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Scope and regioselectivity of the 1,3-dipolar cycloaddition of azides with methyl 2-perfluoroalkynoates for an easy, metal-free route to perfluoroalkylated 1,2,3-triazoles

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ABSTRACT

1,3-Dipolar cycloadditions of methyl 2-perfluoroalkynoates with various azides have been examined, leading to a simple metal-free synthetic protocol for the synthesis of perfluoroalkylated 1,2,3-triazoles. The regiochemical results demonstrated that the cycloaddition was controlled by FMO (the frontier molecular obitals) interaction and steric hindrance in transition states.

1. Introduction

1,2,3-Triazoles are an important class of heterocyclic compounds due to their wide range of applications including uses as building blocks for pharmaceutical agents, agrochemicals, industrial dyes, corrosion inhibition agents (of copper and copper alloys), photostabilizers, and photographic materials [1]. The most widely used method for synthesis of 1,2,3-triazoles is the 1,3-dipolar cycloaddition of organic azides with alkynes pioneered by Huisgen [2]. This method became especially popular after it was found to proceed regioselectively with a base and with copper (I) as a catalyst, yielding 1,4-disubstituted 1,2,3-triazoles [3]. In contrast, 1,5-disubstituted 1,2,3-triazoles can be formed regioselectively from alkynes and azides using a Ru (II) catalyst [4].

Although azide–alkyne cycloadditions are relevant for biological applications and azide–alkyne chemistry constitutes an interesting chemoselective platform for the functionalization or ligation of biological systems, the published methods for regioselective triazole ligations, both for the 1,4- and 1,5-isomers, rely on the use of heavy metal salts, thus limiting applications in the presence of living cells [5]. Therefore, the development of a metal-free method was considered as highly attractive target [6].

Since it is well known that the introduction of polyfluoroalkyl groups into organic molecules can bring about remarkable changes in the properties of the derived fluorinated compounds [7], and that alkynes with an electron-withdrawing functional group favour the traditional irreversible Huisgen cycloaddition [8], herein we report a facile and metal-free route for the introduction of polyfluoroalkyl groups into triazole rings by carrying out 1,3-dipolar cycloaddition between electron-deficient alkynes (methyl 2-perfluoroalkynoates) and a variety of substituted azides. The regioselectivity of the reaction was also investigated, as research on the regioselectivities of the dipolar cycloadditions using perfluoroalkylated internal alkynes has been limited [4b].

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Table 1
Metal-free synthesis of perfluoroalkyl-substituted 1,2,3-triazoles.[a]

Entry	Perfluorinated alkyne	Azide	*T* (°C)	Time (h)	Ratio of (**3**:**4**)[c]		Yield (%)[b]
1	**1a**	**2a**	25	16	**3aa:4aa**	1:0.7	91
2	**1a**	**2b**	25	16	**3ab:4ab**	1:0.6	87
3	**1a**	**2c**	25	16	**3ac:4ac**	1:0.8	92
4	**1a**	**2d**	25	16	**3ad:4ad**	1:0.8	90
5	**1a**	**2e**	25	16	**3ae:4ae**	1:0.8	85
6	**1a**	**2f**	25	16	**3af:4af**	1:0.7	84
7	**1b**	**2c**	25	16	**3bc:4bc**	1:0.9	82
8	**1b**	**2d**	25	16	**3bd:4bd**	1:1.0	80
9	**1c**	**2c**	25	16	**3cc:4cc**	1:1.2	83
10	**1c**	**2d**	25	16	**3cd:4cd**	1:1.3	81
11	**1a**	**2g**	25	16		1:1.8	15
12	**1a**	**2g**	25	40	**3ag:4ag**	1:2.0	24
13	**1a**	**2g**	80	16		1:2.5	70
14	**1a**	**2h**	80	16	**3ah:4ah**	1:2.1	85
15	**1a**	**2i**	80	16	**3ai:4ai**	1:2.2	88
16	**1a**	**2j**	80	16	**3aj:4aj**	1:2.3	89
17	**1a**	**2k**	80	16	**3ak:4ak**	1:2.4	86
18	**1a**	**2l**	80	16	**3al:4al**	1:1.9	87
19	**1a**	**2m**	80	16	**3am:4am**	1:2.3	74
20	**1a**	**2n**	80	16	**3an:4an**	1:2.1	78
21	**1b**	**2j**	80	16	**3bj:4bj**	1:2.6	92
22	**1b**	**2k**	80	16	**3bk:4bk**	1:2.7	80
23	**1c**	**2j**	80	16	**3cj:4cj**	1:3.0	85
24	**1c**	**2k**	80	16	**3ck:4ck**	1:3.1	85

[a] Reaction conditions: methyl 2-perfluoroalkynoate **1** 1.1 mmol, azide **2** 1.0 mmol, ^{t}BuOH 1 mL.
[b] Isolated yields.
[c] The ratio of **3**:**4** was determined by the isolated yields of **3** and **4** respectively.

2. Results and discussion

Our initial studies were focused on the reaction of methyl 2-trifluoromethylalkynoate **1a** with benzyl azide **2a**. Under metal-free conditions, the reaction proceeded smoothly at room temperature after 16 h in ^{t}BuOH to give a mixture of regioisomers **3aa** and **4aa** in 91% isolated yield with a ratio of **3aa**:**4aa** = 1:0.7. Further investigation of this transformation revealed that the electronic effect of the substituted groups on the aromatic ring in these benzyl azides was not apparent (Table 1, entries 2–10). Both the electron-rich and the electron-deficient azides **2a**–**f** provided the desired products in good to excellent yields.

Our next attempt at cycloaddition of the internal alkyne **1** with aryl azide was carried out by mixing compound **1a** with *p*-nitrophenyl azide **2g** under the same conditions. The starting material was consumed slowly at room temperature even at the prolonged time (Table 1, entries 11 and 12). Increasing the reaction temperature to 80 °C resulted in the completion of the reaction and the products **3ag** and **4ag** were obtained in total 70% yield in a ratio of **3ag**:**4ag** = 1:2.5 (Table 1, entry 13). It was observed that aryl azides with either an electron-donating substituent, such as methyl, methoxyl or an electron-withdrawing group including halogens and cyano could perform efficiently with good to excellent yields (Table 1, entries 11–24).

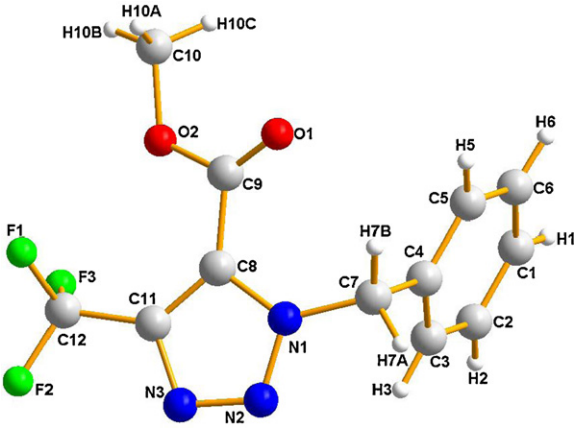


Fig. 1. The crystal structure of **4aa**.

The regiochemistry of **4aa** and **3ai** was determined as 1,5- and 1,4-regioisomers respectively, by X-ray crystallography (Figs. 1 and 2) [9]. Furthermore, the ^{19}F NMR spectra of **4aa** showed the signal of fluorine atoms of polyfluoroalkyl in the α-position to the triazolyl group at higher field (−61.12 ppm, s, CF_3) than those of **3ai** (−55.79 ppm, s, CF_3) and **3aa** (−56.61 ppm, s, CF_3). The ^{19}F NMR spectra of other compounds manifested themselves in a similar manner, such as the regioisomers **4ae** (−61.14 ppm, s, CF_3) and **3ae** (−56.63 ppm, s, CF_3) or **4cj** (−126.05 to −126.00 ppm, m, CF_2) and **3cj** (−123.76 to −123.71 ppm, m, CF_2).

The ratio of 1,4- and 1,5-regioisomers depended to a small extent on the chain length of the perfluoroalkyl group. Larger substituent resulted in a higher ratio of 1,5-regioisomer **4**. It is noteworthy that compound **4** predominated in the reaction of **1c** with **2c** or **2d** (Table 1, entries 9 and 10), and in all the reactions of methyl 2-perfluoroalkynoates **1** with aryl azides (see Scheme 1).

According to previous work on the mechanism of 1,3-dipolar cycloaddition [10], the Huisgen cycloaddition occurs by a concerted process. If steric effects are insignificant, the regiochemistry of the reaction is determined by which pair of frontier orbitals is used. In the case of azides, reactions with electron-deficient dipolarophiles are $HOMO_{dipole}$–$LUMO_{alkyne}$ controlled and in the majority of cases, electrophilic attack occurs at the substituted nitrogen atom in the azido group of the azide to afford the major product as 1,4-regioisomer [10a]. In these reactions, the azide is the donor and the electron-deficient alkyne is the acceptor of electrons.

With respect to the cycloaddition of azides with methyl 2-perfluoroalkynoates, two regioisomers were obtained and regioselectivity was observed favouring the formation of one cycloadduct over the other. This lack of absolute regioselectivity is a direct result of the low-lying unoccupied molecular orbitals of the C–C triple bond and hence leads to the reaction being controlled by both dipole HOMO and dipole LUMO interactions simultaneously (Scheme 2). However, for aryl azides, the aryl group is a π-acceptor

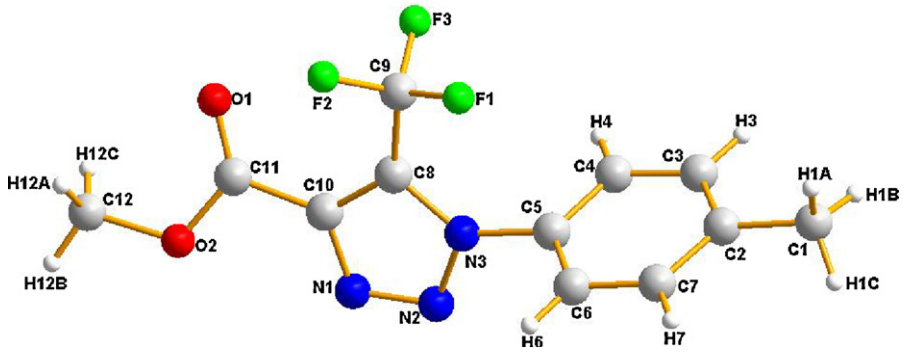
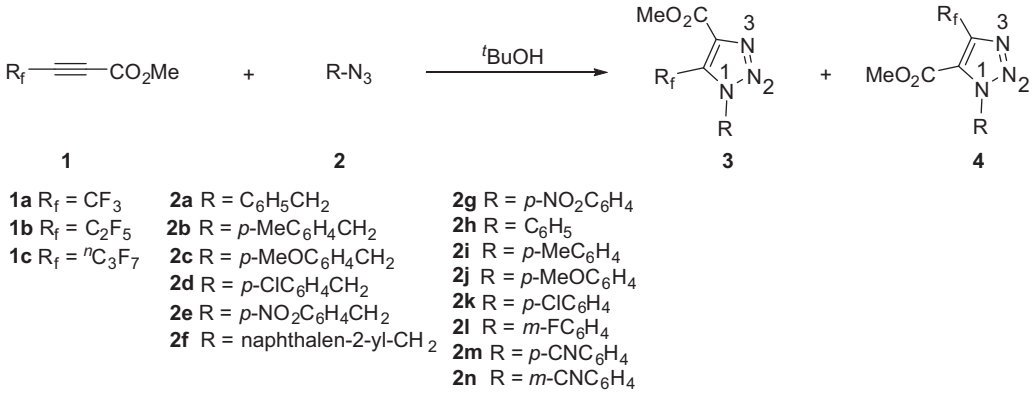


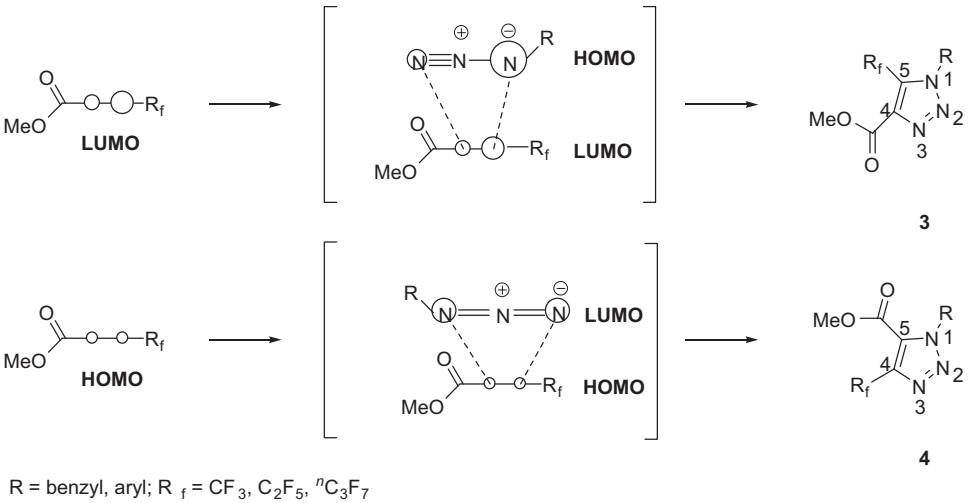
Fig. 2. The crystal structure of **3ai**.

that lowers the energy levels of the frontier orbitals of HOMO and LUMO in comparision with that of benzyl azides. These decrease the contribution of the interaction $HOMO_{azide}$–$LUMO_{alkyne}$ and make more favourable the interaction $LUMO_{azide}$–$HOMO_{alkyne}$. This generates the higher regioselectivity of the aryl azides–methyl 2-perfluoroalkynoates system. Thus, in all reactions of methyl 2-perfluoroalkynoates **1** with aryl azides, 1,5-regioisomer **4** as the major product was formed (Table 1, entries 13–24). Since azide is an electron donor, the strengthening of the donor properties of substituents in azide is accompanied by the increase of the cycloaddition rate, and therefore, the cycloaddition of substituted or unsubstituted benzyl azide proceeds at room temperature and aryl azide at an elevated temperature as 80 °C.

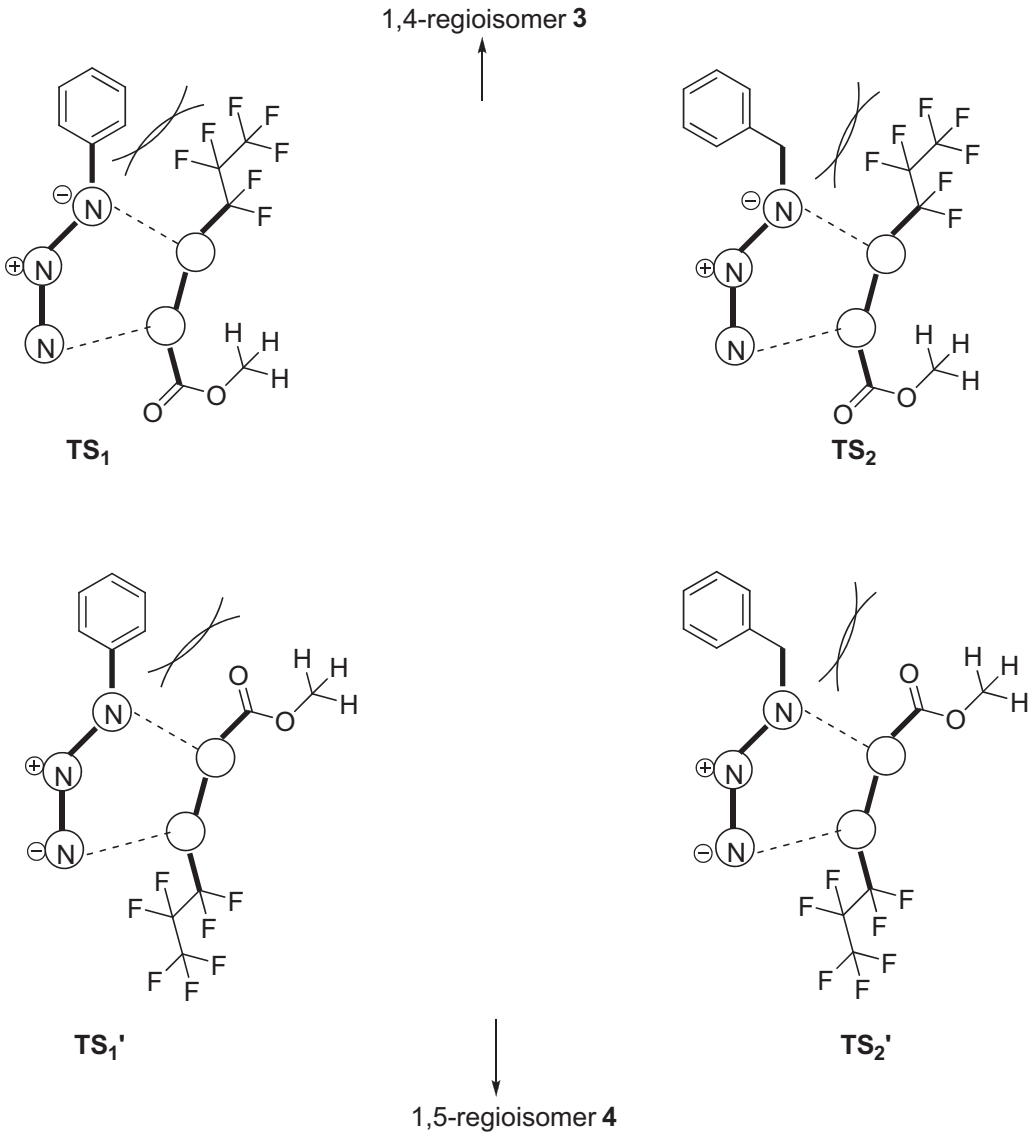
Steric interactions had a slight effect on the ratio of 1,4- and 1,5-regioisomers (Scheme 3) [10c]. As an example, for the transition states of cycloaddition of methyl 4,4,5,5,6,6,6-heptafluorohex-2-ynoate **1c** with phenyl azide **TS$_1$** and **TS$_1$′**, the steric interaction is more significant in **TS$_1$** than that in **TS$_1$′** due to a larger steric repulsion between the aromatic ring and the perfluoroalkyl group on neighbouring atoms, thus giving a triazole mixture with a higher ratio of 1,5-regioisomer **4**. Moreover, with the size of perfluroalkyl group increasing, the ratio of compound **4** increased in a mixture of trizaoles since the alkynoate prefers to approach the dipole from the less sterically hindered side. However, as an another example, although there was unfavorable steric interaction in the transition states of cycloaddition of alkynoate **1c** with



Scheme 1. Synthesis of perfluoroalkyl-substituted 1,2,3-triazoles.



Scheme 2. Formation of product **3** and **4**.



Scheme 3. Sterichindric approach diagram.

benzyl azide, **TS$_2$** is slightly over that in **TS$_2$**′ and 1,4-regioisomer **3** predominates in the reactions of benzyl azides due to the domination of the frontier molecular orbitals.

3. Conclusion

We have shown that the metal-free 1,3-dipolar cycloaddition of electron-deficient internal alkynes (methyl 2-perfluoroalkynoates) with azides is a general process. These cycloadditions proceed under mild conditions, affording perfluoroalkylated 1,2,3-triazoles in good to excellent yields. The regiochemistry of the reactions is determined by the combination of the dominant FMO (frontier molecular orbitals) interaction of substrates with steric interactions between perfluoroalkyl group and aryl or benzyl group in the transition states.

4. Experimental

4.1. General

Methyl 2-perfluoroalkynoates [11] and azides [12,13] were synthesized according to the known procedures. Other 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: $CFCl_3$ 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 analyses were 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 perpration of perfluoroalkylated 1,2,3-triazoles **3** and **4**

To the solution of aryl or benzyl azides (1.0 mmol) in ^{t}BuOH (1 mL), methyl 2-perfluoroalkynoate (1.1 mmol) was added and the mixture was stirred at 80 °C or room temperature for the defined time. After the completion of the reaction, the products were purified by preparative TLC (elutent:petroleum ether (60–90 °C)/ethyl acetate) and recrystallized from ethyl acetate and petroleum ether (60–90 °C) to give pure products **3** and **4**.

*4.2.1. Methyl 1-benzyl-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylate (**3aa**) [14]*

White solid; mp: 40.2–41.0 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.94 (s, 3H, OCH_3), 5.94 (s, 2H, CH_2), 7.33–7.37 (m, 5H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −56.61 (s, CF_3) ppm. MS (EI) m/z 270 (M^+).

*4.2.2. Methyl 3-benzyl-5-(trifluoromethyl)-3H-1,2,3-triazole-4-carboxylate (**4aa**) [14]*

White solid; mp: 63.0–63.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.97 (s, 3H, OCH_3), 5.76 (s, 2H, CH_2), 7.20–7.35 (m, 5H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −61.12 (s, CF_3) ppm. MS (EI) m/z 270 (M^+).

*4.2.3. Methyl 1-(4-methylbenzyl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylate (**3ab**)*

White solid; mp: 37.4–39.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.32 (s, 3H, CH_3), 3.97 (s, 3H, OCH_3), 5.72 (s, 2H, CH_2), 7.12 (d, J = 8.5 Hz, 2H, ArH), 7.20 (d, J = 8.5 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −56.60 (s, CF_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.13, 52.88, 54.92, 55.28, 114.26, 119.16 (q, $^1J_{F-C}$ = 268.75 Hz), 128.66 (q, $^2J_{F-C}$ = 42.5 Hz), 129.83, 130.37, 139.05, 159.42 ppm. MS (EI) m/z 299 (M^+). IR (KBr) 3038, 2956, 1744, 1470, 1354, 818 cm^{-1}. Anal. Calcd. for $C_{13}H_{12}F_3N_3O_2$: C, 52.18; H, 4.04; N, 14.04. Found: C, 52.37; H, 4.03; N, 14.12.

*4.2.4. Methyl 3-(4-methylbenzyl)-5-(trifluoromethyl)-3H-1,2,3-triazole-4-carboxylate (**4ab**)*

White solid; mp: 68.5–69.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.35 (s, 3H, CH_3), 3.97 (s, 3H, OCH_3), 5.92 (s, 2H, CH_2), 7.18 (d, J = 8.0 Hz, 2H, ArH), 7.27 (d, J = 8.0 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −61.10 (s, CF_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.24, 53.36, 54.24, 119.95 (q, $^1J_{F-C}$ = 267.5 Hz), 126.33, 128.32, 129.71, 131.07, 138.96, 140.01 (q, $^2J_{F-C}$ = 39.2 Hz), 157.47 ppm. MS (EI) m/z 299 (M^+). IR (KBr) 3030, 2959, 1739, 1470, 1374, 815 cm^{-1}. Anal. Calcd. for $C_{13}H_{12}F_3N_3O_2$: C, 52.18; H, 4.04; N, 14.04. Found: C, 52.35; H, 4.01; N, 14.07.

*4.2.5. Methyl 1-(4-methoxybenzyl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylate (**3ac**) [15]*

White solid; mp: 77.4–78.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.75 (s, 3H, OCH_3), 3.94 (s, 3H, OCH_3), 5.66 (s, 2H, CH_2), 6.83 (d, J = 9.0 Hz, 2H, ArH), 7.17 (d, J = 9.0 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −56.63 (s, CF_3) ppm. MS (EI) m/z 315 (M^+).

*4.2.6. Methyl 1-(4-methoxybenzyl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylate (**4ac**) [16]*

White solid; mp: 113.6–115.1 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.78 (s, 3H, OCH_3), 3.95 (s, 3H, OCH_3), 5.86 (s, 2H, CH_2), 6.85 (d, J = 8.5 Hz, 2H, ArH), 7.31 (d, J = 8.5 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −61.10 (s, CF_3) ppm. MS (EI) m/z 315 (M^+).

*4.2.7. Methyl 1-(4-chlorobenzyl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylate (**3ad**)*

White solid; mp: 44.4–45.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.94 (s, 3H, OCH_3), 5.71 (s, 2H, CH_2), 7.14 (d, J = 8.5 Hz, 2H, ArH), 7.30 (d, J = 8.5 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −56.65 (s, CF_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.98, 54.36, 119.10 (q, $^1J_{C-F}$ = 268.75 Hz), 128.67 (q, $^2J_{C-F}$ = 41.25 Hz), 129.09, 129.38, 131.79, 135.22, 139.48, 159.28 ppm. MS (EI) m/z 319 (M^+). IR (KBr) 3009, 2957, 1744, 1474, 1357, 814 cm^{-1}. Anal. Calcd. for $C_{12}H_9ClF_3N_3O_2$: C, 45.09; H, 2.84; N, 13.14. Found: C, 45.12; H, 2.82; N, 13.16.

*4.2.8. Methyl 3-(4-nitrobenzyl)-5-(trifluoromethyl)-3H-1,2,3-triazole-4-carboxylate (**4ad**)*

White solid; mp: 67.1–67.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.95 (s, 3H, OCH_3), 5.89 (s, 2H, CH_2), 7.28–7.32 (m, 4H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −61.13 (s, CF_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.48, 53.69, 119.85 (q, $^1J_{C-F}$ = 267.5 Hz), 126.31 (q, $^3J_{C-F}$ = 2.5 Hz), 129.26, 129.85, 132.42, 135.08, 140.08 (q, $^2J_{C-F}$ = 39.58 Hz), 157.41 ppm. MS (EI) m/z 319 (M^+). IR (KBr) 3018, 2962, 1736, 1475, 1377, 832 cm^{-1}. Anal. Calcd. for $C_{12}H_9ClF_3N_3O_2$: C, 45.09; H, 2.84; N, 13.14. Found: C, 45.11; H, 2.81; N, 13.17.

*4.2.9. Methyl 1-(4-nitrobenzyl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylate (**3ae**)*

White solid; mp: 101.2–102.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.95 (s, 3H, OCH_3), 5.88 (s, 2H, CH_2), 7.37 (d, J = 8.5 Hz, 2H, ArH), 8.19 (d, J = 8.5 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −56.63 (s, CF_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.09, 54.08, 119.02 (q, $^1J_{C-F}$ = 270 Hz), 124.39, 128.42, 128.92 (q, $^2J_{C-F}$ = 45 Hz), 139.64, 140.13, 148.30, 159.12 ppm. MS (EI) m/z 330 (M^+). IR (KBr) 3020, 2964, 1740, 1531, 1479, 1347, 1321, 825 cm^{-1}. Anal. Calcd. for $C_{12}H_9F_3N_4O_4$: C, 43.65; H, 2.75; N, 16.97. Found: C, 43.84; H, 2.73; N, 16.91.

*4.2.10. Methyl 3-(4-nitrobenzyl)-5-(trifluoromethyl)-3H-1,2,3-triazole-4-carboxylate (**4ae**)*

White solid; mp: 114.9–115.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.95 (s, 3H, OCH_3), 6.03 (s, 2H, CH_2), 7.51 (d, J = 8.5 Hz, 2H, ArH), 8.19 (d, J = 8.5 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −61.14 (s, CF_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.51, 53.65, 119.74 (q, $^1J_{C-F}$ = 268 Hz), 124.26, 126.49 (d, $^3J_{C-F}$ = 2.5 Hz), 129.26, 140.17 (q, $^2J_{C-F}$ = 39.2 Hz), 140.70, 148.24, 157.33 ppm. MS (EI) m/z 330 (M^+). IR (KBr) 3026, 2966, 1741, 1522, 1473, 1351, 1329, 825 cm^{-1}. Anal. Calcd. for $C_{12}H_9F_3N_4O_4$: C, 43.65; H, 2.75; N, 16.97. Found: C, 43.82; H, 2.74; N, 16.92.

*4.2.11. Methyl 5-(trifluoromethyl)-1-((naphthalen-2-yl)methyl)-1H-1,2,3-triazole-4-carboxylate (**3af**)*

Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.97 (s, 3H, OCH_3), 5.90 (s, 2H, CH_2), 7.31 (d, J = 8.5 Hz, 1H, ArH), 7.47–7.50 (m, 2H, ArH), 7.65 (s, 1H, ArH), 7.78–7.82 (m, 3H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −56.58 (s, CF_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.94, 55.23, 60.41, 119.17 (q, $^1J_{C-F}$ = 269.2 Hz), 124.48, 126.84, 126.92, 127.80, 128.06, 128.86 (q, $^2J_{C-F}$ = 42.5 Hz), 129.17, 130.68, 133.10, 133.26, 139.44, 159.39 ppm. MS (EI) m/z 335 (M^+). IR (KBr) 3027, 2956, 1745, 1473, 1353 cm^{-1}. Anal. Calcd. for $C_{16}H_{12}F_3N_3O_2$: C, 57.32; H, 3.61; N, 12.53. Found: C, 57.22; H, 3.60; N, 12.52.

*4.2.12. Methyl 5-(trifluoromethyl)-1-((naphthalen-2-yl)methyl)-3H-1,2,3-triazole-4-carboxylate (**4af**)*

Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.93 (s, 3H, OCH_3), 6.09 (s, 2H, CH_2), 7.45 (d, J = 8.5 Hz, 1H, ArH), 7.49–7.52 (m, 2H, ArH), 7.81–7.84 (m, 4H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −61.02 (s, CF_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.38, 54.57, 60.48, 119.93 (q, $^1J_{C-F}$ = 269.2 Hz), 125.42, 126.46 (q, $^3J_{C-F}$ = 1.25 Hz), 126.75, 126.85, 127.78, 127.82, 128.15, 128.99, 131.35, 133.17, 140.05 (q, $^2J_{C-F}$ = 39.58 Hz), 157.41 ppm. MS (EI) m/z 335 (M^+). IR (KBr) 3027, 2958, 1740, 1469, 1373 cm^{-1}. Anal. Calcd. for $C_{16}H_{12}F_3N_3O_2$: C, 57.32; H, 3.61; N, 12.53. Found: C, 57.45; H, 3.59; N, 12.49.

*4.2.13. Methyl 1-(4-methoxybenzyl)-5-(pentafluoroethyl)-1H-1,2,3-triazole-4-carboxylate (**3bc**)*

White solid; mp: 40.9–42.5 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.76 (s, 3H, OCH_3), 3.94 (s, 3H, OCH_3), 5.62 (s, 2H, CH_2), 6.84 (d, J = 8.5 Hz, 2H, ArH), 7.21 (d, J = 8.5 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −83.63 (t, J = 4.7 Hz, CF_3), −108.57 to −108.54 (m, CF_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.93, 54.91 (t, $^3J_{C-F}$ = 2.5 Hz), 55.34, 111.49 (tq, $^1J_{C-F}$ = 285.83 Hz, $^2J_{C-F}$ = 41.39 Hz), 114.36, 118.26 (qt, $^1J_{C-F}$ = 303.75 Hz, $^2J_{C-F}$ = 37.19 Hz), 125.46, 126.67 (t, $^2J_{C-F}$ = 31.25 Hz), 132.48, 140.56, 159.28, 160.13 ppm. MS (EI) m/z 365 (M^+). IR (KBr) 3007, 2959, 1747, 1465, 1358,

819 cm^{-1}. Anal. Calcd. for $C_{14}H_{12}F_5N_3O_3$: C, 46.04; H, 3.31; N, 11.50. Found: C, 46.16; H, 3.25; N, 11.42.

*4.2.14. Methyl 3-(4-methoxybenzyl)-5-(pentafluoroethyl)-3H-1,2,3-triazole-4-carboxylate (**4bc**)*

White solid; mp: 46.6–48.1 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 3.78 (s, 3H, OCH_3), 3.93 (s, 3H, OCH_3), 5.84 (s, 2H, CH_2), 6.86 (d, J = 8.5 Hz, 2H, ArH), 7.29 (d, J = 8.5 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −83.09 (t, J = 4.7 Hz, CF_3), −109.99 to −109.96 (m, CF_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.43, 54.02, 55.36, 109.95 (tq, $^1J_{C-F}$ = 250.83 Hz, $^2J_{C-F}$ = 39.58 Hz), 114.93, 118.74 (qt, $^1J_{C-F}$ = 284.58 Hz, $^2J_{C-F}$ = 36.40 Hz), 125.98, 127.96, 129.98, 138.22 (t, $^1J_{C-F}$ = 278.75 Hz), 157.81, 160.14 ppm. MS (EI) m/z 365 (M^+). IR (KBr) 3008, 2961, 1738, 1465, 1342, 817 cm^{-1}. Anal. Calcd. for $C_{14}H_{12}F_5N_3O_3$: C, 46.04; H, 3.31; N, 11.50. Found: C, 46.15; H, 3.19; N, 11.45.

*4.2.15. Methyl 1-(4-chlorobenzyl)-5-(pentafluoroethyl)-1H-1,2,3-triazole-4-carboxylate (**3bd**)*

Yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 3.95 (s, 3H, OCH_3), 5.66 (s, 2H, CH_2), 7.18 (d, J = 8.5 Hz, 2H, ArH), 7.31 (d, J = 8.5 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −83.61 (t, J = 4.7 Hz, CF_3), −108.65 to −108.62 (m, CF_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.04, 54.55 (t, $^3J_{C-F}$ = 3.75 Hz), 110.37 (tq, $^1J_{C-F}$ = 256.88 Hz, $^2J_{C-F}$ = 41.67 Hz), 118.26 (qt, $^1J_{C-F}$ = 285.42 Hz, $^2J_{C-F}$ = 37.03 Hz), 126.90 (t, $^2J_{C-F}$ = 31.88 Hz), 129.07, 129.31, 131.96, 135.21, 140.75, 159.13 ppm. MS (EI) m/z 369 (M^+). IR (KBr) 3035, 2958, 1747, 1464, 1334, 828 cm^{-1}. Anal. Calcd. for $C_{13}H_9ClF_5N_3O_2$: C, 42.24; H, 2.45; N, 11.37. Found: C, 42.37; H, 2.43; N, 11.45.

*4.2.16. Methyl 3-(4-chlorobenzyl)-5-(pentafluoroethyl)-3H-1,2,3-triazole-4-carboxylate (**4bd**)*

White solid; mp: 54.2–55.3 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 3.93 (s, 3H, OCH_3), 5.88 (s, 2H, CH_2), 7.28 (d, J = 8.5 Hz, 2H, ArH), 7.32 (d, J = 8.5 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −83.05 (t, J = 4.7 Hz, CF_3), −109.95 to −109.92 (m, CF_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.54, 53.75, 109.88 (tq, $^1J_{C-F}$ = 251.88 Hz, $^2J_{C-F}$ = 39.58 Hz), 118.72 (qt, $^1J_{C-F}$ = 283.75 Hz, $^2J_{C-F}$ = 36.37 Hz), 128.01, 129.32, 129.85, 132.36, 135.15, 138.41 (t, $^2J_{C-F}$ = 41.88 Hz), 157.68 ppm. MS (EI) m/z 369 (M^+). IR (KBr) 3026, 2960, 1742, 1465, 1344, 813 cm^{-1}. Anal. Calcd. for $C_{13}H_9ClF_5N_3O_2$: C, 42.24; H, 2.45; N, 11.37. Found: C, 42.45; H, 2.43; N, 11.42.

*4.2.17. Methyl 1-(4-methoxybenzyl)-5-(heptafluoropropyl)-1H-1,2,3-triazole-4-carboxylate (**3cc**)*

Yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 3.77 (s, 3H, OCH_3), 3.94 (s, 3H, OCH_3), 5.62 (s, 2H, CH_2), 6.85 (d, J = 8.5 Hz, 2H, ArH), 7.21 (d, J = 8.5 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −79.98 (t, J = 9.4 Hz, CF_3), −105.51 to −105.40 (m, CF_2), −124.50 to −124.45 (m, CF_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.93, 55.00, 55.35, 108.48 (tq, $^1J_{C-F}$ = 263.75 Hz, $^2J_{C-F}$ = 37.92 Hz), 110.15–110.86 (m, 1C), 112.64, 114.36, 117.58 (qt, $^1J_{C-F}$ = 286.25 Hz, $^2J_{C-F}$ = 33.75 Hz), 125.52, 126.61 (t, $^2J_{C-F}$ = 31.88 Hz), 129.34, 140.77, 159.29, 160.15 ppm. MS (EI) m/z 415 (M^+). IR (KBr) 3007, 2959, 1748, 1464, 1352, 818 cm^{-1}. Anal. Calcd. for $C_{15}H_{12}F_7N_3O_3$: C, 43.38; H, 2.91; N, 10.12. Found: C, 43.47; H, 2.85; N, 10.23.

*4.2.18. Methyl 3-(4-methoxybenzyl)-5-(heptafluoropropyl)-3H-1,2,3-triazole-4-carboxylate (**4cc**)*

Yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 3.78 (s, 3H, OCH_3), 3.91 (s, 3H, OCH_3), 5.84 (s, 2H, CH_2), 6.87 (d, J = 8.5 Hz, 2H, ArH), 7.28 (d, J = 8.5 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −80.26 (t, J = 9.4 Hz, CF_3), −108.24 to −108.16 (m, CF_2), −125.72 to −125.65 (m, CF_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.38, 54.08, 55.34, 108.73 (t-q, $^1J_{C-F}$ = 265.00 Hz, $^2J_{C-F}$ = 37.50 Hz), 108.28–111.29 (m, 1C), 111.83 (t, $^2J_{C-F}$ = 32.50 Hz), 114.39, 117.92 (qt, $^1J_{C-F}$ = 285.62 Hz, $^2J_{C-F}$ = 33.44 Hz), 125.99, 128.28, 129.86, 137.82 (t, $^2J_{C-F}$ = 28.75 Hz), 157.86, 160.13 ppm. MS (EI) m/z 415 (M^+). IR (KBr) 3009, 2961, 1740, 1462, 1362, 818 cm^{-1}. Anal. Calcd. for $C_{15}H_{12}F_7N_3O_3$: C, 43.38; H, 2.91; N, 10.12. Found: C, 43.50; H, 2.92; N, 10.25.

*4.2.19. Methyl 1-(4-chlorobenzyl)-5-(heptafluoropropyl)-1H-1,2,3-triazole-4-carboxylate (**3cd**)*

Yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 3.94 (s, 3H, OCH_3), 5.66 (s, 2H, CH_2), 7.17 (d, J = 8.5 Hz, 2H, ArH), 7.30 (d, J = 8.5 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −80.01 (t, J = 9.4 Hz, CF_3), −105.62 to −105.51 (m, CF_2), −124.50 to −124.45 (m, CF_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.98, 54.59, 108.45 (tq, $^1J_{C-F}$ = 265.00 Hz, $^2J_{C-F}$ = 38.33 Hz), 110.11–111.02 (m, 1C), 112.58 (t, $^2J_{C-F}$ = 34.38 Hz), 117.50 (q-t, $^1J_{C-F}$ = 286.25 Hz, $^2J_{C-F}$ = 33.44 Hz), 126.82 (t, $^2J_{C-F}$ = 31.88 Hz), 129.03, 129.28, 132.01, 135.17, 140.93, 159.11 ppm. MS (EI) m/z 419 (M^+). IR (KBr) 3036, 2958, 1749, 1463, 1351, 828 cm^{-1}. Anal. Calcd. for $C_{14}H_9ClF_7N_3O_2$: C, 40.07; H, 2.16; N, 10.01. Found: C, 40.19; H, 2.18; N, 10.25.

*4.2.20. Methyl 3-(4-chlorobenzyl)-5-(heptafluoropropyl)-3H-1,2,3-triazole-4-carboxylate (**4cd**)*

Yellow oil; ^1H NMR (500 MHz, $CDCl_3$) δ 3.92 (s, 3H, OCH_3), 5.89 (s, 2H, CH_2), 7.28 (d, J = 8.5 Hz, 2H, ArH), 7.33 (d, J = 8.5 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −80.31 (t, J = 9.4 Hz, CF_3), −108.28 to −108.15 (m, CF_2), −125.70 to −125.65 (m, CF_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.45, 53.80, 108.72 (tq, $^1J_{C-F}$ = 265.00 Hz, $^2J_{C-F}$ = 37.50 Hz), 110.28–111.30 (m, 1C), 111.94 (t, $^2J_{C-F}$ = 31.88 Hz), 117.90 (q-t, $^1J_{C-F}$ = 285.00 Hz, $^2J_{C-F}$ = 33.75 Hz), 128.33, 129.30, 129.72, 132.42, 135.10, 137.99 (t, $^2J_{C-F}$ = 28.75 Hz), 157.69 ppm. MS (EI) m/z 419 (M^+). IR (KBr) 3035, 2961, 1738, 1461, 1333, 811 cm^{-1}. Anal. Calcd. for $C_{14}H_9ClF_7N_3O_2$: C, 40.07; H, 2.16; N, 10.01. Found: C, 40.25; H, 2.17; N, 10.19.

*4.2.21. Methyl 5-(trifluoromethyl)-1-(4-nitrophenyl)-1H-1,2,3-triazole-4-carboxylate (**3ag**) [14]*

White solid; mp: 112.6–113.4 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 4.04 (s, 3H, OCH_3), 7.73 (d, J = 9.0 Hz, 2H, ArH), 8.47 (d, J = 9.0 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −55.25 (s, CF_3) ppm. MS (EI) m/z: 316 (M^+).

*4.2.22. Methyl 5-(trifluoromethyl)-3-(4-nitrophenyl)-3H-1,2,3-triazole-4-carboxylate (**4ag**)*

White solid; mp: 123.0–123.6 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 3.93 (s, 3H, OCH_3), 7.73 (d, J = 9.0 Hz, 2H, ArH), 8.43 (d, J = 9.0 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −60.97 (s, CF_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.95, 119.66 (q, $^1J_{C-F}$ = 269 Hz), 124.82, 126.96, 128.37, 128.40 (d, $^3J_{C-F}$ = 1.2 Hz), 139.97 (q, $^2J_{C-F}$ = 40 Hz), 148.96, 156.80 ppm. MS (EI) m/z: 316 (M^+). IR (KBr): 3090, 2964, 1738, 1504, 1458, 1356, 1313, 816 cm^{-1}. Anal. Calcd. for $C_{11}H_7F_3N_4O_4$: C, 41.78; H, 2.23; N, 17.72. Found: C, 41.89; H, 2.25; N, 17.81.

*4.2.23. Methyl 5-(trifluoromethyl)-1-phenyl-1H-1,2,3-triazole-4-carboxylate (**3ah**) [14]*

White solid; mp: 32.9–33.8 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 4.02 (s, 3H, OCH_3), 7.45 (d, J = 7.5 Hz, 2H, ArH), 7.54–7.62 (m, 3H, ArH), 7.53–7.60 (m, 3H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −55.68 (s, CF_3) ppm. MS (EI) m/z: 271 (M^+).

*4.2.24. Methyl 5-(trifluoromethyl)-3-phenyl-3H-1,2,3-triazole-4-carboxylate (**4ah**)*

White solid; mp: 43.9–45.2 °C. ^1H NMR (500 MHz, $CDCl_3$) δ 3.89 (s, 3H, OCH_3), 7.48 (d, J = 7.0 Hz, 2H, ArH), 7.55–7.62 (m, 3H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −60.89 (s, CF_3) ppm. ^{13}C NMR (125 MHz, CDCl3) δ 53.60, 119.93 (q, $^1J_{C-F}$ = 267.92 Hz),

125.54, 128.31 (q, $^3J_{C-F}$ = 2.5 Hz), 129.45, 130.93, 135.75, 139.35 (q, $^2J_{C-F}$ = 39.58 Hz), 157.20 ppm. MS (EI) *m*/*z*: 271 (M^+). IR (KBr): 3064, 2963, 1742, 1453, 1384, 816 cm^{-1}. Anal. Calcd. for $C_{11}H_8F_3N_3O_2$: C, 48.72; H, 2.97; N, 15.49. Found: C, 48.85; H, 2.97; N, 15.54.

*4.2.25. Methyl 5-(trifluoromethyl)-1-p-tolyl-1H-1,2,3-triazole-4-carboxylate (**3ai**)*

White solid; mp: 72.3–73.5 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.46 (s, 3H, CH_3), 4.02 (s, 3H, OCH_3), 7.33 (d, *J* = 8.5 Hz, 2H, ArH), 7.36 (d, *J* = 8.5 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −55.79 (s, CF_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.44, 53.14, 118.91 (q, $^1J_{C-F}$ = 270 Hz), 125.58, 129.80 (q, $^2J_{C-F}$ = 39.2 Hz), 130.19, 133.03, 139.07, 141.84, 159.62 ppm. MS (EI) *m*/*z*: 285 (M^+). IR (KBr): 3044, 2956, 1738, 1459, 1364, 822 cm^{-1}. Anal. Calcd. for $C_{12}H_{10}F_3N_3O_2$: C, 50.53; H, 3.53; N, 14.73. Found: C, 50.66; H, 3.58; N, 14.76.

*4.2.26. Methyl 5-(trifluoromethyl)-3-p-tolyl-3H-1,2,3-triazole-4-carboxylate (**4ai**)*

White solid; mp: 104.4–105.2 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.46 (s, 3H, CH_3), 3.88 (s, 3H, OCH_3), 7.35 (s, 4H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −60.91 (s, CF_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.39, 53.56, 119.96 (q, $^1J_{C-F}$ = 268 Hz), 125.28, 128.26 (d, $^3J_{C-F}$ = 1.2 Hz), 130.00, 133.28, 139.24 (q, $^2J_{C-F}$ = 39.6 Hz), 141.35, 157.30 ppm. MS (EI) *m*/*z*: 285 (M^+). IR (KBr): 3019, 2963, 1736, 1461, 1384, 822 cm^{-1}. Anal. Calcd. for $C_{12}H_{10}F_3N_3O_2$: C, 50.53; H, 3.53; N, 14.73. Found: C, 50.62; H, 3.57; N, 14.85.

*4.2.27. Methyl 5-(trifluoromethyl)-1-(4-methoxyphenyl)-1H-1,2,3-triazole-4-carboxylate (**3aj**) [14]*

White solid; mp: 113.2–114.8 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.87 (s, 3H, OCH_3), 4.01 (s, 3H, OCH_3), 7.03 (d, *J* = 9.0 Hz, 2H, ArH), 7.36 (d, *J* = 9.0 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −55.91 (s, CF_3) ppm. MS (EI) *m*/*z*: 301 (M^+).

*4.2.28. Methyl 5-(trifluoromethyl)-3-(4-methoxyphenyl)-3H-1,2,3-triazole-4-carboxylate (**4aj**)*

White solid; mp: 113.2–114.8 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.89 (s, 3H, OCH_3), 3.90 (s, 3H, OCH_3), 7.04 (d, *J* = 9.0 Hz, 2H, ArH), 7.39 (d, *J* = 9.0 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −60.91 (s, CF_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.57, 55.75, 114.50, 119.97 (q, $^1J_{C-F}$ = 268 Hz), 123.18, 128.14, 126.96, 128.40, (d, $^2J_{C-F}$ = 39.2 Hz), 157.31, 161.33 ppm. MS (EI) *m*/*z*: 301 (M^+). IR (KBr): 3016, 2970, 1741, 1462, 1383, 835 cm^{-1}. Anal. Calcd. for $C_{12}H_{10}F_3N_3O_3$: C, 47.85; H, 3.35; N, 13.95. Found: C, 47.92; H, 3.32; N, 13.90.

*4.2.29. Methyl 1-(4-chlorophenyl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylat (**3ak**)*

White solid; mp: 84.1–85.4 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.04 (s, 3H, OCH_3), 7.43 (d, *J* = 9.0 Hz, 2H, ArH), 7.56 (d, *J* = 9.0 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −55.60 (s, CF_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.24, 118.82 (q, $^1J_{C-F}$ = 269.6 Hz), 127.16, 129.83 (d, $^2J_{C-F}$ = 41.25 Hz), 130.03, 133.89, 137.74, 139.33, 159.38 ppm. MS (EI) *m*/*z*: 305 (M^+). IR (KBr): 3032, 2963, 1737, 1452, 1366, 822 cm^{-1}. Anal. Calcd. for $C_{11}H_7ClF_3N_3O_2$: C, 43.23; H, 2.31; N, 13.75. Found: C, 43.29; H, 2.33; N, 13.86.

*4.2.30. Methyl 3-(4-chlorophenyl)-5-(trifluoromethyl)-3H-1,2,3-triazole-4-carboxylate (**4ak**)*

White solid; mp: 90.1–91.0 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.91 (s, 3H, OCH_3), 7.43 (d, *J* = 9.0 Hz, 2H, ArH), 7.54 (d, *J* = 9.0 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −60.93 (s, CF_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.71, 119.82 (q, $^1J_{C-F}$ = 268.75 Hz), 126.99, 128.27 (d, $^3J_{C-F}$ = 2.5 Hz), 129.70, 134.16, 137.18, 139.57 (d, $^2J_{C-F}$ = 40 Hz), 157.02 ppm. MS (EI) *m*/*z*: 305 (M^+). IR (KBr): 3032, 2963, 1737, 1452, 1366, 822 cm^{-1}. Anal. Calcd. for $C_{11}H_7ClF_3N_3O_2$: C, 43.23; H, 2.31; N, 13.75. Found: C, 43.35; H, 2.32; N, 13.79.

*4.2.31. Methyl 5-(trifluoromethyl)-1-(3-fluorophenyl)-1H-1,2,3-triazole-4-carboxylate (**3al**)*

Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.05 (s, 3H, OCH_3), 7.27–7.62 (m, 4H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −55.65 (s, CF_3), −109.30 (m, ArF) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.23, 113.89 (d, $^2J_{C-F}$ = 25 Hz), 118.68 (d, $^2J_{C-F}$ = 21.25 Hz), 118.78 (q, $^1J_{C-F}$ = 270 Hz), 121.82 (d, $^4J_{C-F}$ = 2.5 Hz), 129.84 (d, $^2J_{C-F}$ = 42.08 Hz), 131.12 (d, $^3J_{C-F}$ = 10 Hz), 136.38 (d, $^3J_{C-F}$ = 10 Hz), 139.31, 159.34, 162.52 (d, $^1J_{C-F}$ = 249 Hz) ppm. MS (EI) *m*/*z* 289 (M^+). IR (KBr) 3079, 2959, 1746, 1466, 1364, 878, 792, 715 cm^{-1}. Anal. Calcd. for $C_{11}H_7F_4N_3O_2$: C, 45.69; H, 2.44; N, 14.53. Found: C, 45.79; H, 2.46; N, 14.52.

*4.2.32. Methyl 5-(trifluoromethyl)-3-(3-fluorophenyl)-3H-1,2,3-triazole-4-carboxylate (**4al**)*

White solid; mp: 46.8–48.4 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.92 (s, 3H, OCH_3), 7.27–7.58 (m, 4H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −60.98 (s, CF_3), −109.91 to −109.86 (m, ArF) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.74, 113.64 (d, $^2J_{C-F}$ = 25 Hz), 118.16 (d, $^2J_{C-F}$ = 25 Hz), 119.82 (q, $^1J_{C-F}$ = 267.92 Hz), 121.52 (d, $^4J_{C-F}$ = 3.75 Hz), 128.38 (d, $^3J_{C-F}$ = 1.25 Hz), 130.84 (d, $^3J_{C-F}$ = 8.75 Hz), 136.71 (d, $^3J_{C-F}$ = 10 Hz), 139.50 (q, $^2J_{C-F}$ = 39.58 Hz), 157.00, 162.48 (d, $^1J_{C-F}$ = 249 Hz) ppm. MS (EI) *m*/*z*: 289 (M^+). IR (KBr): 3080, 2871, 1744, 1471, 1384, 884, 792, 706 cm^{-1}. Anal. Calcd. for $C_{11}H_7F_4N_3O_2$: C, 45.69; H, 2.44; N, 14.53. Found: C, 45.75; H, 2.46; N, 14.42.

*4.2.33. Methyl 1-(4-cyanophenyl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylate (**3am**)*

White solid; mp: 98.7–100.6 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.03 (s, 3H, OCH_3), 7.66 (d, *J* = 9.0 Hz, 2H, ArH), 7.91 (d, *J* = 9.0 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −55.31 (s, CF_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.35, 118.72 (q, $^1J_{C-F}$ = 267.5 Hz), 115.66, 117.13, 126.79, 129.84 (q, $^2J_{C-F}$ = 42.5 Hz), 133.69, 138.64, 139.68, 159.12 ppm. MS (EI) *m*/*z*: 296 (M^+). IR (KBr): 3068, 2963, 2240, 1744, 1454, 1365, 819 cm^{-1}. Anal. Calcd. for $C_{12}H_7F_3N_4O_2$: C, 48.66; H, 2.38; N, 18.91. Found: C, 48.78; H, 2.39; N, 18.99.

*4.2.34. Methyl 3-(4-cyanophenyl)-5-(trifluoromethyl)-3H-1,2,3-triazole-4-carboxylate (**4am**)*

White solid; mp: 132.5–133.7 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.92 (s, 3H, OCH_3), 7.66 (d, *J* = 8.5 Hz, 2H, ArH), 7.88 (d, *J* = 8.5 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −60.95 (s, CF_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.88, 115.03, 117.34, 119.65 (q, $^1J_{C-F}$ = 267.92 Hz), 126.65, 128.28 (q, $^3J_{C-F}$ = 1.25 Hz), 133.35, 138.88, 139.74 (q, $^2J_{C-F}$ = 39.58 Hz), 156.79 ppm. MS (EI) *m*/*z*: 296 (M^+). IR (KBr): 3074, 2968, 2239, 1731, 1460, 1386, 816 cm^{-1}. Anal. Calcd. for $C_{12}H_7F_3N_4O_2$: C, 48.66; H, 2.38; N, 18.91. Found: C, 48.81; H, 2.39; N, 19.03.

*4.2.35. Methyl 1-(3-cyanophenyl)-5-(trifluoromethyl)-1H-1,2,3-triazole-4-carboxylate (**3an**)*

White solid; mp: 75.4–76.1 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 34.03 (s, 3H, OCH_3), 7.70–7.76 (m, 2H, ArH), 7.82 (s, 1H, ArH), 7.93–7.95 (m, 1H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −55.35 (s, CF_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.34, 114.39, 116.75, 118.70 (q, $^1J_{C-F}$ = 270 Hz), 129.39, 130.23, 130.32 (q, $^2J_{C-F}$ = 42.5 Hz), 130.91, 134.91, 136.17, 139.56, 159.10 ppm. MS (EI) *m*/*z*: 296 (M^+). IR (KBr): 3079, 2963, 2235, 1740, 1472, 1369, 884, 799, 685 cm^{-1}. Anal. Calcd. for $C_{12}H_7F_3N_4O_2$: C, 48.66; H, 2.38; N, 18.91. Found: C, 48.73; H, 2.38; N, 19.94.

*4.2.36. Methyl 3-(3-cyanophenyl)-5-(trifluoromethyl)-3H-1,2,3-triazole-4-carboxylate (**4an**)*

White solid; mp: 93.5–94.9 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.91 (s, 3H, OCH_3), 7.71–7.77 (m, 2H, ArH), 7.82 (s, 1H, ArH), 7.88–7.90 (m, 1H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −60.98 (s, CF_3) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.83, 113.81, 116.99, 119.64 (q, $^1J_{C-F}$ = 267.92 Hz), 128.28, 129.40, 130.27, 130.49, 134.38, 136.36, 139.78 (q, $^2J_{C-F}$ = 40 Hz), 156.68 ppm. MS (EI) *m*/*z*: 296 (M^+). IR (KBr): 3079, 2975, 2234, 1739, 1457, 1381, 803, 757, 682 cm^{-1}. Anal. Calcd. for $C_{12}H_7F_3N_4O_2$: C, 48.66; H, 2.38; N, 18.91. Found: C, 48.78; H, 2.39; N, 19.97.

*4.2.37. Methyl 1-(4-methoxyphenyl)-5-(pentafluoroethyl)-1H-1,2,3-triazole-4-carboxylate (**3bj**)*

White solid; mp: 57.6–59.3 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.87 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 7.00 (d, *J* = 9.0 Hz, 2H, ArH), 7.29 (d, *J* = 9.0 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −83.20 (t, *J* = 4.7 Hz, CF_3), −107.43 to −107.40 (m, CF_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 52.99, 55.67, 109.79 (tq, $^1J_{C-F}$ = 257.5 Hz, $^2J_{C-F}$ = 41.67 Hz), 114.24, 118.09 (qt, $^1J_{C-F}$ = 285.62 Hz, $^2J_{C-F}$ = 36.67 Hz), 128.07, 128.46 (t, $^2J_{C-F}$ = 30.62 Hz, CCF_2), 129.54, 140.20, 159.29, 161.51 ppm. MS (EI) *m*/*z*: 351 (M^+). IR (KBr): 3014, 2959, 1746, 1453, 1359, 840 cm^{-1}. Anal. Calcd. for $C_{13}H_{10}F_5N_3O_3$: C, 44.46; H, 2.87; N, 11.96. Found: C, 44.57; H, 2.89; N, 12.11.

*4.2.38. Methyl 3-(4-methoxyphenyl)-5-(pentafluoroethyl)-3H-1,2,3-triazole-4-carboxylate (**4bj**)*

White solid; mp: 60.9–62.1 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.85 (s, 6H, OCH_3), 7.01 (d, *J* = 9.0 Hz, 2H, ArH), 7.39 (d, *J* = 9.0 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −83.60 (t, *J* = 4.7 Hz, CF_3), −110.95 to −111.03 (m, CF_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.67, 55.66, 109.34 (tq, $^1J_{C-F}$ = 251.25 Hz, $^2J_{C-F}$ = 40.00 Hz), 114.61, 118.69 (qt, $^1J_{C-F}$ = 285 Hz, $^2J_{C-F}$ = 36.72 Hz), 126.54, 128.36, 130.28, 136.90 (t, $^2J_{C-F}$ = 29.38 Hz), 157.84, 161.3 ppm. MS (EI) *m*/*z*: 351 (M^+). IR (KBr): 3022, 2965, 1741, 1461, 1349, 836 cm^{-1}. Anal. Calcd. for $C_{13}H_{10}F_5N_3O_3$: C, 44.46; H, 2.87; N, 11.96. Found: C, 44.54; H, 2.88; N, 12.07.

*4.2.39. Methyl 1-(4-chlorophenyl)-5-(pentafluoroethyl)-1H-1,2,3-triazole-4-carboxylate (**3bk**)*

White solid; mp: 47.7–49.2 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.01 (s, 3H, OCH_3), 7.34 (d, *J* = 8.5 Hz, 2H, ArH), 7.53 (d, *J* = 8.5 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −83.16 (t, *J* = 4.7 Hz, CF_3), −107.18 to −107.16 (m, CF_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.21, 109.85 (tq, $^1J_{C-F}$ = 257.5 Hz, $^2J_{C-F}$ = 41.67 Hz), 118.14 (qt, $^1J_{C-F}$ = 285.62 Hz, $^2J_{C-F}$ = 36.67 Hz), 128.24, 128.55 (t, $^2J_{C-F}$ = 30.62 Hz), 129.67, 134.03, 137.87, 140.56, 159.16 ppm. MS (EI) *m*/*z*: 355 (M^+). IR (KBr): 3030, 2966, 1740, 1443, 1358, 820 cm^{-1}. Anal. Calcd. for $C_{12}H_7ClF_5N_3O_2$: C, 40.53; H, 1.98; N, 11.82. Found: C, 40.65; H, 1.99; N, 11.85.

*4.2.40. Methyl 3-(4-chlorophenyl)-5-(pentafluoroethyl)-3H-1,2,3-triazole-4-carboxylate (**4bk**)*

White solid; mp: 86.5–88.0 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.88 (s, 3H, OCH_3), 7.44 (d, *J* = 8.5 Hz, 2H, ArH), 7.53 (d, *J* = 8.5 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −83.53 (t, *J* = 4.7 Hz, CF_3),-110.99 to −110.97 (m, CF_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.85, 109.84 (tq, $^1J_{C-F}$ = 251.88 Hz, $^2J_{C-F}$ = 40.14 Hz), 118.52 (qt, $^1J_{C-F}$ = 285 Hz, $^2J_{C-F}$ = 36.41 Hz), 126.59, 129.84, 130.20, 134.06, 137.18, 137.43 (t, $^2J_{C-F}$ = 29.38 Hz), 157.54 ppm. MS (EI) *m*/*z*: 355 (M^+). IR (KBr): 3030, 2964, 1734, 1453, 1346, 837 cm^{-1}. Anal. Calcd. for $C_{12}H_7ClF_5N_3O_2$: C, 40.53; H, 1.98; N, 11.82. Found: C, 40.59; H,1.99; N, 11.91.

*4.2.41. Methyl 1-(4-methoxyphenyl)-5-(heptafluoropropyl)-1H-1,2,3-triazole-4-carboxylate (**3cj**)*

Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.87 (s, 3H, OCH_3), 4.00 (s, 3H, OCH_3), 7.00 (d, *J* = 8.5 Hz, 2H, ArH), 7.30 (d, *J* = 8.5 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −80.10 (t, *J* = 9.4 Hz, CF_3), −104.29 to −104.16 (m, CF_2), −123.76 to −123.71 (m, CF_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.11, 55.78, 108.36 (tq, $^1J_{C-F}$ = 265.00 Hz, $^2J_{C-F}$ = 37.92 Hz), 109.87–110.94 (m, 1C), 112.21 (t, $^2J_{C-F}$ = 34.38 Hz), 114.31, 117.52 (qt, $^1J_{C-F}$ = 286.25 Hz, $^2J_{C-F}$ = 33.75 Hz), 128.26, 128.75, 128.50, 140.56, 159.43, 161.62 ppm. MS (EI) *m*/*z* 401 (M^+). IR (KBr) 3011, 2959, 1748, 1448, 1358, 839 cm^{-1}. Anal. Calcd. for $C_{14}H_{10}F_7N_3O_3$: C, 41.91; H, 2.51; N, 10.47. Found: C, 41.99; H, 2.53; N, 10.56.

*4.2.42. Methyl 3-(4-methoxyphenyl)-5-(heptafluoropropyl)-3H-1,2,3-triazole-4-carboxylate (**4cj**)*

White solid; mp: 82.0–84.0 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.84 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 7.02 (d, *J* = 8.5 Hz, 2H, ArH), 7.40 (d, *J* = 8.5 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −80.24 (t, *J* = 9.4 Hz, CF_3), −109.05 to −108.94 (m, CF_2), −126.05 to −126.00 (m, CF_2) (m, CF_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.70, 55.69, 108.69 (tq, $^1J_{C-F}$ = 265.00 Hz, $^2J_{C-F}$ = 37.50 Hz), 108.24–111.25 (m, 1C), 111.95 (t, $^2J_{C-F}$ = 31.88 Hz), 114.67, 117.92 (q-t, $^1J_{C-F}$ = 286.25 Hz, $^2J_{C-F}$ = 33.75 Hz,), 126.49, 128.39, 130.57, 136.60 (t, $^2J_{C-F}$ = 28.75 Hz), 157.99, 161.36 ppm. MS (EI) *m*/*z*: 401 (M^+). IR (KBr): 3020, 2968, 1747, 1448, 1377, 836 cm^{-1}. Anal. Calcd. for $C_{14}H_{10}F_7N_3O_3$: C, 41.91; H, 2.51; N, 10.47. Found: C, 42.18; H, 2.56; N,10.50.

*4.2.43. Methyl 1-(4-chlorophenyl)-5-(heptafluoropropyl)-1H-1,2,3-triazole-4-carboxylate (**3ck**)*

Yellow oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.01 (s, 3H, OCH_3), 7.35 (d, *J* = 8.5 Hz, 2H, ArH), 7.53 (d, *J* = 8.5 Hz, 2H, ArH) ppm. ^{19}F NMR (470 MHz, $CDCl_3$) δ −80.05 (t, *J* = 9.4 Hz, CF_3), −104.09 to −103.98 (m, CF_2), −123.72 to −123.67 (m, CF_2) (m, CF_2) ppm. ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.21, 108.33 (tq, $^1J_{C-F}$ = 265.00 Hz, $^2J_{C-F}$ = 30.67 Hz), 109.84–110.90 (m, 1C), 112.18 (t, $^2J_{C-F}$ = 33.75 Hz), 117.46 (qt, $^1J_{C-F}$ = 286.25 Hz, $^2J_{C-F}$ = 33.12 Hz, CF_3), 128.32, 128.46 (t, $^2J_{C-F}$ = 30.25 Hz), 129.63, 134.05, 137.87, 140.81, 159.18 ppm. MS (EI) *m*/*z* 405 (M^+). IR (KBr) 3008, 2958, 1749, 1443, 1356, 838 cm^{-1}. Anal. Calcd. for $C_{13}H_7ClF_7N_3O_2$: C, 38.49; H, 1.74; N, 10.36. Found: C, 38.61; H, 1.76; N, 10.51.

*4.2.44. Methyl 3-(4-chlorophenyl)-5-(heptafluoropropyl)-3H-1,2,3-triazole-4-carboxylate (**4ck**)*

White solid; mp: 60.9–62.3 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.87 (s, 3H, OCH_3), 7.45 (d, *J* = 8.5 Hz, 2H, ArH), 7.53 (d, *J* = 8.5 Hz, 2H, ArH). ^{19}F NMR (470 MHz, $CDCl_3$) δ −80.22 (t, *J* = 9.4 Hz, CF_3), −108.99 to −108.89 (m, CF_2), −125.97 to −125.92 (m, CF_2). ^{13}C NMR (125 MHz, $CDCl_3$) δ 53.86, 108.67 (tq, $^1J_{C-F}$ = 265.00 Hz, $^2J_{C-F}$ = 37.50 Hz), 108.22–111.87 (m, 1C), 111.87 (t, $^2J_{C-F}$ = 31.35 Hz), 117.89 (q-t, $^1J_{C-F}$ = 286.25 Hz, $^2J_{C-F}$ = 33.75 Hz), 126.50, 129.90, 130.47, 134.07, 137.13 (t, $^2J_{C-F}$ = 28.75 Hz), 137.20, 157.69 ppm. MS (EI) *m*/*z*: 405 (M^+). IR (KBr): 3022, 2964, 1737, 1447, 1343, 829 cm^{-1}. Anal. Calcd. for $C_{13}H_7ClF_7N_3O_2$: C, 38.49; H, 1.74; N, 10.36. Found: C, 38.58; H, 1.75; N, 10.49.

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