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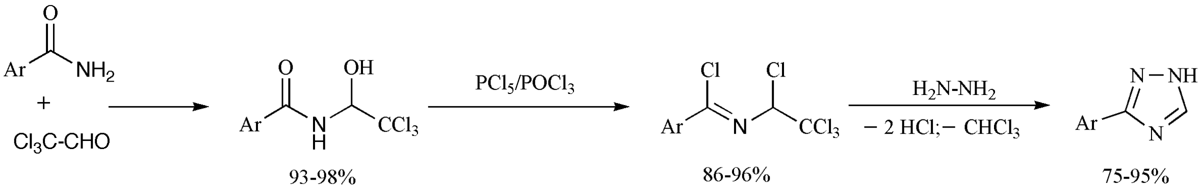
Ar
NH2
+
Cl3C-CHO
Ar
N
H
OH
CCl3
93-98%
PCl5/POCl3
Cl
Cl
Ar
N
CCl3
86-96%
H2N-NH2
− 2 HCl;− CHCl3
Ar
N − NH
N
75-95%

A new, high-yield synthesis of 3-aryl-1,2,4-triazoles

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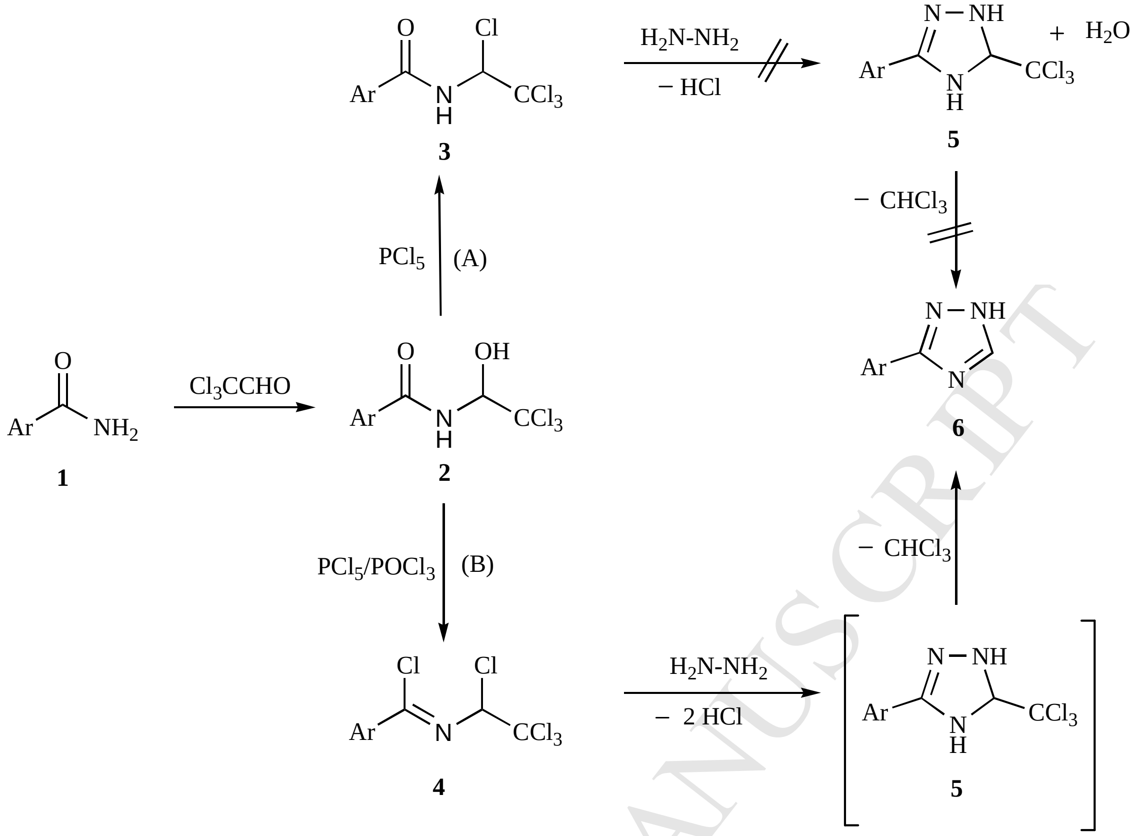
Abstract- A convenient new synthetic approach to 3-aryl-1,2,4-triazoles has been developed. Chloralamides were obtained by high yield reactions between benzamides and chloral hydrate. These reacted with a phosphorus pentachloride/phosphorus oxychloride mixture undergoing a near quantitative conversion to N-(1,2,2,2-tetrachloroethyl)benzimidoyl chlorides, which were treated with hydrazine hydrate to directly give 3-aryl-1,2,4-triazoles in high to quantitative yields. The formation of these products involves a double condensation process followed by a spontaneous β-elimination of chloroform. The molecular structure of 1-(4-chlorobenzoyl)-3-(4-methoxyphenyl)-1,2,4-triazole was determined by X-ray crystallography. Theoretical computational studies on aromatization of 3-aryl-5-trichloromethyl-1,2,4-triazolines via chloroform elimination and to determine relative stabilities of 3-phenyl-1,2,4-triazole tautomers were performed using ab initio, density functional (B3LYP), Moller-Plesset (MP2), and the thermochemical recipe T1.

1. Introduction

The synthesis and properties of 1,2,4-triazoles have been thoroughly reviewed,[1-24] showing that the presence of a triazole nucleus is essential for a wide assortment of biological activities and pharmacological applications. It should also be noted that 3-aryl-1,2,4-triazoles are currently being used as intermediates in a variety of chemical and medicinal chemistry works.[25-33] Regarding the synthesis of these substances, the first preparation[34,35] of the parent compound, 3-phenyl-1,2,4-triazole, was carried out by oxidation of 2-benzylidene-1-methylhydrazinecarboxamide to 5-hydroxy-1-methyl-3-phenyl-1,2,4-triazole, which was treated with phosphorus pentasulfide to give the final product in a very unsatisfactory yield.[36] Reactions between benzoylhydrazides and formamide or between formylhydrazide and benzamides were also found to be of little synthetic utility.[37] 3-Phenyl-1,2,4-triazole and some other similar ones were obtained through a fairly efficient procedure involving reactions of aroylisothiocyanates with hydrazines to give the corresponding 3-aryl-1,2,4-triazol-5-thioles, which were subjected to desulfuration with Raney nickel leading to the targeted products.[36] Reactions of benzamides with N,N-dimethylformamide dimethyl acetal gave N'-benzoyl-N,N-dimethylamidines, whose treatment with hydrazines led to isolable intermediates that when they were subjected to high temperature cyclized giving the corresponding triazoles in better yields.[38,39] In this paper we report a new, high-yield synthetic approach to 3-aryl-1,2,4-triazoles starting from chloral, which is an inexpensive multipurpose starting material for organic synthesis.[40]

On studying reactions of trichloroethylideneacetophenones with benzamidines, we noticed the formation of isolable 2,4-diaryl-6-trichloromethyl-1,6-dihidropyrimidines, whose treatment with potassium tert-butoxide promoted aromatization processes via β-elimination of chloroform to give 2,4-diarylpyrimidines in high yields.[41,42] These successful results strongly suggested continuing this promising line of work. Thus, we envisioned a new preparative methodology for 3-aryl-1,2,4-triazoles based on chloralamides **2**, which are available by facile near quantitative reactions[43,44] between chloral and carboxamides **1** (Scheme 1). First, compounds **2** would be converted to *N*-(1,2,2,2-tetrachloroethyl)benzamides **3** by treatment with phosphorous pentachloride.[44] Secondly reactions of compounds **3** with hydrazine were found to be unsuccessful for generating trichloromethyltriazolines **5** neither aryltriazoles **6**, leading to a complex mixture of unidentified products. Alternatively, intermediates **2** were efficiently transformed to N-(1-chloro-2,2,2-trichloroethyl)benzimidoyl chlorides **4**, which reacted with hydrazine directly yielding 3-aryl-1,2,4-triazoles **6** in whose formation undetected 3-aryl-5-trichloromethyl-2-triazolines **5** intermediates would participate.



Scheme 1. Synthesis of compounds **2**, **4** and **6**.

2. Results and discussion

Chloralbenzamides **2** and N-(1,2,2,2-tetrachloroethyl)benzamides **3** were sequentially synthesized in high yields as previously reported[44] by heating of benzamides and chloral hydrate mixtures followed by treatment of the obtained reaction adducts with phosphorous pentachloride. In an earlier work, we had recognized that compounds **3** undergo clean and efficient reactions with primary amines leading to N-(1-amino-2,2,2-trichloroethyl)benzamides.[45] On the other hand, it was take into account that thermal cyclodehydration of N-(2-aminoethyl)benzamides are able to produce the corresponding 2-arylimidazolines.[46] Therefore, one would expect that reactions of compounds **3** with hydrazine might provide 3-aryl-5-trichloromethyl-1,2,4-triazolines **5** (Scheme 1, route A), whose chemical behaviour could be expected to be similar to that we observed in the synthesis of 2,4-diarylpyrimidines,[41,42] in this case chloroform eliminations giving 3-aryl-1,2,4-triazoles **6**. Nevertheless, this possibility of conversion was discarded since experiments led to a complex mixture of unidentified reaction products. These disappointing results could perhaps be caused by a relatively low electrophilic activity at the carbonyl centre, thus offering an opportunity for adverse competitive reactions. In order to overcome this difficulty we designed an alternative synthesis (route B), involving more active electrophilic that a carbonyl amide group, such as imidoyl chloride function. Focusing the work on preparing N-(1,2,2,2-tetrachloroethyl)benzimidoyl chlorides **4**, reaction of chloralamides **2** with phosphorus pentachloride carried out in carbon tetrachloride solutions has been the only reported preparing method.[47] In spite of the attractive structure of compounds **4**, clearly favourable to undergo reactions with dienucleophiles to close heterocyclic rings, these reagents remain scarcely exploited, perhaps due to the lack of a good preparative procedure for them. Low to moderate yields, generation of impurities, and difficulty of purification were the main problems we found when working with this method. However, we improved it by treatment of compounds **2** with a mixture of phosphorus pentachloride and phosphorus oxychloride in the absence of carbon tetrachloride. Fortunately, this more active chlorinating agent was found to be able to obtain the targeted compounds in high to near quantitative yields (Table 1). Advantageously, a simple extraction allows the isolation of intermediates **4** in a high pure state, sufficient for use without needing any purification.

Table 1. Products **4**,**6** and yields.

entry	**Ar**	**4 (%)**	**6 (%)**
a	C_6H_5	98	82
b	2-ClC_6H_4	98	87
c	$3\text{-O}_2NC_6H_4$	95	95
d	$3,5\text{-(O}_2N)_2C_6H_3$	91	75
e	$2\text{-CH}_3C_6H_4$	81	95
f	3-FC_6H_4	86	84
g	$4\text{-CH}_3OC_6H_4$	93	77
h	$4\text{-O}_2NC_6H_4$	94	86
i	$4\text{-CH}_3C_6H_4$	88	79
j	4-ClC_6H_4	90	93

When compounds **4** were treated with hydrazine hydrate at room temperature the progressive formation of single products was observed in all cases. After isolation and purification they were identified as the corresponding 3-aryl-1,2,4-triazoles **6** instead of the expected triazolines **5**. Yields ranged from high to near quantitative (Table 1). As far as we know, this is the first time that triazoles have been synthesized starting from chloral. Single crystals suitable for an X-ray diffraction analysis of any of the prepared aryltriazoles **6** could not be obtained despite intensive effort. Instead, we were successful in analyzing a 4-chlorobenzoyl derivative of **6g**. The molecular structure determined corresponds to 1-(4-chlorobenzoyl)-3-(4-methoxyphenyl)-1,2,4-triazole **7** (Fig. 1).

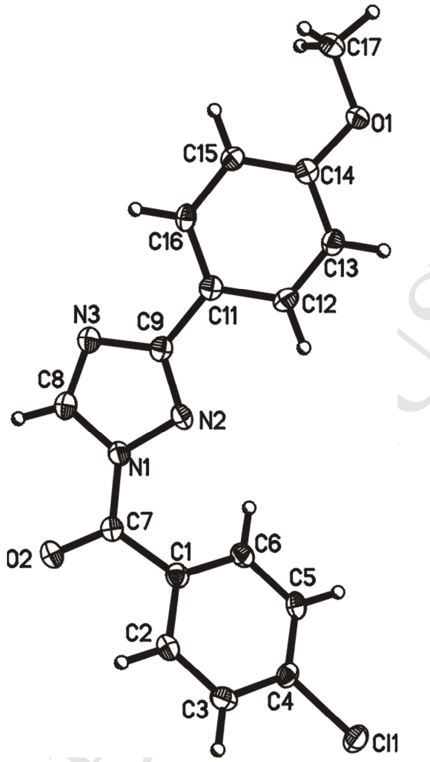
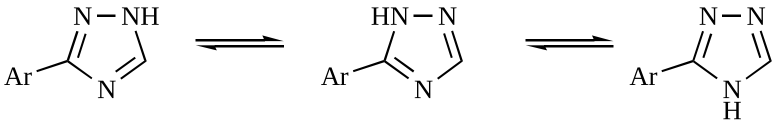


Figure 1. Thermal ellipsoid plot (50% level) of compound **7** in the crystal.

It should be noted that in a previous work we reported that reactions of trichloroethylideneacetophenones with benzamidines followed by dehydration lead to isolable 2,4-diaryl-6-trichloromethyl-1,6-dihidropyrimidines, which needed treatment with a strong base, such as potassium *t*-butoxide, to promote aromatization by chloroform elimination.[41,42] However, 3-aryl-5-trichloromethyl-1,2,4-triazolines **5** were non detectable intermediates in the direct synthetic process of triazoles **6** described here. This contrast evidences a greater proclivity to undergo loss of chloroform from **5** than from trichloromethyldihidropyrimidines. This experimental observation has been found to be fully consistent with a comparative theoretical DFT computational study[48] carried out at the B3LYP/6-311++G(d,p) level, where aromatization by chloroform elimination from **5a** is a more exothermic process (-15.77 kcal/mol) than from 2,4-diphenyl-6-trichloromethyl-1,6-dihidropyrimidine (-9.24 kcal/mol).



6(1) **6(2)** **6(3)**

Scheme 2. Tautomeric forms of 3-aryl-1,2,4-triazoles **6**.

In order to gain further insights into the structure and relative populations of tautomers (Scheme 2) in samples of triazoles **6** subjected to NMR spectroscopy, computational calculations[48] were carried out on the parent compound **6a** (Ar= Ph) using different methods: ab initio (HF), density functional (B3LYP), Moller-Plesset (MP2), and the thermochemical recipe T1. Two basis sets of different sizes, 6-31G(d) and 6-311++G(d,p), were applied. All procedures gave similar results, showing completely planar structures for the three tautomeric forms, but with significant differences in stability. Thus, at the B3LYP/6-311++G(d,p) level **6a**(**1**) is the most stable tautomer (rel. E= 0 kcal/mol) exhibiting a relative stability very close to 6a(2) (rel. E= 0.2 kcal/mol), whereas **6a**(**3**) is the most unstable tautomer (rel. E= 7.17 kcal/mol). From the Boltzmann distribution law it can be concluded that, at room temperature, isomers **6a**(**1**) and **6a**(**2**) would be in a comparable ratio (about 58% and 42%, respectively), whereas the presence of **6a**(**3**) would be negligible.

Finally, the accuracy of the above computational methodology was checked by comparing the molecular structure obtained by X-ray crystallography of **7** (Figure 1) and the corresponding calculated molecular structure. An excellent agreement for bond lengths and bond angles was found, as is shown in Table 2.

Table 2. Selected bond lengths and bond angles of crystal and calculated structures in crystal structure of compound **7**

Bond	**Calculated[a](Å)**	**Crystal[b](Å)**	**Angle**	**Calculated[a](º)**	**Crystal[b](º)**
N1-C8	1.371	1.367	C9-N2-N1	103.19	102.79
N1-N2	1.370	1.328	C8-N3-C9	103.72	102.85
N1-C7	1.426	1.415	C14-O1-C17	118.79	116.71
N2-C9	1.322	1.310	O2-C7-C1	117.49	117.99
N3-C8	1.303	1.305	O2-C7-C1	122.85	122.42
N3-C9	1.384	1.392	N1-C7-C1	119.67	119.58
Cl1-C4	1.754	1.739	N3-C8-N1	110.39	110.78
O1-C14	1.361	1.367	N2-C9-N3	113.89	114.75
O1-C17	1.423	1.430	N2-C9-C11	123.49	122.67
O2-C7	1.212	1.209	C6-C1-C2	119.15	119.28
C1-C17	1.426	1.415	O1-C14-C15	124.68	123.98
C9-C11	1.463	1.467	O1-C14-C13	115.70	116.01

a) Geometry optimized at the B3LYP/6-311++G(d,p) level; b) Crystal structure

3. Conclusions

To conclude, an excellent new synthetic method on 1,2,4-triazole chemistry is reported. Versatility, good yields, easy availability of starting materials, mildness and a simple experimental procedure are noteworthy advantages of this approach. The development of syntheses for some other classes of heterocycles by applying a similar strategy also appears feasible.

4. Experimental Section

4.1. General

NMR spectra were determined on Bruker AV-200, Bruker AV-300 or Bruker AV-400 with tetramethylsilane as internal reference. High-resolution mass spectra (HRMS) were obtained using a time-of-flight (TOF) instrument equipped with electrospray ionization (ESI). IR spectra were recorded on a Nicolet Impact 400 Spectrometer. Microanalyses were performed on a Carlo Erba EA- 1108 analyzer. Melting points were determined on a Büchi Melting point B-540, and are uncorrected. Chloralbenzamides **2** and N-(1,2,2,2-tetrachloroethyl)benzamides **3** were prepared as previously described.[44]

All computations were performed with the Spartan’14 package program.[48] The most stable conformers were determined with the MMFF molecular mechanics method. Next, these conformers were used as input for ab initio molecular orbital and density functional theory calculations of geometry optimizations at the HF, B3LYP, and MP2 levels of theory with the 6-31G(d) and 6-311++G(d,p) basis sets. There were no significant differences between the results obtained with the different procedures.

4.2. General procedure for the synthesis of N-(1,2,2,2-tetrachloroethyl)benzimidoyl chlorides 4

To a solution of compound **2** (16 mmol) in phosphorus oxychloride (25 mL) phosphorus pentachloride (39 mmol) was added in small portions. The reaction mixture was refluxed for 2 h, cooled, and carefully added to crushed ice-water (300 mL). Then, chloroform (300 mL) was added and the mixture was vigorously stirred for 5 min, the organic layer was separated, dried, and evaporated under low pressure, leaving compound **4** as a highly pure pale green oil.

4.2.1. *N-(1,2,2,2-tetrachloroethyl)benzimidoyl chloride* ***(4a)****.* $C_9H_6Cl_5N$ (305.42). ^1H NMR δ ($CDCl_3$, 200 MHz): 6.17 (s, 1H), 7.44-7.64 (m, 3H), 8.14-8.18 (m, 2H); ^{13}C NMR δ ($CDCl_3$, 50.4 MHz): 83.30 (CH), 99.87 (C), 128.73 (CH), 129.90 (CH), 133.46 (CH), 134.39 (C), 153.61 (C); MS (EI) m/z (%): 268 (M^+ -Cl, 7), 198 (26), 188 (43), 186 (42), 149 (25), 104 (100); IR (Nujol): 1642, 1448, 1306, 1225, 1065, 1030, 904, 832, 767, 749, 685, 665, 623, 542 cm^{-1}.

4.2.2. *N-(1,2,2,2-tetrachloroethyl)-3-chlorobenzimidoyl chloride* ***(4b)****.* $C_9H_5Cl_6N$ (339.86). ^1H NMR δ ($CDCl_3$, 200 MHz): 6.14 (s, 1H), 7.34-7.49 (m, 3H), 7.58-7.61 (m, 1H); ^{13}C NMR δ ($CDCl_3$, 50.4 MHz): 83.03 (CH), 99.22 (C), 126.90 (CH), 130.37 (CH), 130.77 (CH), 132.15 (CH), 132.27 (C), 135.70 (C), 151.25 (C); MS (EI) m/z (%): 302 (M^+ -Cl, 3), 270 (21), 268 (16), 232 (19), 222 (56), 167 (16), 138 (100); IR (Nujol): 1660, 1590, 1471, 1438, 1304, 1269, 1224, 1058, 1023, 905, 831, 756, 727, 709, 647 cm^{-1}.

4.2.3. *N-(1,2,2,2-tetrachloroethyl)-3-nitrobenzimidoyl chloride* ***(4c)****.* $C_9H_5Cl_5N_2O_2$ (350.41). ^1H NMR δ ($CDCl_3$, 200 MHz): 6.15 (s, 1H), 7.68-7.75 (m, 1H), 8.43-8.53 (m, 2H), 8.95-8.97 (m, 1H); ^{13}C NMR δ ($CDCl_3$, 50.4 MHz): 82.86 (CH), 99.39 (C), 124.73 (CH), 127.72 (CH), 129.98 (CH), 135.08 (CH), 136.00 (C), 148.46 (C), 151.26 (C); MS (EI) m/z (%): 313 (M^+ -Cl, 8), 243 (19), 231 (100), 197 (23), 149 (87); IR (Nujol): 1645, 1612, 1577, 1532, 1473, 1348, 1223, 1067, 951, 849, 835, 751, 705, 676, 649 cm^{-1}.

4.2.4. *N-(1,2,2,2-tetrachloroethyl)-3,5-dinitrobenzimidoyl chloride* ***(4d)****.* $C_9H_4Cl_5N_3O_4$ (395.41). ^1H NMR δ ($CDCl_3$, 200 MHz): 6.16 (s, 1H), 9.26 (s, 3H); ^{13}C NMR δ ($CDCl_3$, 50.4 MHz): 82.59 (CH), 98.98 (C), 122.48 (CH), 129.17 (CH), 137.78 (C), 148.83 (C), 149.21 (C); MS (EI) m/z (%): 358 (M^+ -Cl, 7), 280 (18), 278 (91), 276 (99), 196 (15), 167 (40); IR (Nujol): 1647, 1593, 1546, 1343, 1309, 1244, 1118, 1071, 994, 918, 834, 753, 732, 715, 669, 545 cm^{-1}.

4.2.5. *N-(1,2,2,2-tetrachloroethyl)-2-methylbenzimidoyl chloride* ***(4e)****.* $C_{10}H_8Cl_5N$ (319.44). ^1H NMR δ ($CDCl_3$, 300 MHz): 2.54 (s, 3H), 6.07 (s, 1H), 7.17-7.20 (m, 2H), 7.21-7.29 (m, 1H), 7.33 (dd, 1H, J= 7.4, J= 1.4 Hz, Hz); ^{13}C NMR δ ($CDCl_3$, 75.4 MHz): 21.86 (CH_3), 83.57 (CH), 99.49 (C), 125.93 (CH), 130.54 (CH), 131.57 (CH), 134.89 (C), 138.37 (C), 153.19 (C); MS (EI) m/z (%): 282 (M^+ -Cl, 19), 166.8 (26), 149

(59), 118 (100); IR (Nujol): 1646, 1569, 1457, 1303, 1222, 1069, 1025, 898, 830, 762, 750, 717, 658, 629, 573 cm^{-1}.

4.2.6. *N-(1,2,2,2-tetrachloroethyl)-3-fluorobenzimidoyl chloride **(4f)**.* $C_9H_5Cl_5FN$ (323.41). ^{1}H NMR δ ($CDCl_3$, 300 MHz): 6.11 (s, 1H), 7.24-7.47 (m, 2H), 7.80-7.94 (m, 2H); ^{13}C NMR δ ($CDCl_3$, 75.4 MHz): 83.07 (CH), 99.68 (C), 116.716 (CH, d, J= 24.4 Hz), 120.49 (CH, d, J= 21.3 Hz), 125.63 (CH, d, J= 2.9 Hz), 130.31 (CH, d, J= 8.0 Hz), 136.46 (C, d, J= 8.0 Hz), 152.22 (C, d, J= 3.4 Hz), 162.63 (C, d, J= 247.5 Hz); MS (EI) m/z (%): 286 (M^+ -Cl, 19), 218 (15), 216 (25), 204 (100), 167 (17), 122 (66); IR (Nujol): 1697, 1644, 1588, 1483, 1439, 1311, 1275, 1261, 1172, 1151, 1066, 1032, 967, 879, 833, 803, 750, 684, 661 cm^{-1}.

4.2.7. *N-(1,2,2,2-tetrachloroethyl)-4-methoxybenzimidoyl chloride **(4g)**.* $C_{10}H_8Cl_5NO$ (335.44): ^{1}H NMR δ ($CDCl_3$, 300 MHz): 3.89 (s, 3H), 6.16 (s, 1H), 6.96 (d, 2H, J= 9.1 Hz), 8.12 (d, 2H, J= 9.1 Hz); ^{13}C NMR δ ($CDCl_3$, 75.4 MHz): 55.69 (CH_3), 83.65 (CH), 100.10 (C), 114.04 (CH), 126.82 (C), 132.01 (CH), 152.90 (C), 163.97 (C); MS (EI) m/z (%): 298 (M^+ -Cl, 32), 230 (26), 228 (42), 219 (18), 165 (14), 135 (36), 134 (100), 119 (18), 90 (27); IR (Nujol): 1633, 1598, 1506, 1460, 1441, 1310, 1269, 1169, 1062, 1026, 905, 822, 750, 664, 608, 544 cm^{-1}.

4.2.8. *N-(1,2,2,2-tetrachloroethyl)-4-nitrobenzimidoyl chloride **(4h)**.* $C_9H_5Cl_5N_2O_2$ (350,41) ^{1}H NMR δ ($CDCl_3$, 200 MHz): 6.12 (s, 1H), 8.30 (br s, 4H); ^{13}C NMR δ ($CDCl_3$, 75.4 MHz): 82.71 (CH), 99.32 (C), 123.73 (CH), 130.71 (CH), 139.42 (C), 150.49 (C), 151.42 (C); MS (EI) m/z (%): 313 (M^+ -Cl, 3), 243 (45), 231 (100), 197 (35), 150 (84); IR (Nujol): 3453, 3101, 2947, 1666, 1610, 1573, 1529, 1443, 1310, 1229, 1062, 1030, 909, 831, 751, 644, 630, 558 cm^{-1}.

4.2.9. *N-(1,2,2,2-tetrachloroethyl)-4-methylbenzimidoyl chloride **(4i)**.* $C_{10}H_8Cl_5N$ (319.44); ^{1}H NMR δ ($CDCl_3$, 400 MHz): 2.43 (s, 3H), 6.16 (s, 1H), 7.25-7.29 (m, 2H), 8.03-806 (m, 2H); ^{13}C NMR δ ($CDCl_3$, 100.8 MHz): 21.70 (CH_3), 83.48 (CH), 100.00 (C), 129.45 (CH), 129.95 (CH), 131.77 (C), 144.46 (C), 153.53 (C), MS (EI) m/z (%): 282 (M^+ - Cl, 3), 182 (13), 149 (29), 119 (100), 65(53); IR (KBr): 3269, 1630, 1525, 1503, 1247, 1182, 1069, 1034, 905, 821, 786, 739, 706, 621, 612, 586 cm^{-1}.

4.2.10. *N-(1,2,2,2-tetrachloroethyl)-4-chlorobenzimidoyl chloride (**4j**).* $C_9H_5Cl_6N$ (339,86); ^1H NMR δ ($CDCl_3$, 200 MHz): 6.16 (s, 1H), 7.44 (d, 2H, J= 8.7 Hz), 8.08 (d, 2H, J= 8.7 Hz); ^{13}C NMR δ ($CDCl_3$, 75.4 MHz): 83.09 (CH), 99.64 (C), 128.97 (CH), 131.01 (CH), 132.69 (C), 139.99 (C), 152.31 (C), MS (EI) m/z (%): 302 (M^+ -Cl, 3), 270 (21), 268 (16), 232 (19), 222 (56), 167 (16), 138 (100); IR (KBr): 3070, 2938, 1661, 1590, 1471, 1438, 1304, 1269, 1224, 1058, 1023, 905, 831, 727, 709, 647,558 cm^{-1}.

4.3. General procedure for the synthesis 3-aryl-1,2,4-triazoles 6

A mixture of compound 4 (10 mmol) and hydrazine hydrate (50-60%, 5.0 mL), in chloroform (25 mL), was stirred at room temperature for 24 h and washed twice with water (50 mL). The organic solvent was removed under low pressure, leaving crude product **6** as a solid residue, which was purified by crystallization from the appropriate solvent.

4.3.1. *3-Phenyl-1,2,4-triazole (**6a**).* $C_8H_7N_3$ (145.16).Crystallization from isopropanol gave white needles; mp 118 ºC (Lit[34], mp 118.5-119 °C).^1H NMR δ ($CDCl_3$, 400 MHz): 7.36-7.43 (m, 3H), 7.98-8.02 (m, 2H), 8.23 (s, 1H), 11.48 (br s, 1H); ^{13}C NMR δ ($CDCl_3$, 50.4 MHz): 126.50 (CH), 128.36 (C), 128.89 (CH), 130.11 (CH), 147.51 (CH), 158.74 (C); IR (Nujol): 3445, 2918, 2776, 2724, 1563, 1474, 1407, 1272, 1112, 964, 866, 715, 687, 663, 495 cm^{-1}. HRMS (ESI) calcd for $C_8H_8N_3$ $(M+H)^+$: 146.0713. Found 146.0712.

4.3.2. *3-(3-Chlorophenyl)-1,2,4-triazole (**6b**).* $C_8H_6ClN_3$ (179.61). Crystallization from acetonitrile/toluene gave a beige powder; mp 153-154 ºC. ^1H NMR δ (DMSO-d_6, 70 ºC, 300 MHz): 7.42-7.57 (m, 3H), 7.80-7.83 (m, 1H), 8.39 (s, 1H), 13.95 (br s, 1H); ^{13}C NMR δ (DMSO-d_6, 70 ºC, 100.8MHz): 126.60 (CH), 129.18 (C), 129.85 (CH), 130.03 (CH), 130.89 (CH), 131.36 (C), 145.62 (CH), 156.64 (C); IR (Nujol): 3054, 2898, 2751, 2704, 1609, 1571, 1492, 1459, 1399, 1273, 1194, 1126, 1036, 997, 909, 767, 744, 671, 458 cm^{-1}. HRMS (ESI) calcd for $C_8H_7ClN_3$ $(M+H)^+$: 180.0323. Found 180.0322.

4.3.3. *3-(3-Nitrophenyl)-1,2,4-triazole (**6c**).* $C_8H_6N_4O_2$ (190.16). Crystallization from methanol gave pale yellow needles; mp 214 ºC. ^1H NMR δ (DMSO-d_6, 200 MHz): 7.74 (t, 1H, J= 8.0 Hz), 8.23 (d, 1H, J=7.8 Hz), 8.21-8.43 (m, 1H), 8.73 (s, 2H), 14.36 (br s, 1H); ^{13}C NMR δ (DMSO-d_6, 50.4MHz): 120.09 (CH), 123.51 (CH), 130.56 (CH), 131.89 (CH), 132.85(C), 145.14 (CH), 148.18 (C), 159.18 (C); IR (Nujol): 3318, 3132, 1534, 1508 1349, 1274, 1117, 1089, 981, 874, 743, 725, 672, 618, 463 cm^1. HRMS (ESI) calcd for $C_8H_5N_4O_2$ $(M-H)^-$: 189.0418. Found 189.0409.

4.3.4. *3-(3,5-Dinitrophenyl)-1,2,4-triazole* ***(6d)****.* $C_8H_5N_5O_4$ (235.16). Crystallization from methanol gave brown prisms; mp 252-254 ºC. ^1H NMR δ (DMSO-d_6 + TFA-d, 70 ºC, 400 MHz): 7.54-7.55 (m, 1H), 7.75-7.76 (m, 1H), 8.03-8.04 (m, 1H), 8.56 (s, 1H); ^{13}C NMR δ (DMSO-d_6 + TFA-d, 70 ºC, 100.8 MHz): 109.15 (CH), 109.34 (CH), 118.05 (CH), 131.72 (C), 145.62 (CH), 148.40 (C), 149.40 (C), 157.62 (C); IR (Nujol): 3456, 3375, 3219, 3113, 1629, 1617, 1528, 1502, 1484, 1346, 1266, 1013, 975, 861, 737, 662, 577, 452 cm^{-1}. HRMS (ESI) calcd for $C_8H_4N_5O_4$ $(M-H)^-$: 234.0269. Found 234.0261.

4.3.5. *3-(2-Methylphenyl)-1,2,4-triazole* ***(6e)****.* $C_9H_9N_3$ (159.19). Crystallization from isopropanol gave a pale yellow powder; mp 158-160 ºC. ^1H NMR δ (Pyr-d_5 + D_2O, 90 ºC, 200 MHz): 4.15 (s, 3H), 8.67-8.76 (m, 3H), 9.51-9.56 (m, 1H), 9.97 (s, 1H); ^{13}C NMR δ (DMSO-d_6 + TFA-d, 90 ºC, 100.8 MHz): 20.40 (CH_3), 125.79 (CH), 127.21 (C), 129.45 (CH), 129.75 (CH), 131.02 (CH), 136.94 (C), 144.86 (CH), 156.58 (C); IR (Nujol): 3090, 1611, 1565, 1534, 1516, 1456, 1403, 1185, 1169, 955, 870, 772, 729, 627, 631, 449 cm^{-1}. HRMS (ESI) calcd for $C_9H_{10}N_3$ $(M+H)^+$: 160.0869. Found 160.0876.

4.3.6. *3-(3-Fluorophenyl)-1,2,4-triazole* ***(6f)****.* $C_8H_6FN_3$ (163.15). Crystallization from isopropanol gave a beige powder; mp 111-113 ºC. ^1H NMR δ (DMSO-d_6 70 ºC, 200 MHz): 7.17-7.56 (m, 2H), 7.72-7.89 (m, 2H), 8.40 (s, 1H); ^{13}C NMR δ (DMSO-d_6, 100.8 MHz): 112.93 (CH, d, J= 23.0 Hz), 116.21 (CH, d, J= 21.0 Hz), 122.41 (CH), 131.22 (CH, d, J= 8.0 Hz), 133.24 (C), 146.90 (CH), 158.51 (C), 162.9 (C, d, J= 244.0 Hz); IR (Nujol): 3441, 3059, 2815, 2759, 1559, 1501, 1463, 1386, 1280, 1226, 1189, 1097, 1006, 860, 799, 738, 665, 527, 454 cm^{-1}. HRMS (ESI) calcd for $C_8H_7FN_3$ $(M+H)^+$: 164.0619. Found 164.0621.

4.3.7. *3-(4-Methoxyphenyl)-1,2,4-triazole (**6g**).* $C_9H_9N_3O$ (175.19). Crystallization from isopropanol gave white needles; mp 186 ºC (Lit,[36] mp 186 °C). ^1H NMR δ (DMSO-d_6 90 ºC, 400 MHz): 3.82 (s, 3H), 7.03 (d, 2H J= 9.2 Hz), 7.95 (d, 2H J= 9.2 Hz), 8.22 (s, 1H), 9.97 (br s, 1H); ^{13}C NMR δ (DMSO-d_6 90 ºC, 100.8 MHz): 54.85 (CH_3), 113.86 (CH), 122.08 (C), 127.09 (CH), 146.62 (CH), 157.10 (C), 159.98 (C); IR (Nujol): 3442, 2998, 2932, 2836, 2664, 1614, 1512, 1474, 1427, 1289, 1256, 1177, 1115, 1026, 991, 963, 836, 748, 613, 530 cm^{-1}. HRMS (ESI) calcd for $C_9H_{10}N_3O$ $(M+H)^+$: 176.0818. Found 176.0819.

4.3.8. *3-(4-Nitrophenyl)-1,2,4-triazole (**6h**).* $C_8H_6N_4O_2$ (190,16). Crystallization from ethanol gave a yellow powder; mp 226-229 ºC (Lit,[38] mp 228-229 °C). ^1H NMR δ (DMSO-d_6 90 ºC, 300 MHz): 8.27 (br, 4H), 8.54 (s, 1H); ^{13}C NMR δ (DMSO-d_6, 90 ºC, 75.4 MHz): 123.42 (CH), 126.40 (CH), 136.15 (C), 145.62 (CH), 147.31 (C), 157.57 (C); IR(KBr): 3354, 3318, 2940, 1602, 1577, 1514, 1436, 1337, 1317, 1097, 1066, 900, 865, 855, 778, 716, 696, 682,cm^{-1}. HRMS (ESI) calcd for $C_8H_5N_4O_2$ $(M-H)^-$: 189.0418. Found 189.0416.

4.3.9. *3-(4-Methylphenyl)-1,2,4-triazole (**6i**).* $C_9H_9N_3$ (159,19). Crystallization from isopropanol gave a light grey powder; mp 169-171 ºC. ^1H NMR δ (DMSO-d_6, 90 ºC, 400 MHz): 2.34 (s, 3H), 7.26 (d, 2H, J= 8.0 Hz), 7.90 (d, 2H, J= 8.0 Hz), 8.24 (s, 1H); ^{13}C NMR δ (DMSO-d_6 90 ºC, 100.8 MHz): 20.26 (CH_3), 125.51 (CH), 126.68 (C), 128.70 (CH), 138.31 (C), 146.64 (CH), 157.60 (C); IR (KBr): 3152, 3094, 2769, 2653, 1732, 1615, 1569, 1510, 1470, 1422, 1397, 1271, 1202, 1111, 992, 963, 821, 737, 701, 663 cm^{-1}. HRMS (ESI) calcd for $C_9H_{10}N_3$ $(M+H)^+$: 160.0869. Found 160.0873.

4.3.9. *3-(4-Chlorophenyl)-1,2,4-triazole (**6j**).* $C_8H_6ClN_3$ (179,61). Crystallization from chloroform/petroleum ether gave a white powder; mp 180-181 ºC (Lit,[36] mp 182 °C). ^1H NMR δ (DMSO-d_6 90 ºC, 400 MHz): 7.51 (d, 2H J= 8.4 Hz), 8.02 (d, 2H J= 8.4 Hz), 8.49 (s, 1H); ^{13}C NMR δ (DMSO-d_6 90 ºC, 100.8 MHz): 127.07 (CH), 127.96 (CH), 128.67 (C), 133.31 (C), 145.77 (CH), 157.34 (C); IR (KBr): 3431, 3085, 3043,2905, 2766, 2650, 1610, 1495, 1472, 1424, 1406, 1275, 1116, 1094,1013, 993, 960, 878, 830, 741, 698, 664 cm^{-1}. HRMS (ESI) calcd for $C_8H_7ClN_3$ $(M+H)^+$: 180.0323. Found 180.0321.

4.4. Preparation of 1-(4-chlorobenzoyl)-3-(4-methoxyphenyl)-1,2,4-triazole 7

To a stirred solution of 3-(4-methoxyphenyl)-1,2,4-triazole **6g** (0.57 mmol) and triethylamine (0.93 mmol) in dichloromethane (1 mL) a solution of p-chlorobenzoyl chloride (1.2 mmol) in dichloromethane (1 mL) was added. After 16 h the solvent was removed under reduced pressure leaving a residue that was washed with aqueous solution of sodium bicarbonate and crystallized from ethanol. (92%), white needles; mp 125-126 ºC. ^{1}H NMR δ ($CDCl_3$, 400 MHz): 3.82 (s, 3H), 6.95 (m, 2H), 7.50 (m, 2H), 8.07 (m, 2H), 8.28 (m, 2H), 9.03 (s, 1H); ^{13}C NMR δ ($CDCl_3$, 100.8 MHz): 55.46, 114.24, 122.02, 128.62, 128.75, 128.93, 133.42, 140.96, 146.52, 161.61, 163.64, 164.16; MS (EI) m/z (%): 313 (M^+, 35), 141 (63), 139 (100), 119 (9), 113 (20), 111 (53), 76 (11), 75 (18); IR (Nujol): 3121, 2972, 2839, 1703, 1614, 1507, 1372, 1249, 1170, 1092, 909, 838, 744, 657, 594, 516, 482 cm-1.

4.5. X-ray structure determination of compound 7

$C_{16}H_{12}ClN_3O_2$, M = 313.74, orthorhombic, a = 17.567(2) Å, b = 20.530(3) Å, c = 3.9152(5) Å, α = 90.00°, β = 90.00°, γ = 90.00°, V = 1412.0(3) Å^3, T = 100(2) K, space group *Pna*2*(*1*)*, Z = 4, 9038 reflections measured, 2980 independent reflections (R_{int} = 0.0296). *Data collection*: A colourless needle 0.43 × 0.12 × 0.08 mm was mounted in inert oil on a glass fibre and transferred to the cold gas stream of the diffractometer (Bruker SMART APEX). Measurements were performed to $2\theta_{max}$ 52° with monochromated Mo-$K\alpha$ radiation. Of 9038 measured reflections, 2980 were unique (R_{int} = 0.0296) and were used for all calculations. *Structure refinement*: The structures were refined anisotropically against F^2 (program SHELXL-97).[49] Hydrogen atoms were included with a riding model. The final $wR(F^2)$ values were 0.0927 for all data and 200 parameters, with a final R_1 value of 0.0395 ($I > 2\sigma(I)$). Δr 0.431 e/Å^3, S 1.125. Complete crystallographic data (excluding structure factors) have been deposited at the Cambridge Crystallographic Data Centre under the number CCDC 933675. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (0)1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

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