenient tool in the good-yield synthesis of the novel fluoroalkyl-tetrahydroimidazoisoxazole bicyclic system **3** with high regio- and stereo- selectivity.

2. Results and discussion

The Δ^3-imidazoline 3-oxides **1**, prepared according to the reported procedure [7], undergo 1,3-cycloaddition with methyl 2-perfluoroalkynoates **2** [8] to give 2-perfluoroalkyl-3a,4,5,6-tetrahydroimidazo[1,5-*b*]isoxazoles **3** at room temperature in good to excellent yields, using CH_2Cl_2 as solvent (Scheme 1, Table 1).

All reactions went rapidly and completely within 4 h, though it was found that cyclic nitrones **1** with an electron-donating group on R_2 reacted more readily with methyl 2-perfluoroalkynoates **2** to give the product in higher yields than those with an electron-withdrawing group on R_2 (Table 1, **3d** and **3g**, **3h**; **3m** and **3n**, **3p**). The high efficiency in the reaction between **1** and **2** may be ascribed to strong electron-withdrawal of the R_F group according to the theory of frontier molecular orbitals (FMO theory) [6a,e]. Based on the theory, nitrone is a donor and alkyne is an acceptor of electrons. Thus the strengthening of the acceptor properties of substituents in alkyne explains why electron-withdrawing group substituted-2-alkynoates such as perfluoro-2-alkynoates

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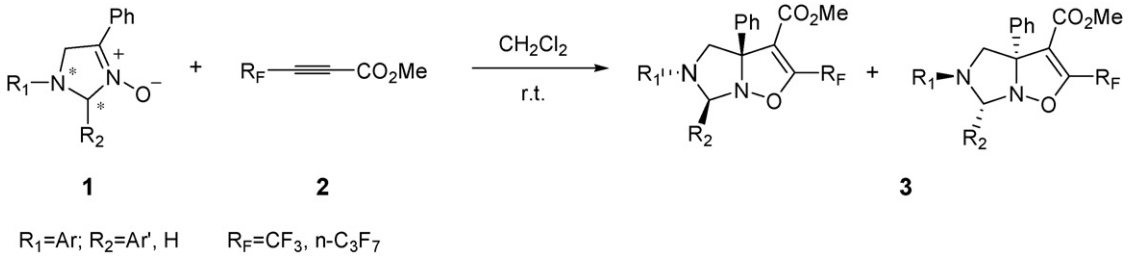


Scheme 1. Synthesis of 3a,4,5,6-tetrahydroimidazo[1,5-*b*]isoxazoles **3**.

Table 1
Synthesis of 3a,4,5,6-tetrahydroimidazo[1,5-*b*]isoxazoles **3**.

Entry	*N*-oxide **1**	R_1	R_2	R_F	Product	Yield[a] (%)	Mp (°C)
1	**1a**	*p*-$MeOC_6H_4$	Ph	CF_3	**3a**	92	107.0–107.7
2	**1b**	*p*-$MeOC_6H_4$	H	CF_3	**3b**	90	108.7–109.8
3	**1c**	*p*-MeC_6H_4	*p*-MeC_6H_4	CF_3	**3c**	96	112.1–112.6
4	**1d**	*p*-MeC_6H_4	*p*-$MeOC_6H_4$	CF_3	**3d**	89	92.3–93.1
5	**1e**	*p*-$MeOC_6H_4$	*p*-MeC_6H_4	CF_3	**3e**	87	103.4–103.7
6	**1f**	*p*-$MeOC_6H_4$	*p*-$MeOC_6H_4$	CF_3	**3f**	92	89.8–90.7
7	**1g**	*p*-MeC_6H_4	*p*-$NO_2C_6H_4$	CF_3	**3g**	73	68.2–69.4
8	**1h**	*p*-MeC_6H_4	*p*-ClC_6H_4	CF_3	**3h**	76	54.1–55.7
9	**1i**	*p*-$MeOC_6H_4$	*p*-ClC_6H_4	CF_3	**3i**	78	59.3–61.5
10	**1j**	*p*-MeC_6H_4	Ph	*n*-C_3F_7	**3j**	92	98.1–100.2
11	**1k**	*p*-MeC_6H_4	H	*n*-C_3F_7	**3k**	98	104.6–108.2
12	**1b**	*p*-$MeOC_6H_4$	H	*n*-C_3F_7	**3l**	95	86.5–88.0
13	**1c**	*p*-MeC_6H_4	*p*-MeC_6H_4	*n*-C_3F_7	**3m**	89	92.5–95.2
14	**1h**	*p*-MeC_6H_4	*p*-ClC_6H_4	*n*-C_3F_7	**3n**	81	70.3–73.1
15	**1i**	*p*-$MeOC_6H_4$	*p*-ClC_6H_4	*n*-C_3F_7	**3o**	76	64.3–66.7
16	**1g**	*p*-MeC_6H_4	*p*-$NO_2C_6H_4$	*n*-C_3F_7	**3p**	79	79.5–81.3

[a] Isolated yields.

like 4,4,4-trifluorobutynoates or acetylenedicarboxylates can increase the rate of cycloaddition [3c,5,6,9].

Furthermore, the distinguishing feature of the studied reaction is its high regioselectivity: only one regioisomer containing stronger electron-withdrawing substituent at position 2 of the tetrahydroimidazo[1,5-b]isoxazol is formed (Scheme 1). Dipolar cycloaddition of nitrones to electron-deficient alkynes is probably a type I cycloaddition and is controlled by the interaction of HOMO of the dipole and LUMO of the alkyne [4e,6b,c,9a]. Based on FMO theory, high regioselectivity is the result of the significant difference of coefficients squares of atomic wave functions at reaction centers in LUMO of asymmetrically substituted alkyne(φ_1^2 and φ_2^2)s and in HOMO of the nitrone group (φ_3^2 and φ_4^2). Interaction of the centers with maximum values of φ_i^2 is preferred. Maximum atomic coefficients in the interacting molecular orbitals pertain to the oxygen atom of the nitrone and to the carbon atom β to ester group in alkyne. Regioisomer **3** is formed as a result of such overlapping, that is observed in the experiment.

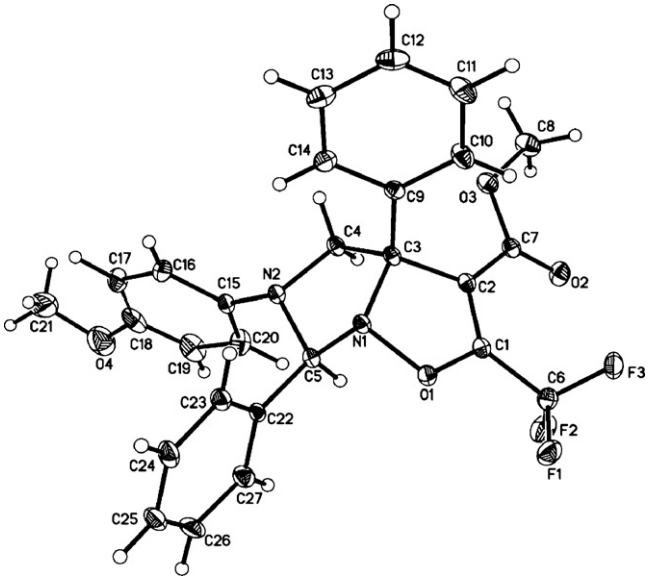


Fig. 1. X-ray structure of **3a**.

Since the assignment of configuration of **3** is difficult to be made on the basis of ^{1}H NMR spectroscopic data and NOESY experiments, an X-ray diffraction analysis was used to elucidate the structures of **3**. A 3D perspective view of the crystal structure of **3a** is shown in Fig. 1 [10]. The adduct is proved unequivocally to be the *cis*-isomer by X-ray differaction analysis, that is, the Ph ring and R_2 were on the same side of the bicyclic ring system [5b]. The fact that only one signal observed in ^{19}F NMR spectroscopy of **3a** proves further that the reactions of **1** with alkyne **2** are not only regiospecific but also diastereospecific, affording only one diastereoisomer. Take **3a** for an example, Δ^3-imidazoline 3-oxide **1a** possesses two chiral centers, thus there exist four possible stereoisomers: **A**, **B**, **C** and **D** (Fig. 2). In **C** and **D**, the *N*-anisyl group is in a *cis* relationship with the phenyl group on *C-3a*. Accordingly, the steric interactions between two vicinal aryl groups become so significant that **C** and **D** are thermally too unstable to undergo the 1,3-dipolar cycloaddition with alkynoates, which was proved by the fact that no corresponding products were detected in the experiment. For **A** and **B**, the fact that only one diastereoisomer was obtained demonstrated that the reaction was a concerted process guided with the Woodward–Hoffman rule. When the linear molecule of 4,4,4-trifluorobutynoate approaches planar dipole *N*-oxide **1a** with the CF_3 group being oriented towards the oxygen atom of the *N*-oxide function, there are four different routes, which are **E**, **F**, **G** and **H**, respectively. The alkynoate prefers to approach the dipole from the less sterically hindered side of the plane and thus afforded a pair of enantiomers (Scheme 2 and Fig. 3).

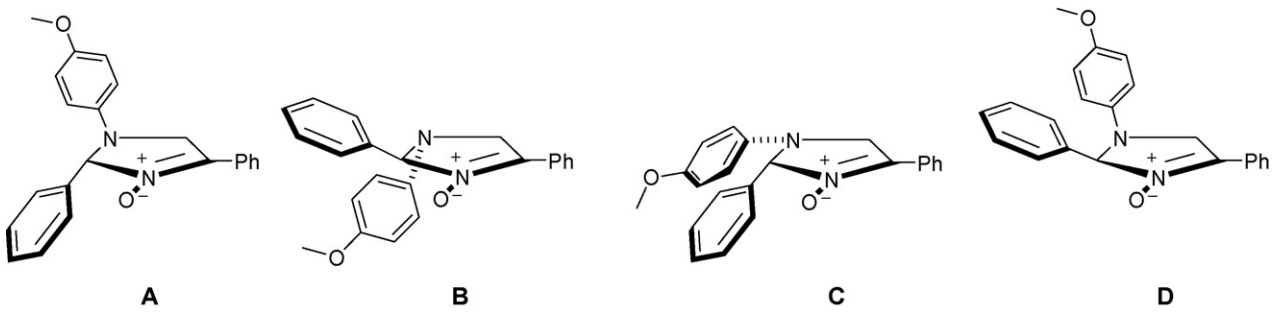
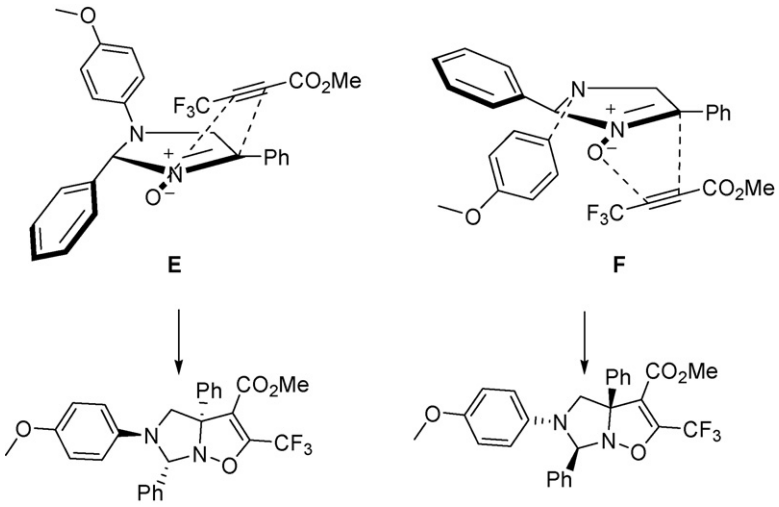


Fig. 2. Four possible stereoisomers of **1**.



Scheme 2. Formation of product **3**.

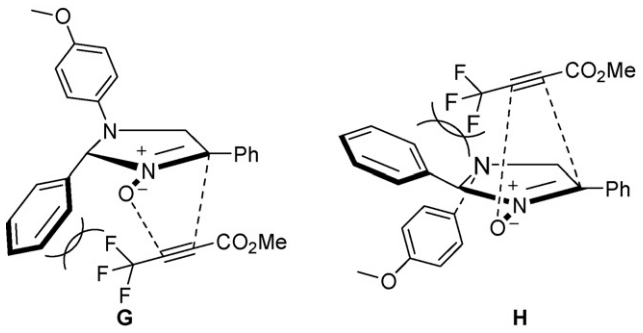


Fig. 3. Sterichindric approach diagram.

3. Conclusion

In summary, we developed a convenient method to synthesize the regiospecific 2-perfluoroalkylsubstituted isoxazoles **3** with high diasterselectivity, which were prepared readily from the 1,3-dipolar cycloaddition reactions of cyclic nitrones **1** with methyl 2-perfluoroalkynoates **2** in good to excellent yields. This work provides a simple procedure for the synthesis of fluorine-containing bicyclic nitrogen heterocycles. Considering the contributions of the method such as mild reaction conditions, easy manipulation, simple work-up, etc., it should found applications in organic synthesis.

4. Experimental

4.1. General

All reagents and solvents were purchased from commercial sources and used without further purification. Melting points were recorded on a WRS-1 instrument and uncorrected. IR spectra were obtained on a Bruker Spectrometer. ^{1}H, ^{19}F and ^{13}C NMR spectra were recorded on a Bruker AVANCE-500 MHz instrument. All chemical shifts are reported in parts per million downfield (positive) of the standard: C_6F_6 for ^{19}F, TMS for ^{1}H and ^{13}C NMR spectra. Elemental analyses were performed on an Elementar Vario EL-III instrument. MS spectra were run on an Agilent LC spectrometer. X-ray analysis was performed on a Bruker Smart Apex2 CCD Spectrometer. Preparative TLC on silica gel was performed by using self-coated GF_{254} plates, which were activated immediately before use.

4.2. General procedure for the preparation of compounds 1

At room temperature, α-bromoacetophenone oxime (2.5 mmol) was added to a solution of aromatic amine (5 mmol) in ethanol and the mixture was stirred for 20 min followed by adding aromatic aldehyde (5 mmol) or 35% water solution of formaldehyde (5 mL) and then stirred for another 3 h at same temperature. The formed precipitate was collected by filtration and recrystallized from acetone to get **1a–e**, **1j–k** [7d] and **1f–i**, respectively.

*4.2.1. 1,2-Bis(4-methoxyphenyl)-4-phenyl-2,5-dihydro-1H-imidazole 3-oxide (**1f**)*

White solid; mp: 165–167.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.73 (3H, s, CH_3O), 3.80 (3H, s, CH_3O), 4.80 (1H, dd, J = 14.5, 2.8 Hz, CH_2), 5.14 (1H, dd, J = 14.5, 5.0 Hz, CH_2), 6.09 (1H, m, CH), 6.57–8.35 (13H, m, Ph). ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.31, 55.47, 55.82, 73.45, 89.89, 113.83, 114.45, 115.19, 127.04, 127.41, 128.19, 128.85, 128.97, 129.51, 131.00, 138.76, 152.96. MS (ESI) m/z 397 $(M + Na)^+$. IR (KBr) 3088, 3000, 2935, 2837, 1611, 1515 cm^{-1}. Anal. Cacld for $C_{23}H_{22}N_2O_3$: C 73.78, H 5.92, N 7.48; Found: C 73.82, H 5.76, N 7.44.

*4.2.2. 2-(4-Nitrophenyl)-4-phenyl-1-p-tolyl-2,5-dihydro-1H-imidazole 3-oxide (**1g**)*

Yellow solid; mp: 174.5–175.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.25 (3H, s, CH_3), 4.89 (1H, dd, J = 14.5, 2.0 Hz, CH_2), 5.21 (1H, dd, J = 14.5, 5.0, CH_2), 6.27 (1H, m, CH), 6.47–8.33 (13H, m, Ph). ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.45, 53.27, 73.78, 88.65, 112.84, 124.10, 126.87, 127.32, 129.12, 129.01, 129.35, 130.36, 131.53, 131.76, 141.50, 142.79. MS (ESI) m/z 375.1 $(M + 1)^+$. IR (KBr) 3067, 3030, 2861, 1617, 1522, 1447, 1349 cm^{-1}. Anal. Cacld for $C_{22}H_{19}N_3O_3$: C 70.76, H 5.13, N 11.25; Found: C 70.28, H 4.99, N 11.03.

*4.2.3. 2-(4-Chlorophenyl)-4-phenyl-1-p-tolyl-2,5-dihydro-1H-imidazole 3-oxide (**1h**)*

White solid; mp: 143.7–145 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.41 (3H, s, CH_3), 4.83 (1H, dd, J = 14.5, 3.0 Hz, CH_2), 5.14 (1H, dd, J = 14.5, 5.0 Hz, CH_2), 6.14 (1H, m, CH), 6.48–8.33 (13H, m, Ph). ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.44, 53.06, 89.13, 112.78, 127.06, 126.14, 128.57, 128.90, 129.24, 129.54, 130.20, 131.22, 134.55, 134.68, 136.16, 141.77. MS (ESI) m/z 385.0 $(M + Na)^+$. IR (KBr) 3093, 3029, 2860, 1618, 1519, 1447, 1352 cm^{-1}. Anal. Cacld for $C_{22}H_{19}ClN_2O$: C 72.82, H 5.28, N 7.72; Found: C 72.83, H 5.17, N 7.71.

*4.2.4. 2-(4-Chlorophenyl)-1-(4-methoxyphenyl)-4-phenyl-2,5-dihydro-1H-imida zole 3-oxide (**1i**)*

White solid; mp: 169.8–172.4 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.73 (3H, s, CH_3O), 4.80 (1H, dd, J = 14.5, 3.0 Hz, CH_2), 5.14 (1H, dd, J = 14.5, 5.5 Hz, CH_2), 6.10 (1H, m, CH), 6.53–8.33 (13H, m, Ph). ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.42, 55.79, 89.42, 113.88, 115.23, 127.04, 127.15, 128.90, 129.24, 129.62, 131.20, 134.61, 134.77, 136.19, 138.40, 153.18. MS (ESI) m/z 379.1 $(M + 1)^+$. IR (KBr) 3048, 3000, 2929, 2832, 1620, 1515, 1490, 1352 cm^{-1}. Anal. Cacld for $C_{22}H_{19}ClN_2O_2$: C 69.75, H 5.05, N 7.39; Found: C 69.53, H 5.24, N 7.43.

*4.3. General procedure for the preparation of compounds **3***

To the solution of imidazoline oxides (1.0 mmol) in CH_2Cl_2, methyl 2-perfluoroalkynoates (1.1 mmol) was added and the mixture was stirred at room temperature for 0.5–3 h. After the completion of the reaction (monitored by TLC), the products were purified by preparative TLC (elutent: petroleum ether 60–90 °C-ethyl acetate) and recrystallized from dichloromethane and petroleum ether (60–90 °C) to get pure product **3**.

*4.3.1. Methyl cis-5-(4-methoxyphenyl)-3a,6-diphenyl-2-(trifluoromethyl)-3a,4,5,6-tetrahydroimidazo[1,5-b]isoxazole-3-carboxylate (**3a**)*

White solid; mp: 107.0–107.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.72 (3H, s, CH_3O), 3.73 (3H, s, CH_3O), 4.15 (1H, d, J = 11.0 Hz, CH_2), 4.65 (1H, d, J = 11.0 Hz, CH_2), 5.88 (1H, s, CH), 6.73–7.54 (14H, m, Ph). ^{19}F NMR (470 MHz, $CDCl_3$) δ −63.74 (s, CF_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.30, 55.37, 58.68, 81.53, 88.73, 111.66 (d, ^3J_F = 2.5), 114.78, 116.98, 117.52 (q, ^1J_F = 254.0 Hz), 126.80, 127.74, 128.18, 128.50, 128.63, 128.71, 130.72, 140.13, 140.91, 149.96 (d, ^2J_F = 40.0 Hz), 153.65, 161.88. MS (ESI) m/z 497.2 $(M + 1)^+$. IR (KBr) 3031, 2949, 2836, 1718, 1669, 1512, 1457, 1340 cm^{-1}. Anal. Cacld for $C_{27}H_{23}F_3N_2O_4$: C 65.32, H 4.67, N 5.64; Found: C 65.37, H 4.63, N 5.68.

*4.3.2. Methyl cis-5-(4-methoxyphenyl)-3a-phenyl-2-(trifluoromethyl)-3a,4,5,6-tetrahydroimidazo[1,5-b]isoxazole-3-carboxylate (**3b**)*

White solid; mp: 108.7–109.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.43 (1H, d, J = 9.0 Hz, CH_2), 3.69 (3H, s, CH_3O), 3.78 (3H, s, CH_3O), 4.13 (1H, d, J = 11.5 Hz, CH_2), 4.67 (1H, d, J = 9.0 Hz, CH_2), 5.03 (1H, d, J = 11.5 Hz, CH_2), 6.78–7.59 (9H, m, Ph). ^{19}F NMR (470 MHz, $CDCl_3$) δ −63.50 (s, CF_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.14, 55.79, 57.99, 83.94, 110.82 (d, ^3J_F = 2.5), 114.98, 116.91, 117.65 (q, ^1J_F = 272.0 Hz), 127.26, 128.41, 128.52, 140.18, 140.60, 149.84 (d, ^2J_F = 39.5 Hz), 153.96, 161.69. MS (ESI) m/z 421.1 $(M + 1)^+$. IR (KBr) 3060, 2957, 2829, 1710, 1668, 1515, 1443, 1347 cm^{-1}. Anal. Cacld for $C_{21}H_{19}F_3N_2O_4$: C 60.00, H 4.56, N 6.66; Found: C 60.02, H 4.59, N 6.64.

*4.3.3. Methyl cis-3a-phenyl-5,6-di-p-tolyl-2-(trifluoromethyl)-3a,4,5,6-tetrahydroimidazo[1,5-b]isoxazole-3-carboxylate (**3c**)*

White solid; mp: 112.1–112.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.23 (3H, s, CH_3), 2.25 (3H, s, CH_3), 3.70 (3H, s, CH_3O), 4.12 (1H, d, J = 11.0 Hz, CH_2), 4.77 (1H, d, J = 11.0 Hz, CH_2), 5.98 (1H, s, CH), 6.66–7.52 (13H, m, Ph). ^{19}F NMR (470 MHz, $CDCl_3$) δ −63.74 (s, CF_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.48, 21.25, 52.24, 57.17, 81.86, 111.64 (d, ^3J_F = 2.5 Hz), 114.78, 117.68 (q, ^1J_F = 272.0 Hz), 126.86, 127.46, 128.13, 128.45, 128.58, 129.37, 129.90, 134.04, 138.38, 140.76, 148.81, 149.00 (d, ^2J_F = 39.5 Hz), 161.87. MS (ESI) m/z 495.1 $(M + 1)^+$. IR (KBr) 3030, 2951, 2924, 1722, 1685, 1513, 1422, 1353 cm^{-1}. Anal. Cacld for $C_{28}H_{25}F_3N_2O_3$: C 68.01, H 5.10, N 5.66; Found: C 68.03, H 5.13, N 5.65.

*4.3.4. Methyl cis-6-(4-methoxyphenyl)-3a-phenyl-5-p-tolyl-2-(trifluoromethyl)-3a,4,5,6-tetrahydroimidazo[1,5-b]isoxazole-3-carboxylate (**3d**)*

White solid; mp: 92.3–93.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.24 (3H, s, CH_3), 3.71 (3H, s, CH_3O), 3.72 (3H, s, CH_3O), 4.13 (1H, d, J = 10.5 Hz, CH_2), 4.74 (1H, d, J = 10.5 Hz, CH_2), 5.95 (1H, s, CH), 6.66–7.51 (13H, m, Ph). ^{19}F NMR (470 MHz, $CDCl_3$) δ −63.77 (s, CF_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.49, 52.26, 55.33, 57.33, 81.72, 87.59, 111.68 (d, ^3J_F = 2.5 Hz), 114.91, 117.67 (q, ^1J_F = 272.0 Hz), 126.85, 128.15, 128.45, 128.66, 128.84, 128.96, 129.90, 140.77, 143.78, 149.00 (d, ^2J_F = 39.5 Hz), 159.78, 161.87. MS (ESI) m/z 511.2 $(M + 1)^+$. IR (KBr) 3060, 3034, 2997, 2894, 1723, 1687, 1512, 1442, 1353 cm^{-1}. Anal. Cacld for $C_{28}H_{25}F_3N_2O_4$: C 65.88, H 4.94, N 5.49; Found: C 65.90, H 4.96, N 5.46.

*4.3.5. Methyl cis-5-(4-methoxyphenyl)-3a-phenyl-6-p-tolyl-2-(trifluoromethyl)-3a,4,5,6-tetrahydroimidazo[1,5-b]isoxazole-3-carboxylate (**3e**)*

White solid; mp: 103.4–103.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.26 (3H, s, CH_3), 3.71 (3H, s, CH_3O), 3.72 (3H, s, CH_3O), 4.15 (1H, d, J = 11.0 Hz, CH_2), 4.63 (1H, d, J = 11.0 Hz, CH_2), 5.83 (1H, s, CH), 6.74–7.54 (13H, m, Ph). ^{19}F NMR (470 MHz, $CDCl_3$) δ −63.74 (s, CF_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.16, 52.17, 55.62, 58.55, 81.27, 88.54, 111.53 (d, ^3J_F = 2.5 Hz), 114.65, 116.92, 117.58 (q, ^1J_F = 272.0 Hz), 126.69, 127.54, 128.39, 129.25, 138.38, 140.07, 140.96, 148.90 (d, ^2J_F = 39.5 Hz), 153.49, 161.81. MS (ESI) m/z 511.2 $(M + 1)^+$. IR (KBr) 3060, 3033, 2997, 2894, 1722, 1687, 1512, 1442, 1352 cm^{-1}. Anal. Cacld for $C_{28}H_{25}F_3N_2O_4$: C 65.88, H 4.94, N 5.49; Found: C 65.94, H 4.86, N 5.52.

*4.3.6. Methyl cis-5,6-bis(4-methoxyphenyl)-3a-phenyl-2-(trifluoromethyl)-3a,4,5,6-tetrahydroimidazo[1,5-b]isoxazole-3-carboxylate (**3f**)*

White solid; mp: 89.8–90.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.70 (9H, s, $3CH_3O$), 4.16 (1H, d, J = 11.0 Hz, CH_2), 4.61 (1H, d, J = 11.0 Hz, CH_2), 5.80 (1H, s, CH), 6.74–7.55 (13H, m, Ph). ^{19}F NMR (470 MHz, $CDCl_3$) δ −63.69 (s, CF_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.25, 55.65, 58.84, 61.95, 81.17, 88.41, 111.66 (d, ^3J_F = 2.5 Hz), 113.97, 114.70, 117.24 (q, ^1J_F = 272.0 Hz), 126.75, 126.98, 128.13, 128.48, 128.90, 129.01, 130.44, 140.08, 141.08, 148.78 (d, ^2J_F = 39.0 Hz), 153.66, 161.85. MS (ESI) m/z 527.1 $(M + 1)^+$. IR (KBr) 3001, 2954, 2837, 1716, 1675, 1512, 1441, 1346 cm^{-1}. Anal. Cacld for $C_{28}H_{25}F_3N_2O_5$: C 63.87, H 4.79, N 5.32; Found: C 63.71, H 4.86, N 5.61.

*4.3.7. Methyl cis-6-(4-nitrophenyl)-3a-phenyl-5-p-tolyl-2-(trifluoromethyl)-3a,4,5,6-tetrahydroimidazo[1,5-b]isoxazole-3-carboxylate (**3g**)*

Yellow solid; mp: 68.2–69.4 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.26 (3H, s, CH_3), 3.72 (3H, s, CH_3O), 4.10 (1H, d, J = 11.0 Hz, CH_2), 4.82 (1H, d, J = 11.0 Hz, CH_2), 6.10 (1H, s, CH), 6.66–8.10 (13H, m, Ph). ^{19}F NMR (470 MHz, $CDCl_3$) δ −63.71 (s, CF_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.50, 52.42, 61.30, 82.30, 87.13, 114.87, 111.84 (d, ^3J_F = 2.5 Hz), 117.51 (q, ^1J_F = 273.0 Hz), 123.89, 126.74, 128.52, 128.58, 128.63, 128.75, 129.63, 129.98, 130.15, 139.24, 143.24, 144.38, 148.44 (d, ^2J_F = 39.0 Hz), 161.58. MS (ESI) m/z 548.0 $(M + Na)^+$. IR (KBr) 3032, 2954, 2860, 1720, 1668, 1521, 1441, 1347 cm^{-1}. Anal. Cacld for $C_{27}H_{22}F_3N_3O_5$: C 61.71, H 4.22, N 8.00; Found: C 61.48, H 4.56, N 7.87.

*4.3.8. Methyl cis-6-(4-chlorophenyl)-3a-phenyl-5-p-tolyl-2-(trifluoromethyl)-3a,4,5,6-tetrahydroimidazo[1,5-b]isoxazole-3-carboxylate (**3h**)*

White solid; mp: 54.1–55.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.25 (3H, s, CH_3), 3.71 (3H, s, CH_3O), 4.09 (1H, d, J = 11.0 Hz, CH_2), 4.77 (1H, d, J = 11.0 Hz, CH_2), 5.98 (1H, s, CH), 6.65–7.50 (13H, m, Ph). ^{19}F NMR (470 MHz, $CDCl_3$) δ −63.76 (s, CF_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.45, 52.44, 57.37, 82.06, 88.05, 114.98, 111.84 (d, ^3J_F = 2.5 Hz), 117.88 (q, ^1J_F = 273.0 Hz), 127.05, 127.66, 128.33, 128.64, 128.78, 129.57, 130.09, 134.24, 138.58, 140.96, 144.01, 149.20 (d, ^2J_F = 39.0 Hz), 162.07. MS (ESI) m/z 515.1 $(M + 1)^+$. IR (KBr) 3032, 2953, 2921, 2854, 1717, 1668, 1516, 1440, 1346 cm^{-1}. Anal. Cacld for $C_{27}H_{22}ClF_3N_2O_3$: C 62.98, H 4.31, N 5.44; Found: C 61.81, H 4.28, N 5.61.

*4.3.9. Methyl cis-6-(4-chlorophenyl)-5-(4-methoxyphenyl)-3a-phenyl-2-(trifluoromethyl)-3a,4,5,6-tetrahydroimidazo[1,5-b]isoxazole-3-carboxylate (**3i**)*

White solid; mp: 59.3–61.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.71 (3H, s, CH_3O), 3.73 (3H, s, CH_3O), 4.12 (1H, d, J = 10.5 Hz, CH_2), 4.64 (1H, d, J = 10.5 Hz, CH_2), 5.84 (1H, s, CH), 6.71–7.53 (13H, m, Ph). ^{19}F NMR (470 MHz, $CDCl_3$) δ −63.71 (s, CF_3). ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.82, 56.27, 59.20, 81.91, 89.19, 112.18 (d, ^3J_F = 2.5 Hz), 115.30, 117.56, 118.22 (q, ^1J_F = 273.0 Hz), 127.34, 128.19, 128.68, 129.04, 129.89, 134.57, 139.03, 140.72, 141.60, 149.55 (d, ^2J_F = 39.0 Hz), 154.14, 162.45. MS (ESI) m/z 531.0 $(M + 1)^+$. IR (KBr) 3061, 3000, 2954, 2839, 1717, 1668, 1512, 1441, 1345 cm^{-1}. Anal. Cacld for $C_{27}H_{22}ClF_3N_2O_4$: C 61.08, H 4.18, N 5.28; Found: C 61.10, H 4.28, N 5.57.

*4.3.10. Methyl cis-2-(perfluoropropyl)-3a,6-diphenyl-5-p-tolyl-3a,4,5,6-tetrahydroimidazo[1,5-b]isoxazole-3-carboxylate (**3j**)*

White solid; mp: 98.1–100.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.22 (3H, s, CH_3), 3.64 (3H, s, CH_3O), 4.17 (1H, d, J = 10.5 Hz, CH_2), 4.83 (1H, d, J = 10.5 Hz, CH_2), 5.99 (1H, s, CH), 6.68–7.50 (14H, m, Ph). ^{19}F NMR (470 MHz, $CDCl_3$) δ −80.44 (q, J = 9.4 Hz, CF_3), −112.49 (m, CF_2), −125.65 (m, CF_2). ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.43, 52.26, 57.37, 82.32, 88.00, 108.54 (t–t, ^1J_F = 250.5 Hz, ^2J_F = 35.4 Hz), 114.49 (t–t, ^1J_F = 254.6 Hz, ^2J_F = 32.3 Hz), 114.91, 117.56 (q–t, ^1J_F = 275.8 Hz, ^2J_F = 30.8 Hz), 126.74, 127.56, 128.22, 128.49, 128.62, 128.71, 129.14, 129.64, 129,90, 137.04, 140.55, 143.82, 146.52 (d, ^2J_F = 29.4 Hz), 161.76. MS (ESI) m/z 603.2 $(M + Na)^+$. IR (KBr) 3031, 2951, 1710, 1656, 1520, 1443, 1333 cm^{-1}. Anal. Cacld for $C_{29}H_{23}F_7N_2O_3$: C 60.00, H 3.99, N 4.83; Found: C 60.27, H 4.25, N 5.02.

*4.3.11. Methyl cis-2-(perfluoropropyl)-3a-phenyl-5-p-tolyl-3a,4,5,6-tetrahydroimidazo[1,5-b]isoxazole-3-carboxylate (**3k**)*

White solid; mp: 104.6–108.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.27 (3H, s, CH_3), 3.50 (1H, d, J = 10.0 Hz, CH_2), 3.63 (3H, s, CH_3O), 4.15 (1H, d, J = 11.5 Hz, CH_2), 4.75 (1H, d, J = 10.0 Hz, CH_2), 5.03 (1H, d, J = 11.5, CH_2), 6.71–7.56 (9H, m, Ph). ^{19}F NMR (470 MHz, $CDCl_3$) δ −80.52 (t, J = 9.4, CF_3), −112.97 (m, CF_2), −125.92 (m, CF_2). ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.51, 52.13, 57.49, 76.12, 84.30, 108.39 (t–t, ^1J_F = 266.9 Hz, ^2J_F = 37.5 Hz), 110.38 (t–t, ^1J_F = 258.75 Hz, ^2J_F = 32.5 Hz), 114.17, 115.51, 117.70 (q–t, ^1J_F = 286.3 Hz, ^2J_F = 33.8 Hz), 127.12, 128.47, 128.61, 129.54, 130.05, 140.43, 143.85, 147.13 (t, ^2J_F = 28.8), 161.60. MS (ESI) m/z 505.1 $(M + 1)^+$. IR (KBr) 3065, 3007, 2959, 2847, 1708, 1655, 1521, 1445, 1334 cm^{-1}. Anal. Cacld for $C_{23}H_{19}F_7N_2O_3$: C 54.77, H 3.80, N 5.55; Found: C 54.84, H 3.71, N 5.53.

*4.3.12. Methyl cis-5-(4-methoxyphenyl)-2-(perfluoropropyl)-3a-phenyl-3a,4,5,6-tetrahydroimidazo[1,5-b]isoxazole-3-carboxylate (**3l**)*

White solid; mp: 86.5–88.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.45 (1H, d, J = 10.0, CH_2), 3.64 (3H, s, CH_3O), 3.75 (3H, s, CH_3O), 4.10 (1H, d, J = 11.0 Hz, CH_2), 4.73 (1H, d, J = 10.0 Hz, CH_2), 5.00 (1H, d, J = 11.0 Hz, CH_2), 6.77–7.55 (9H, m, Ph). ^{19}F NMR (470 MHz, $CDCl_3$) δ −80.53 (t, J = 9.4 Hz, CF_3), −112.16 (m, CF_2), −125.93 (m, CF_2). ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.12, 55.71, 58.09, 76.84, 84.39, 108.91 (t–t, ^1J_F = 258.8 Hz, ^2J_F = 32.5 Hz), 110.29 (t–t, ^1J_F = 258.8 Hz, ^2J_F = 32.5 Hz), 114.05, 114.96, 116.93, 117.69 (q–t, ^1J_F = 286.3 Hz, ^2J_F = 33.8 Hz), 127.12, 128.44, 128.59, 140.19, 140.51, 147.17 (t, ^2J_F = 28.75 Hz), 153.97, 161.60. MS (ESI) m/z 521.0 $(M + 1)^+$. IR (KBr) 3065, 3003, 2955, 2838, 1734, 1672, 1516, 1475, 1353 cm^{-1}. Anal. Cacld for $C_{23}H_{19}F_7N_2O_4$: C 53.08, H 4.03, N 5.73; Found: C 53.32, H 3.59, N 5.33.

*4.3.13. Methyl cis-2-(perfluoropropyl)-3a-phenyl-5,6-di-p-tolyl-3a,4,5,6-tetrahydroimidazo[1,5-b]isoxazole-3-carboxylate (**3m**)*

White solid; mp: 92.5–95.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.21 (3H, s, CH_3), 2.23 (3H, s, CH_3), 3.65 (3H, s, CH_3O), 4.17 (1H, d, J = 11.0 Hz, CH_2), 4.81 (1H, d, J = 11.0 Hz, CH_2), 5.95 (1H, s, CH), 6.68–7.71 (13H, m, Ph). ^{19}F NMR (470 MHz, $CDCl_3$) δ −80.44 (t, J = 9.4, CF_3), −112.11 (m, CF_2), −125.63 (m, CF_2). ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.44, 21.20, 52.25, 57.40, 82.17, 87.95, 108.59 (t–t, ^1J_F = 267.5 Hz, ^2J_F = 37.5 Hz), 110.39 (t–t, ^1J_F = 258.8 Hz, ^2J_F = 32.5 Hz), 114.86, 114.92, 117.68 (q–t, ^1J_F = 286.3 Hz, ^2J_F = 33.8 Hz), 126.74, 127.49, 128.18, 128.49, 128.64, 129.36, 129.87, 134.07, 138.39, 140.73, 143.87, 146.59 (t, ^2J_F = 28.8 Hz), 161.79. MS (ESI) m/z 595.1 $(M + 1)^+$. IR (KBr) 3031, 2953, 2862, 1716, 1655, 1517, 1440, 1329 cm^{-1}. Anal. Cacld for $C_{30}H_{25}F_7N_2O_3$: C 60.61, H 4.24, N 4.71; Found: C 60.88, H 4.58, N 4.62.

*4.3.14. Methyl cis-6-(4-chlorophenyl)-2-(perfluoropropyl)-3a-phenyl-5-p-tolyl-3a,4,5,6-tetrahydroimidazo[1,5-b]isoxazole-3-carboxylate (**3n**)*

White solid; mp: 70.3–73.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.22 (3H, s, CH_3), 3.64 (3H, s, CH_3O), 4.13 (1H, d, J = 11.0 Hz, CH_2), 4.83 (1H, d, J = 11.0 Hz, CH_2), 5.97 (1H, s, CH), 6.67–7.50 (13H, m, Ph). ^{19}F NMR (470 MHz, $CDCl_3$) δ −80.45 (t, J = 9.4 Hz, CF_3), −113.68 (m,

CF_2), −125.67 (m, CF_2). ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.39, 52.26, 57.35, 82.40, 87.49, 108.08 (t–t, ^1J_F = 243.8 Hz, ^2J_F = 38.8 Hz), 110.33 (t–t, ^1J_F = 258.8 Hz, ^2J_F = 32.5 Hz), 114.97, 117.71 (q–t, ^1J_F = 270.0 Hz, ^2J_F = 32.5 Hz), 126.68, 128.34, 128.57, 128.83, 128.98, 129.11, 129.71, 129.97, 134.50, 135.63, 140.34, 143.64, 146.32 (t, ^2J_F = 29.38 Hz), 161.64. MS (ESI) *m/z* 615.0 $(M + 1)^+$. IR (KBr) 3062, 3032, 2953, 2858, 1716, 1657, 1517, 1441, 1330 cm^{-1}. Anal. Cacld for $C_{29}H_{22}ClF_7N_2O_3$: C 56.64, H 3.61, N 4.56; Found: C 56.87, H 3.85, N 4.21.

*4.3.15. Methyl cis-6-(4-chlorophenyl)-5-(4-methoxyphenyl)-2-(perfluoropropyl)-3a-phenyl-3a,4,5,6-tetrahydroimidazo[1,5-b]isoxazole-3-carboxylate (**3o**)*

White solid; mp: 64.3–66.7 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 3.65 (3H, s, CH_3O), 3.68 (3H, s, CH_3O), 4.16 (1H, d, *J* = 11.5 Hz, CH_2), 4.70 (1H, d, *J* = 11.5 Hz, CH_2), 5.82 (1H, s, CH), 6.71–7.52 (13H. m, Ph). ^{19}F NMR (470 MHz, $CDCl_3$) δ −80.44 (t, *J* = 9.4 Hz, CF_3), −112.14 (m, CF_2), −125.68 (m, CF_2). ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.26, 55.55, 58.88, 81.94, 88.34, 108.06 (t–t, ^1J_F = 243.8 Hz, ^2J_F = 38.8 Hz), 110.33 (t–t, ^1J_F = 258.8 Hz, ^2J_F = 32.5 Hz), 117.43, 117.50 (q–t, ^1J_F = 292.5 Hz, ^2J_F = 31.9 Hz), 126.59, 127.12, 128.31, 128.60, 128.79, 129.16, 130.76, 134.56, 135.61, 139.85, 140.68, 146.32 (t, ^2J_F = 30.0 Hz), 154.02, 161.64. MS (ESI) *m/z* 631.0 $(M + 1)^+$. IR (KBr) 3061, 3000, 2954, 2837, 1716, 1658, 1512, 1441, 1330 cm^{-1}. Anal. Cacld for $C_{29}H_{22}ClF_7N_2O_4$: C 55.21, H 3.51, N 4.44; Found: C 55.59, H 3.77, N 4.26.

*4.3.16. Methyl cis-6-(4-nitrophenyl)-2-(perfluoropropyl)-3a-phenyl-5-p-tolyl-3a,4,5,6-tetrahydroimidazo[1,5-b]isoxazole-3-carboxylate (**3p**)*

Yellow solid; mp: 79.5–81.3 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 2.24 (3H, s, CH_3), 3.68 (3H, s, CH_3O), 4.14 (1H, d, *J* = 11.5 Hz, CH_2), 4.86 (1H, d, *J* = 11.5 Hz, CH_2), 6.08 (1H, s, CH), 6.68–8.07 (13H, m, Ph). ^{19}F NMR (470 MHz, $CDCl_3$) δ −80.47 (t, *J* = 10.0 Hz, CF_3), −114.29 (m, CF_2), −125.77 (m, CF_2). ^{13}C NMR (125 MHz, $CDCl_3$) δ 20.43, 52.40, 57.38, 83.65, 87.26, 108.23 (t–t, ^1J_F = 258.5 Hz, ^2J_F = 35.5 Hz), 110.26 (t–t, ^1J_F = 258.8 Hz, ^2J_F = 32.5 Hz), 114.98, 117.60 (q–t, ^1J_F = 285.0 Hz, ^2J_F = 31.3 Hz), 123.82, 126.63, 126.99, 128.54, 128.59, 128.66, 129.65, 130.12, 139.87, 143.31, 144.38, 146.15 (t, ^2J_F = 30.0 Hz), 148.12, 161.48. MS (ESI) *m/z* 626.0 $(M + 1)^+$. IR (KBr) 3035, 2960, 2854, 1734, 1660, 1523, 1442, 1349 cm^{-1}. Anal. Cacld for $C_{29}H_{22}F_7N_3O_5$: C 55.69, H 3.55, N 6.72; Found: C 55.49, H 3.50, N 6.47.

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References

[1] (a) K. Burger, U. Wucherpfenning, E. Brunner, Adv. Heterocycl. Chem. 60 (1994) 1–64;
(b) R. Filler, in: R.E. Banks (Ed.), Organofluorine Chemicals and Their Industrial Applications, Ellis Horwood, Chichester, 1979;
(c) R. Filler, Y. Kobayashi, Biomedical Aspects of Fluorine Chemistry, Kodansha & Elsevier Biomedical, Tokyo, 1982;
(d) J.T. Welch, Tetrahedron 43 (1987) 3123–3197;
(e) R. Filler, Y. Kobayashi, L.M. Yagupolskii, Organofluorine Compounds in Medicinal Chemistry and Biomedical Applications, Elsevier, Amsterdam, 1993.

[2] (a) R.E. Banks, B.E. Smart, J.C. Tatlow, Organofluorine Chemistry, Principles and Commercial Applications, Plenum Press, New York, 1994;
(b) G.G. Furin, in: O.A. Attanasi, D. Spinelli (Eds.), Targets in Heterocyclic Systems, vol. 2, Societa Chimica Italiana, Roma, 1998, pp. 355–441;
(c) S. Zhu, Y. Wang, W. Peng, L. Song, G. Jin, Curr. Org. Chem. 6 (2002) 1057–1096;
(d) Y.V. Burgart, V.I. Saloutin, O. Chupakhin, Heterocycles 69 (2006) 593–620;
(e) K. Burger, L. Hennig, J. Spengler, F. Albericio, Heterocycles 69 (2006) 569–592;
(f) A. Pace, I. Pibiri, S. Buscemi, N. Vivona, L. Malpezzi, J. Org. Chem. 69 (2004) 4108–4115;
(g) V. Petrov, W. Marshall, J. Fluorine Chem. 128 (2007) 729–735;
(h) K.A. Khistiaey, M.S. Novikov, A.F. Khlebnikov, J. Magull, Tetrahedron Lett. 49 (2008) 1237–1240;
(i) G.G. Furin, Chem. Heterocycl. Compd. 42 (2006) 285–319.

[3] (a) K.V. Gothelf, K.A. Jorgensen, Chem. Commun. 16 (2000) 1449–1458;
(b) R.F. Jones, J.N. Martin, Chemistry of Heterocyclic Compounds, vol. 59, John Wiley & Sons Ltd., 2002, pp. 1–81;
(c) K. Rueck-Braun, T.E. Freysoldt, F. Wierschem, Chem. Soc. Rev. 34 (2005) 507–516;
(d) P.C.R. Pedro Merino, Chimie 8 (2005) 775–788;
(e) H. Pellissier, Tetrahedron 63 (2007) 3235–3285;
(f) V. Nair, T.D. Suja, Tetrahedron 63 (2007) 12247–12275;
(g) J. Revuelta, S. Cicchi, A. Goti, A. Brandi, Synthesis (2007) 485–504.

[4] (a) V. Jäger, P.A. Colinas, in: A. Padwa, W.H. Pearson (Eds.), Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry Toward Heterocycles and Natural Products, Wiley, New Jersey, 2003, p. 416;
(b) M. Frederickson, Tetrahedron 53 (1997) 403–425;
(c) U. Chiacchio, A. Rescifina, G. Romeo, in: O.A. Attanasi, D. Spinelli (Eds.), Targets in Heterocyclic Systems, vol. 1, Italian Society of Chemistry, Rome, 1997, p. 225;
(d) K.B.G. Torssell, Nitrile Oxides Nitrones and Nitronates in Organic Synthesis, VCH, Weinheim, 1988;
(e) A. Padwa, W.H. Pearson (Eds.), The Chemistry of Heterocyclic Compounds, Vol. 59, Synthetic Applications of 1,3-Dipolar Cycloaddition Chemistry, Wiley, New York, 2002.

[5] (a) N. Coskun, B. Yilmaz, Syn. Commun. 34 (2004) 1617–1623;
(b) N. Coskun, F. Tirli Tat, O. Ozel Guven, Tetrahedron 57 (2001) 3413–3417;
(c) M. Nishiuchi, H. Sato, N. Umemoto, S. Murakami, Chem. Lett. 37 (2008) 146–147;
(d) M. Lager, P. Dietrich, D. Weinrich, K. Rueck-Braun, Heterocycles 74 (2007) 743–761;
(e) E. Coutouli-Argyropoulou, C. Xatzis, N.G. Argyropoulos, Nucleos. Nucleot. Nucl. Acids 27 (2008) 84–100;
(f) F. Machetti, L. Cecchi, E. Trogu, F. De Sarlo, Eur. J. Org. Chem. 26 (2007) 4352–4359;
(g) C. Pillard, V. Desvergnes, S. Py, Tetrahedron Lett. 48 (2007) 6209–6213.

[6] For some examples, see:
(a) K. Funabiki, T. Ishihar, H. Yamanak, J. Fluorine Chem. 71 (1995) 5–7;
(b) W.V. Murray, D. Francois, A. Maden, I. Turchi, J. Org. Chem. 72 (2007) 3097–3099;
(c) S.A. Popov, N.V. Chukanov, G.V. Romanenko, T.V. Rybalova, Y.V. Gatilov, V.A. Reznikov, J. Heterocycl. Chem. 43 (2006) 277–291;
(d) Y. Shen, J. Zheng, Y. Huang, Synthesis (1985) 970–971;
(e) J.P. Bégué, D. Bonnet-Delpon, T. Lequeux, Tetrahedron Lett. 34 (1993) 3279–3282;
(f) S. Man, M. Nečas, J.-P. Bouillon, H. Baillia, D. Harakat, M. Potáček, Tetrahedron 61 (2005) 2387–2393;
(g) S.J. Coats, J.S. Link, D. Gauthier, D.J. Hlasta, Org. Lett. 7 (2005) 1469–1472;
(h) P. He, S. Zhu, Mini-Rev. Org. Chem. 1 (2004) 417–435.

[7] (a) N.A. LeBel, J.J. Whang, J. Am. Chem. Soc. 81 (1959) 6334–6335;
(b) N. Coskun, D. Sűmengen, Syn. Commun. 23 (1993) 1699–1706;
(c) N. Coskun, O. Asutay, Chim. Acta Turc 25 (1997) 69–72;
(d) N. Coskun, O. Asutay, Chim. Acta Turc 27 (1999) 17–23.

[8] (a) B.C. Hamper, Org. Synth. 70 (1992) 246–255;
(b) O. Jeannin, M. Fourmigué, Chem. Eur. J. 12 (2006) 2994–3005.

[9] (a) K.V. Gothelf, K.A. Jørgensen, Chem. Rev. 98 (1998) 863–909;
(b) Y. Tomioka, C. Nagahiro, Y. Nomura, H. Maruoka, J. Heterocycl. Chem. 40 (2003) 121–127;
(c) F. Heaney, J. Fenlon, C. O'Mahony, P. McArdle, D. Cunningham, J. Chem. Soc., Perkin Trans. 1 (24) (2001) 3382–3392.

[10] CCDC-651153 (3a) contains all crystallographic details of this publication and is available free of charge at www.ccdc.cam.ac.uk/consts/retrieving.html or can be ordered from the following address: Cambridge Crystallographic Data Centre, 12 Union Road, GB-Cambridge CB21EZ; Fax: +44 1223 336 033 or deposit@ccdc.cam.ac.uk.;
Unit cell parameters (**3a**): a: 10.8599 Å; b: 10.9551 Å; c: 11.3368 Å; alpha: 90.300; beta: 110.034; gamma: 106.2780; space group: P-1.