

Full Paper

Regioselective Synthesis of 1-(2,6-Dichloro-4-Trifluoromethylphenyl)-4-Alkyl-1*H*-[1,2,3]-Triazoles

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Abstract: A new and efficient method for the synthesis of 1-(2,6-dichloro-4-trifluoromethylphenyl)-4-alkyl-1*H*-[1,2,3]-triazoles by the room temperature 1,3-dipolar cycloaddition of (2-azido-1,3-dichloro-5-trifluoromethyl)benzene with terminal alkynes in the presence of Cu (I) salt as catalyst is reported. All the reactions gave 1,4-disubstituted products with high regioselectivity, as no 1,5-disubstituted product was formed. The structures of all the title compounds have been confirmed by elemental analysis, ¹H- and ¹³C-NMR and in addition, the structure of compound **5a** was investigated by X-ray crystallography.

Keywords: 1,3-Dipolar cycloaddition, 1,2,3-triazole, internal alkyne, regioselective

Introduction

[1,2,3]-Triazoles have found wide use in pharmaceuticals, agrochemicals, dyes, photographic materials and corrosion inhibition, etc. [1]. For example, there are numerous examples in the literature of the biological activity of triazole compounds, including anti-HIV activity [2], antimicrobial activity

against Gram positive bacteria [3] and selective β_3 adrenergic receptor agonism [4]. Several methods have been described for the synthesis of [1,2,3]-triazoles. Among them, the most important and useful one is the 1,3-dipolar cycloaddition of azides with alkynes [5]. However, this reaction suffers from some drawbacks, usually needs elevated temperature and also forms a mixture of 1,4 and 1,5 regioisomers when unsymmetrical alkynes are used.

It has been known for some time that fluorine atom can lead to unexpected biological activity results arising due to the special properties of the fluorine atom, such as the highest electronegativity of fluorine and high carbon-fluorine bond energy [6]. As a consequence, trifluoromethyl-containing molecules have seen considerable utilization in pharmaceutical and agrochemical industry [6-8]. For example, heterocyclic compounds containing the (2,6-dichloro-4-trifluoromethyl)phenyl group are important intermediates in synthesis of biologically active compounds used as medicines and agrochemicals [9-11]. We desired to develop a new and convenient method for synthesizing (2,6-dichloro-4-trifluoromethyl)phenyltriazoles with good biological activity [10-11]. Herein, we present a method for the synthesis of (2-azido-1,3-dichloro-5-trifluoromethyl)benzenes **3** and their regioselective reaction with terminal alkynes in the presence of Cu(I) salt as catalyst, and further studies on the reaction of other fluorine-containing azides with terminal alkynes.

Results and Discussion

Synthesis of the azides

Azides **3** were synthesized from the appropriate fluorine-containing phenylamine (Scheme 1) [3]. Phenylamine was diazotized with sodium nitrite, and then the azide derivatives were prepared in more than 90 % yields by the reaction of the diazotized solution with sodium azide using NaOAc as a stabilizer. The results are summarized in Table 1.

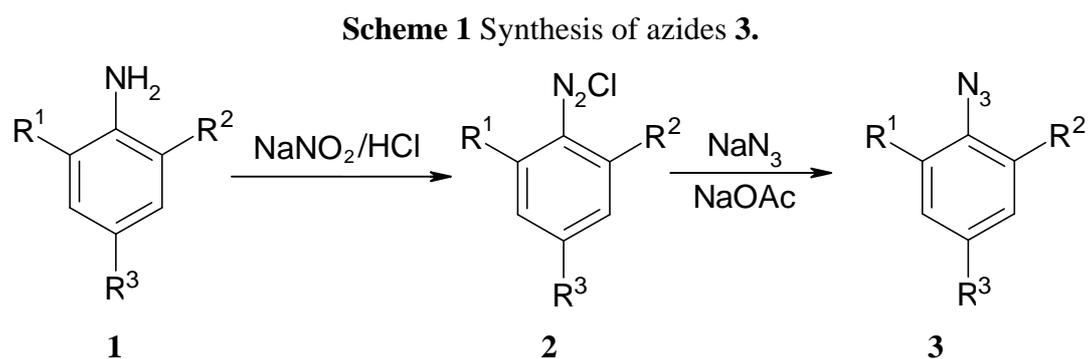


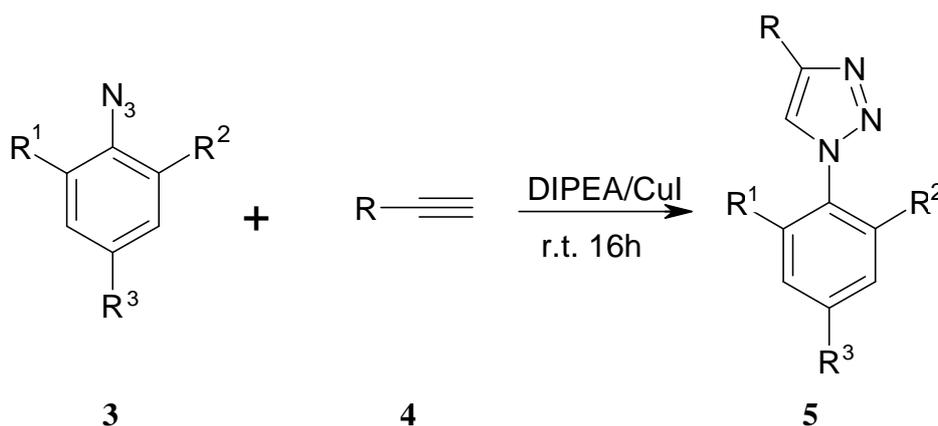
Table 1. The results of the synthesis of azides **3**.

Entry	R ¹ /R ²	R ³	Product 3	Yield/% 3
1	Cl	CF ₃	3a	95
2	H	F	3b	92
3	H	CF ₃	3c	93

Synthesis of [1,2,3]-Triazoles

Several different methods have been described for the synthesis of [1,2,3]-triazoles, including the intramolecular cyclization of bishydrazones or mixed hydrazones, miscellaneous oxidations, as well as the 1,3-dipolar cycloaddition of azides to alkynes [1,12,13]. The cycloaddition between azides and alkynes is typically carried out in refluxing toluene, but labile molecules may not survive these conditions. Nevertheless, by using sodium [14], lithium or magnesium [15] salts of the alkyne, lower temperatures can be employed, although often with limited or little success. In a word, these methods are typically difficult to perform, need elevated temperature or, in the case of unsymmetrical alkynes, lead to a mixture of 1,4- and 1,5-regioisomers. Recently, studies on 1,4- versus 1,5-regioselectivity were reported. Sharpless [16] used a Cu(I) salt as a catalyst to promote the reaction of azide with terminal alkynes to give 1,4-substituted products with high regioselectivity. However, Chen has reported that when they used similar conditions as described by Sharpless, after stirring for 20 h at room temperature, the isolated yield of fluoroalkylated [1,2,3]-triazoles in their reactions was very poor [15]. Meldal [17] also regioselectively synthesized 1,4-substituted [1,2,3]-triazoles by 1,3-dipolar reaction of azides with polymer-supported terminal alkynes. The resin-bound copper acetylide was reacted with primary, secondary, and tertiary alkyl azides, aryl azides, and an azido sugar at 25 °C, affording diversely 1,4-substituted 1*H*-[1,2,3]-triazoles with quantitative conversions and purities ranging from 75 % to 99 %. The mechanism of that reaction may be suitable for other types of reactions, so we used similar conditions as described by Meldal (Scheme 2), and produced a series of 1-(2,6-dichloro-4-trifluoromethylphenyl)-4-alkyl-1*H*-[1,2,3]-triazoles in good yields. No 1,5-disubstituted product was found in these reactions.

Scheme 2 1,3-Dipolar reaction of azide with terminal alkynes.

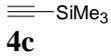
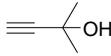
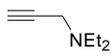
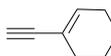
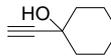
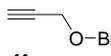


With another two fluorine-containing azides in hand, we started the study on the 1,3-dipolar cycloaddition reaction of other two fluorine-containing azides with 1-ethynylbenzene and hex-1-yne. We also observed that all the reactions were highly regioselective towards 1,4-disubstitution, and no 1,5-disubstituted products were seen. The results are summarized in Table 2.

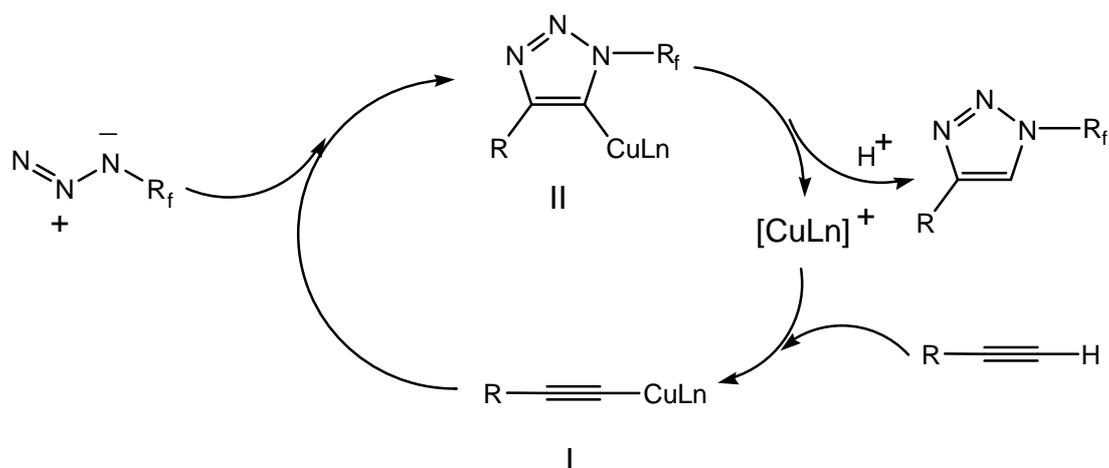
As proposed by Sharpless [16], the following reaction mechanism is suggested: Cu(I) first is inserted into the terminal alkyne, forming copper(I) acetylide **I**, then compound **I** reacts with azide to

form the final product (Scheme 3). Because of the existence of copper(I) acetylide **I**, the reaction was regiospecific in that only a 1,4-disubstituted 1,2,3-triazole was formed.

Table 2. The results of the reactions of azide with terminal alkynes.

Entry	R ¹ /R ²	R ³	Terminal alkyne(4)	Product (5)	Yield/%(5) *
1	Cl	CF ₃	 4a	5a	93
2	Cl	CF ₃	 4b	5b	91
3	Cl	CF ₃	 4c	5c	88
4	Cl	CF ₃	 4d	5d	86
5	Cl	CF ₃	 4e	5e	82
6	Cl	CF ₃	 4f	5f	87
7	Cl	CF ₃	 4g	5g	85
8	Cl	CF ₃	 4h	5h	87
9	Cl	CF ₃	 4i	5i	88
10	Cl	CF ₃	 4j	5j	83
11	H	F	 4k	5k	91
12	H	F	 4l	5l	90
13	H	CF ₃	 4m	5m	92
14	H	CF ₃	 4n	5n	90

* Isolated yields.

Scheme 3. Mechanism of 1,3-dipolar reaction catalyzed with Cu(I) salt.

X ray diffraction

To verify the structural assignment compound **5a** was selected as an example for an X-ray diffraction study. The purified product **5a** was dissolved in 50 % ethanol/acetone (1:1 v/v) and kept at room temperature for 5 days until single crystals of **5a** had formed. The structure of **5a** assigned on the basis of its X-ray crystal structure (Figure 1 and Table 3) [18].

Conclusions

In summary, we have successfully developed a general method for the synthesis of a series of 1-(2,6-dichloro-4-trifluoromethylphenyl)-4-alkyl-1*H*-[1,2,3]-triazoles by the room temperature 1,3-dipolar cycloaddition of (2-azide-1,3-dichloro-5-trifluoromethyl)benzene and other two fluorine-containing azides with terminal alkynes in the presence of Cu (I) salt as catalyst for a short reaction time. All the reactions were performed in highly regioselective with only 1,4-disubstituted and no 1,5-disubstituted product being formed.

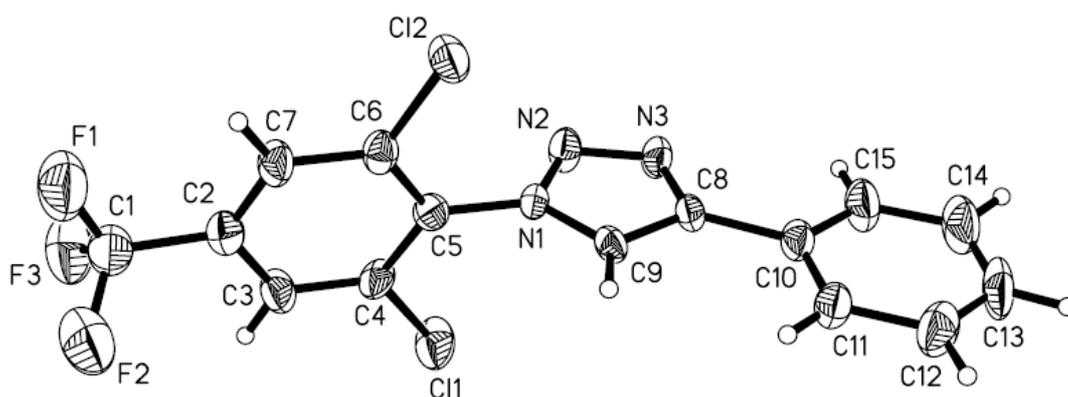
Figure 1. ORTEP drawing of the compound **5a** showing the atom numbering scheme.

Table 3 Crystal data and summary of data collection and structure refinement.

Compound	C ₁₅ H ₈ C ₁₂ F ₃ N ₃
Color	Colorless
Formula weight	358.14
Crystal system	Orthorhombic
Temperature, °K	25(298K)
Cell constants	
a (Å)	15.5358(16)
b (Å)	10.4697(11)
c (Å)	9.3675(9)
α (°)	90
β (°)	90
γ (°)	90
Volume (Å ³)	1523.7(3)
Formula units	4
Calculated density (g/cm ⁻³)	1.561
F(000)	720
Absorption coefficient, mμ ⁻³	0.459
Limiting indices	-9<=h<=18, -12<=k<=12, -11<=l<=10
Reflections collected / unique	7651 / 2703 [R(int) = 0.0371]
Absorption correction	Multi-scan
Max. and min. transmission	0.958 and 0.921
Refinement method	Full-matrix least-squares on F ²
Data / restraints / parameters	2703 / 35 / 208
Goodness-of-fit on F ²	1.160
Final R indices	R ₁ = 0.0973, wR ₂ = 0.2342
Largest diff. peak and hole (e Å ⁻³)	0.678 and -0.372

Experimental

General

All melting points were determined on an XT-4A apparatus and are uncorrected. TLC was performed using precoated silica gel GF₂₅₄ (0.25mm), column chromatography was performed using silica gel (200-300 mesh). The ¹H- and ¹³C-NMR spectra were measured at 25 °C at 300 and 75 MHz, respectively, on a Bruker Advance 300 spectrometer, using TMS as internal standard. *J*-values are given in Hz. The IR spectra were taken on a Bruker Vector 55 spectrometer. Elemental analyses were carried out with an EA 1112 elemental analyzer. All the reagents used were AR grade.

General procedure for the preparation of fluorine-containing azides **3**

Phenylamine (7.5 mmol) was dissolved in concentrated HCl (10 mL) and water (10 mL) and then cooled to 0 °C, sodium nitrite (0.62 g, 9.0 mmol) was added and the yellow solution was stirred at 0 °C

for 2 h. A solution of NaN₃ (0.97 g, 15 mmol) and NaOAc (12.3 g, 150 mmol) was added dropwise to the mixture, the mixture was extracted with EtOAc and the combined extracts were washed with brine, and then dried by Na₂SO₄. Removal of solvent gave the products **3a-c** as brown oils that were used without further purification.

(2-azido-1,3-dichloro-5-trifluoromethyl) benzene (**3a**). ¹H-NMR (CDCl₃) δ: 7.57 (s, 2H, Ar-H); ¹³C-NMR (CDCl₃) δ: 136.1, 133.8 (q, J = 33.8 Hz), 129.5, 125.6, 123.2 (q, J = 271.6 Hz); IR (film, cm⁻¹) v: 3055 (ArH), 2115 (N₃).

2-azido-5-fluorobenzene (**3b**). ¹H-NMR (CDCl₃) δ: 7.79 (d, J = 7.5 Hz, 2H, Ar-H), 7.67 (d, J = 7.5 Hz, 2H, Ar-H); ¹³C-NMR (CDCl₃) δ: 135.3, 129.1 (q, J = 8.5 Hz), 126.3, 116.3 (q, J = 21.7 Hz); IR (film, cm⁻¹) v: 3050 (ArH), 2114 (N₃).

(2-azido-5-trifluoromethyl) benzene (**3c**). ¹H-NMR (CDCl₃) δ: 7.65 (d, J = 8.6 Hz, 2H, Ar-H), 7.59 (d, J = 8.6 Hz, 2H, Ar-H); ¹³C-NMR (CDCl₃) δ: 135.9, 133.6 (q, J = 34.7 Hz), 126.5, 125.1, 123.0 (q, J = 272.4 Hz); IR (film, cm⁻¹) v: 3049 (ArH), 2115 (N₃).

General procedure for the preparation of 1-(2,6-dichloro-4-trifluoromethylphenyl)-4-alkyl-1H-[1,2,3]-triazoles 5

The terminal alkyne (1 mmol) was added to a stirred solution of DIPEA (25 mmol), CuI (1 mmol), and R-N₃ (1 mmol) and reacted for 16 h at 25 °C. Then, the volatile substances were removed under reduced pressure. The residue was subjected to a chromatography on a column of silica gel, eluting with petroleum ether and ethyl acetate, solution was removed under reduced pressure, giving compounds **5a-n** as solids.

1-((2,6-Dichloro-4-trifluoromethyl) phenyl)-4-phenyl-1H-[1,2,3]-triazole (**5a**). White solid; yield: 93%; M.p. 160-161 °C (lit. [10] 158.2-158.6 °C); ¹H-NMR (CDCl₃) δ: 8.01 (s, 1H, triazole H), 7.96 (d, J = 9.6 Hz, 2H, Ar-H), 7.82 (s, 2H, Ar-H), 7.41-7.52 (m, 3H, Ar-H); ¹³C-NMR (CDCl₃) δ: 147.8, 135.9, 134.7, 133.6 (q, J = 34.5 Hz), 129.4, 128.8, 128.5, 125.8, 121.8 (q, J = 272.2 Hz), 121.2, 119.9; IR (KBr, cm⁻¹) v: 3090, 1596 (ArH); Anal. Calcd. (%) for C₁₅H₈Cl₂F₃N₃: C, 50.30; H, 2.25; N, 11.73. Found: C, 50.40; H, 2.17; N, 11.82.

4-Butyl-1-((2,6-dichloro-4-trifluoromethyl) phenyl)-1H-[1,2,3]-triazole (**5b**). White solid; yield: 91%; M.p. 51-52 °C (lit. [10] 48.4-49.9 °C); ¹H-NMR (CDCl₃) δ: 7.75 (s, 2H, Ar-H), 7.50 (s, 1H, triazole H), 2.82 (t, J = 7.5 Hz, 2H, -CH₂CH₂CH₂CH₃), 1.70-1.76 (m, 2H, -CH₂CH₂CH₂CH₃), 1.37-1.44 (m, 2H, -CH₂CH₂CH₂CH₃), 0.94 (t, J=7.2Hz, 3H, -CH₂CH₂CH₂CH₃); ¹³C-NMR (CDCl₃) δ: 148.4, 136.2, 134.7, 133.6 (q, J = 34.3 Hz), 125.6, 122.3, 121.8 (q, J = 272.1 Hz), 31.0, 24.9, 21.9, 13.5; IR (KBr, cm⁻¹) v: 3077 (ArH), 2963, 2930 (CH₃), 2863 (CH₂); Anal. Calcd. (%) for C₁₃H₁₂Cl₂F₃N₃: C, 46.17; H, 3.58; N, 12.43. Found: C, 46.20; H, 3.53; N, 12.46.

1-((2,6-Dichloro-4-trifluoromethyl) phenyl)-4-trimethylsilanyl-1H-[1,2,3]-triazole (5c). White solid; yield: 88%; M.p. 131-132 °C; $^1\text{H-NMR}$ (CDCl_3) δ : 7.79 (s, 2H, Ar-H), 7.73 (s, 1H, triazole H), 0.42 (s, 9H, $-\text{CH}_3$); $^{13}\text{C-NMR}$ (CDCl_3) δ : 146.7, 136.0, 134.7, 133.6 (q, $J = 34.2$ Hz), 130.4, 125.7, 121.8 (q, $J = 272.6$ Hz), -1.35; IR (KBr, cm^{-1}) ν : 3111(ArH), 2962 (CH_3); Anal. Calcd. (%) for $\text{C}_{12}\text{H}_{12}\text{Cl}_2\text{F}_3\text{N}_3\text{Si}$: C, 40.69; H, 3.41; N, 11.86. Found: C, 40.61; H, 3.51; N, 11.91.

2-[1-(2,6-Dichloro-4-trifluoromethylphenyl)-1H-[1,2,3]-triazole-4-yl]-propan-2-ol (5d). White solid; yield: 86%; M.p. 83-85 °C; $^1\text{H-NMR}$ (CDCl_3) δ : 7.75 (s, 2H, Ar-H), 7.70 (s, 1H, triazole H), 3.32 (br, 1H, O-H), 1.70 (s, 6H, $-\text{CH}_3$); $^{13}\text{C-NMR}$ (CDCl_3) δ : 155.8, 136.0, 134.7, 133.6 (q, $J = 34.5$ Hz), 130.5, 125.7, 121.8 (q, $J = 271.6$ Hz), 68.4, 30.2; IR (KBr, cm^{-1}) ν : 3370 (OH), 3115 (ArH), 2958 (CH_3); Anal. Calcd. (%) for $\text{C}_{12}\text{H}_{10}\text{Cl}_2\text{F}_3\text{N}_3\text{O}$: C, 42.38; H, 2.96; N, 12.35. Found: C, 42.41; H, 2.88; N, 12.46.

1-[1-(2,6-Dichloro-4-trifluoromethylphenyl)-1H-[1,2,3]-triazole-4-ylmethyl]-diethyl-amine (5e). Light reddish solid; yield: 82%; M.p. 90-92 °C; $^1\text{H-NMR}$ (CDCl_3) δ : 7.76 (s, 2H, Ar-H), 7.65 (s, 1H, triazole H), 3.93 (s, 2H, $-\text{CH}_2-$), 2.57 (q, $J = 6.9$ Hz, 4H, $-\text{CH}_2\text{CH}_3$), 1.10 (t, $J = 6.9$ Hz, 6H, $-\text{CH}_2\text{CH}_3$); $^{13}\text{C-NMR}$ (CDCl_3) δ : 145.4, 135.9, 134.7, 133.6 (q, $J = 334.5$ Hz), 125.8, 124.2, 121.8 (q, $J = 272.0$ Hz), 47.2, 46.8, 11.9; IR (KBr, cm^{-1}) ν : 3112 (ArH), 2961 (CH_3), 2866 (CH_2); Anal. Calcd. (%) for $\text{C}_{14}\text{H}_{12}\text{Cl}_2\text{F}_3\text{N}_4$: C, 45.79; H, 4.12; N, 15.26. Found: C, 45.69; H, 4.20; N, 15.32.

4-(1-Cyclohexenyl)-1-((2,6-dichloro-4-trifluoromethyl) phenyl)-1H-[1,2,3]-triazole (5f). Light yellow solid; yield: 87%; M.p. 109-111 °C; $^1\text{H-NMR}$ (CDCl_3) δ : 7.77 (s, 2H, Ar-H), 7.62 (s, 1H, triazole H), 6.68-6.71 (m, 1H, =CH), 2.42-2.47 (m, 2H), 2.23-2.27 (m, 2H), 1.68-1.82 (m, 4H); $^{13}\text{C-NMR}$ (CDCl_3) δ : 149.4, 136.1, 134.7, 133.6 (q, $J = 34.6$ Hz), 126.3, 126.1, 125.7, 121.8 (q, $J = 272.2$ Hz), 119.7, 26.1, 25.4, 22.2, 21.9; IR (KBr, cm^{-1}) ν : 3135 (ArH), 3016 (=CH), 2836 (CH_2), 1635 (C=C); Anal. Calcd. (%) for $\text{C}_{15}\text{H}_{12}\text{Cl}_2\text{F}_3\text{N}_3$: C, 49.74; H, 3.34; N, 11.60. Found: C, 49.83; H, 3.27; N, 11.71.

1-[1-(2,6-Dichloro-4-trifluoromethylphenyl)-1H-[1,2,3]-triazole-4-yl]-cyclohexanol (5g). White solid; yield: 85%; M.p. 129-130 °C; $^1\text{H-NMR}$ (CDCl_3) δ : 7.77 (s, 2H, Ar-H), 7.72 (s, 1H, triazole H), 2.86 (br, 1H, O-H), 2.04-2.14 (m, 2H), 1.41-1.97 (m, 6H), 1.24-1.38 (m, 2H); $^{13}\text{C-NMR}$ (CDCl_3) δ : 147.5, 136.5, 134.7, 133.6 (q, $J = 33.8$ Hz), 125.8, 124.6, 121.8 (q, $J = 272.2$ Hz), 75.1, 40.2, 27.6, 18.3; IR (KBr, cm^{-1}) ν : 3380 (OH), 3114 (ArH), 2825 (CH_2); Anal. Calcd. (%) for $\text{C}_{15}\text{H}_{14}\text{Cl}_2\text{F}_3\text{N}_3\text{O}$: C, 47.39; H, 3.71; N, 11.05. Found: C, 47.27; H, 3.83; N, 11.00.

[1-(2,6-Dichloro-4-trifluoromethylphenyl)-1H-[1,2,3]-triazole-4-yl]-methanol (5h). White solid; yield: 87%; M.p. 130-131 °C; $^1\text{H-NMR}$ (CDCl_3) δ : 7.81 (s, 1H, triazole H), 7.77 (s, 2H, Ar-H), 4.92 (d, $J = 5.7$ Hz, 2H, $-\text{CH}_2$), 4.06 (br, 1H, O-H); $^{13}\text{C-NMR}$ (CDCl_3) δ : 148.0, 136.0, 134.1, 133.8 (q, $J = 34.6$ Hz), 125.8, 123.7, 121.8 (q, $J = 272.0$ Hz), 55.9; IR (KBr, cm^{-1}) ν : 3370 (OH), 3115 (ArH), 2832 (CH_2); Anal. Calcd. (%) for $\text{C}_{10}\text{H}_6\text{Cl}_2\text{F}_3\text{N}_3\text{O}$: C, 38.49; H, 1.94; N, 13.46. Found: C, 38.47; H, 1.96; N, 13.51.

4-Benzyloxymethyl-1-((2,6-dichloro-4-trifluoromethyl) phenyl)-1H-[1,2,3]-triazole (5i). White solid. yield: 88%; M.p. 72-73 °C; $^1\text{H-NMR}$ (CDCl_3) δ : 7.80 (s, 2H, Ar-H), 7.77 (s, 1H, triazole H), 7.38-7.40

(m, 5H), 4.84 (s, 2H), 4.69 (s, 2H); ^{13}C -NMR (CDCl_3) δ : 145.5, 137.3, 134.7, 133.6 (q, $J = 33.6$ Hz), 128.3, 127.8, 127.7, 125.7, 124.22, 121.8 (q, $J = 272.3$ Hz), 119.5, 72.5, 63.3; IR (KBr, cm^{-1}) ν : 3112 (ArH), 2835 (CH_2); Anal. Calcd. (%) for $\text{C}_{17}\text{H}_{12}\text{Cl}_2\text{F}_3\text{N}_3\text{O}$: C, 50.77; H, 3.01; N, 10.45. Found: C, 50.88; H, 3.10; N, 10.48.

4-Bromomethyl-1-((2,6-dichloro-4-trifluoromethyl)phenyl)-1H-[1,2,3]-triazole (5j). White solid. yield: 83%; M.p. 135-137 °C; ^1H -NMR (CDCl_3) δ : 7.81 (s, 2H, $J = 8.0$ Hz, Ar-H), 7.79 (s, 1H, triazole H), 4.70 (s, 2H, $-\text{CH}_2$); ^{13}C -NMR (CDCl_3) δ : 146.5, 136.1, 134.7, 133.6 (q, $J = 33.8$ Hz), 125.8, 124.6, 121.8 (q, $J = 272.0$ Hz), 21.6; IR (KBr, cm^{-1}) ν : 3316 (ArH), 2825 (CH_2); Anal. Calcd. (%) for $\text{C}_{10}\text{H}_5\text{BrCl}_2\text{F}_3\text{N}_3$: C, 32.03; H, 1.34; N, 11.21. Found: C, 32.16; H, 1.25; N, 11.24.

1-(4-Fluorophenyl)-4-phenyl-1H-[1,2,3]-triazole (5k). White solid. yield: 91%; M.p. 157-158 °C; ^1H -NMR (CDCl_3) δ : 7.85 (s, 1H, triazole H), 7.77 (d, 2H, Ar-H), 7.47-7.52 (m, 4H, Ar-H), 7.39 (m, 1H, Ar-H), 7.25-7.29 (m, 2H, Ar-H); ^{13}C -NMR (CDCl_3) δ : 147.8, 137.3, 134.7, 129.4 (q, $J = 8.6$ Hz), 129.6, 129.2, 127.9, 125.8, 121.2, 116.2 (q, $J = 21.7$ Hz); IR (KBr, cm^{-1}) ν : 3111, 1596 (ArH); Anal. Calcd. (%) for $\text{C}_{14}\text{H}_{10}\text{FN}_3$: C, 70.28; H, 4.21; N, 17.56. Found: C, 70.16; H, 4.32; N, 18.32.

4-Butyl-1-(4-fluorophenyl)-1H-[1,2,3]-triazole (5l). White solid. yield: 90%; M.p. 54-55 °C; ^1H -NMR (CDCl_3) δ : 7.83 (s, 1H, triazole H), 7.74-7.79 (m, 2H, Ar-H), 7.44-7.53 (m, 2H, Ar-H), 2.82 (t, $J = 7.5$ Hz, 2H, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 1.70-1.74 (m, 2H, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 1.38-1.44 (m, 2H, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 0.89 (t, $J = 7.2$ Hz, 3H, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$); ^{13}C -NMR (CDCl_3) δ : 146.7, 137.3, 132.7, 129.4 (q, $J = 8.6$ Hz), 129.2, 116.2 (q, $J = 21.7$ Hz), 31.0, 24.9, 21.9, 13.5; IR (KBr, cm^{-1}) ν : 3087 (ArH), 2961, 2930 (CH_3), 2863 (CH_2); Anal. Calcd. (%) for $\text{C}_{12}\text{H}_{14}\text{FN}_3$: C, 65.74; H, 6.44; N, 19.16. Found: C, 65.89; H, 6.55; N, 19.07.

4-Phenyl-1-(4-(trifluoromethyl)phenyl)-1H-[1,2,3]-triazole (5m). White solid. yield: 92%; M.p. 158-160 °C; ^1H -NMR (CDCl_3) δ : 7.91 (d, $J = 8.5$ Hz, 2H, Ar-H), 7.79-7.81 (m, 4H, Ar-H), 7.73 (s, 1H, triazole H), 7.41-7.52 (m, 3H, Ar-H); ^{13}C -NMR (CDCl_3) δ : 146.8, 137.9, 134.7, 132.7 (q, $J = 34.6$ Hz), 129.4, 128.6, 128.0, 125.8, 121.8 (q, $J = 272.2$ Hz), 121.2, 119.9; IR (KBr, cm^{-1}) ν : 3088, 1596 (ArH); Anal. Calcd. (%) for $\text{C}_{15}\text{H}_{10}\text{F}_3\text{N}_3$: C, 62.29; H, 3.48; N, 14.53. Found: C, 62.11; H, 3.58; N, 14.68.

4-Butyl-1-(4-(trifluoromethyl)phenyl)-1H-[1,2,3]-triazole (5n). White solid. yield: 91%; M.p. 57-58 °C; ^1H -NMR (CDCl_3) δ : 7.89 (d, $J = 8.5$ Hz, 2H, Ar-H), 7.79 (d, $J = 8.5$ Hz, 2H, Ar-H), 7.76 (s, 1H, triazole H), 2.82 (t, $J = 7.5$ Hz, 2H, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 1.70-1.75 (m, 2H, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 1.37-1.44 (m, 2H, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 0.94 (t, $J = 7.2$ Hz, 3H, $-\text{CH}_2\text{CH}_2\text{CH}_2\text{CH}_3$); ^{13}C -NMR (CDCl_3) δ : 147.4, 136.2, 134.5, 133.5 (q, $J = 34.4$ Hz), 126.6, 122.3, 121.0 (q, $J = 272.1$ Hz), 31.0, 24.7, 21.8, 13.5; IR (KBr, cm^{-1}) ν : 3079 (ArH), 2966, 2926 (CH_3), 2870 (CH_2); Anal. Calcd. (%) for $\text{C}_{13}\text{H}_{14}\text{F}_3\text{N}_3$: C, 57.99; H, 5.24; N, 15.61. Found: C, 56.81; H, 5.34; N, 15.80.

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18. CCDC 668922 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge, CB2 1EZ, UK; E-mail: deposit@ccdc.cam.ac.uk

Sample Availability: Samples of the compounds **5a-n** are available from the authors.

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