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Hydroarylation of (*E*)-5-(2-Arylethenyl)-2-methyl-2*H*-tetrazoles under Superelectrophilic Activation

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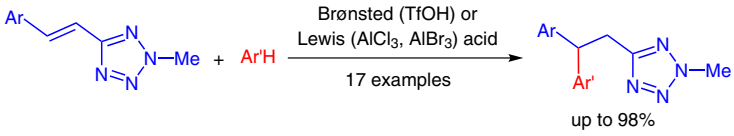

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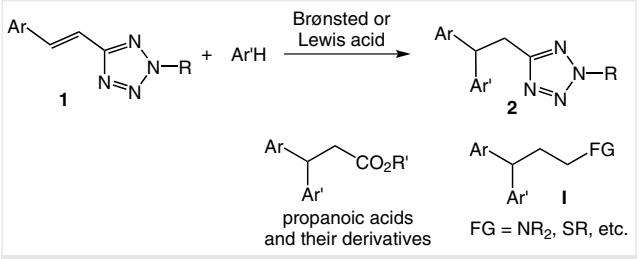
Abstract The reaction of 5-(2-arylethenyl)-2-methyl-2*H*-tetrazoles with arenes (benzene, xylenes, *tert*-butylbenzene, anisole, veratrole, 1,2-dichlorobenzene) under conditions of superelectrophilic activation under the action of Brønsted superacids (CF_3SO_3H, FSO_3H) or strong Lewis acids ($AlCl_3$, $AlBr_3$) leads regioselectively to the products of hydroarylation of the carbon–carbon double bond, viz., 5-(2,2-diarylethenyl)-2-methyl-2*H*-tetazoles, in yields of up to 95%.

Key words tetrazoles, superelectrophilic activation, hydroarylation, Brønsted superacid, Lewis superacid, Friedel–Crafts reaction

At the present time, the dynamic development of the chemistry of tetrazole is observed.[1] Tetrazole-containing compounds and compositions based on them find application as corrosion inhibitors,[2] components of energetic materials,[3] ionic liquids,[4] etc. They are used in schemes for the total synthesis of practically important compounds, the preparation of which by other ways is associated with serious experimental difficulties or impossible at all.[1,5–9] Vinyltetrazoles are also promising monomers for the synthesis of appropriate tetrazole-containing polymers.[1,4] Tetrazoles containing substituents at endocyclic nitrogen and carbon atoms exhibit antimicrobial,[5] antidiabetic,[6] and other types of the biological activity.

5-(2-Arylethenyl)-2-methyl-2*H*-tetrazoles (5-styryltetrazoles) containing a carbon–carbon double bond in the side chain can take part in chemical transformations with the participation of this multiple bond. Reactions of styryltetrazoles proceeding under superelectrophilic activation conditions with Brønsted or Lewis superacids are of special interest. In preliminary brief communications,[10] we showed that (*E*)-2-methyl-5-(2-phenylethenyl)-2*H*-tetrazole gave hydroarylation products of the C=C bond of the styryl fragment in electrophilic aromatic substitution with selected arenes under the action of the Brønsted superacid CF_3SO_3H (TfOH) or strong Lewis acids AlX_3 ($AlCl_3$, $AlBr_3$).

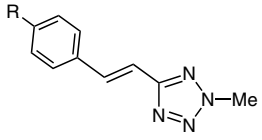
In general, the hydroarylation of 5-styryltetrazoles **1** gives rise to 5-(2,2-diarylethyl)tetrazoles **2** (Scheme 1). Compounds **2** are close structural analogues of substances **I** consisting of a chain of three carbon atoms and a functional group (FG) on its one end and two aryl substituents on the other one (Scheme 1). The structure **I** is general for many bioactive substances. Compounds **I**, in which FG = NR_2 exhibit antihistaminic, choleretic, and anti-anginal activities, and they are inhibitors of serotonin reuptake.[11] Propanoic acids and their derivatives possess properties of antagonists of endothelinic receptors of A type (ET_A), and are also characterized by a high affinity and selectivity to these receptors.[12] In the case, when FG = SR, compounds **I** show antitumor activity.[13] One may expect that 5-(2,2-diarylethyl)tetrazoles **2** containing the same structural fragments, viz., two aryl groups, three carbon atoms and four nitrogen atoms of the tetrazole ring, which can be considered as a



Scheme 1 Hydroarylation of 5-styryltetrazoles **1** leading to compounds **2**; general structure **I** for various biologically active compounds

functional group, may also exhibit various types of biological activity. In this regard, the synthesis of 5-(2,2-diarylethyl)-substituted tetrazoles is an important task.

The goal of the present work was a systematic study of the reactions of 5-(2-arylethenyl)-2-methyl-2*H*-tetrazoles **1a–e** (Figure 1) with various arenes under the superelectrophilic activation for the development of a general synthesis of 5-(2,2-diarylethyl)-2-methyl-2*H*-tetrazoles **2**, as a result of hydroarylation of the C=C bond of substrates **1**.

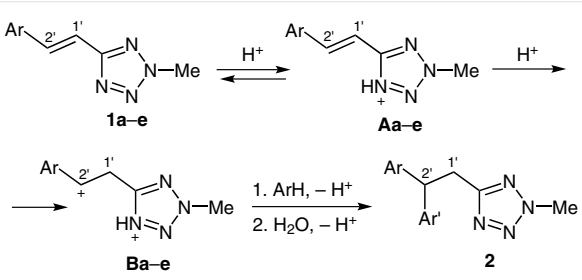


1a R = H
1b R = Me
1c R = *t*-Bu
1d R = Cl
1e R = MeO

Figure 1 (*E*)-5-(2-Arylethenyl)-2-methyl-2*H*-tetrazoles **1a–e** used in this study

It should be noted that the interaction of alkenes with arenes under the action of Brønsted or Lewis superacids is one of the major hydroarylation ways of the C=C bond.[14] Apart from that, metal-catalyzed processes for alkene hydroarylation have a wide application (see reviews[15a,b]). The most efficient catalysts for these purposes are complexes of the following transition metals: Pt,[15c] Au,[15d] Ru,[15e] Rh,[15f–h] Ni,[15i] Pd,[15j] or Pd/Ag.[15k]

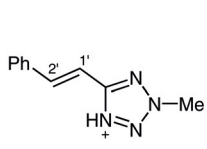
The protonation of 5-styryltetrazoles **1a–e** in Brønsted acids (H_2SO_4, $HClO_4$, etc.)[16] first goes at the nitrogen atom N[4] of the tetrazole ring with the formation of cations **Aa–e** (Scheme 2). Further, in stronger superacids, the protonation of the atom C1′ of the C=C bond of the arylethenyl fragment proceeds leading to dications **Ba–e** (Scheme 2). Such species refer to the class of highly reactive superelectrophiles.[17] Analogously to related dications generated from conjugated enone structures in superacids,[11] dications **B** are reaction intermediates under the superelectrophilic activation conditions. The further interaction of dications **B** with arenes gives hydroarylation products of the C=C bond **2**.



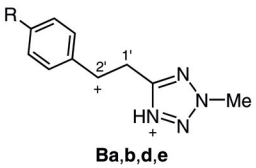
Scheme 2 Protonation of 5-styryltetrazoles **1**

First, using quantum-chemical calculation by the DFT method we studied cations **A** and **B**. The energies of HOMO and LUMO, charges on atoms, contributions of the atomic orbitals into LUMO, and indexes of the global electrophilicity ω[18] for the assessment of the reactivity of cations were calculated. Table 1 contains electronic characteristics of the species **Aa**, **Ba**,**b**,**d**,**e**. In comparison with cation **Aa**, dications **Ba**,**b**,**d**,**e** have larger values of the electrophilicity index ω that reflects their high reactivity. Dications **Bb** and **Be**, generated from compounds **1b** and **1e**, respectively, with electron-donating substituents at the aromatic ring have a smaller value of the index ω, compare to the phenyl-substituted dication **Ba** (Table 1). Dications **Ba**,**b**,**d**,**e** are characterized by a small positive charge on atom C2′, but on this atom, a much larger part of LUMO of ~15–19% is located (see Table 1). This indicates a pronounced orbital control in the reactivity of such electrophiles.

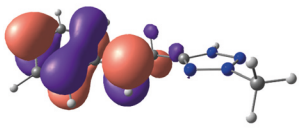
Table 1 Selected Calculated (DFT) Electronic Characteristics of Species **Aa**, **Ba**,**b**,**d**,**e**, Generated on Protonation of Tetrazoles **1a**,**b**,**d**,**e**



Aa



Ba,**b**,**d**,**e**



LUMO isosurface for **Ba**

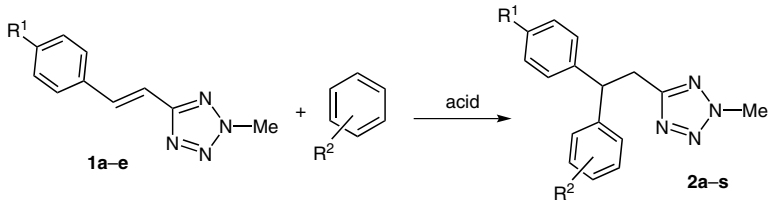
Entry	Species, R	E_{HOMO} (eV)	E_{LUMO} (eV)	ω[a] (eV)	$q(C^{2'})$[b] (e)	$k(C^{2'})_{LUM}$[c] (%)
1	**Aa**	–10.0	–6.5	9.7	–0.04	12.4
2	**Ba**, R = H	–15.0	–11.5	25.0	0.13	17.2
3	**Bb**, R = Me	–14.7	–11.0	22.3	0.09	14.5
4	**Bd**, R = Cl	–14.5	–11.2	25.0	0.09	15.0
5	**Be**, R = OMe	–14.3	–10.4	19.6	0.04	18.8

[a] Global electrophilicity index $\omega = (E_{HOMO} + E_{LUMO})^2/8(E_{LUMO} - E_{HOMO})$.
[b] Natural charges.
[c] Contribution of atomic orbital into the molecular orbital.

We tried to register species **B** in superacids by means of NMR. However, according to the data of ^1H and ^{13}C NMR, upon dissolving in TfOH at room temperature or in FSO_3H at –80 °C, tetrazoles **1a–e** formed oligomeric substances. This indicates an extreme instability and high reactivity of dications **B**. Then, we carried out reactions of tetrazoles **1a** and **1e** in TfOH at room temperature and isolated products of cationic oligomerization. According to the data of MALDI mass spectrometry, the oligomers consist of no more than 9 subunits of the initial tetrazoles **1a** and **1e** (see the Supporting Information).

Then, hydroarylation reactions of the C=C bond of styryltetrazoles **1a–e** by arenes under the superelectrophilic activation conditions leading to 5-(2,2-diarylethyl)-2-methyl-2*H*-tetrazoles) **2a–s** were carried out (Table 2). It should be noted that reactions of tetrazoles **1a**, **1e** with benzene in H_2SO_4 do not lead to the expected hydroarylation products (Table 2, entries 1, 24), that is for implementing such transformations stronger acids should be used. Hydroarylation proceeds efficiently under the action of both the Brønsted acids TfOH, FSO_3H (entries 2, 6–23, 25, 28–31), and strong Lewis acids $AlCl_3$, $AlBr_3$ (entries 3, 4, 18, 26, 27). Benzene, xylenes, *tert*-butylbenzene, anisole, and veratrole, and even a low-nucleophilic arene, such as 1,2-dichlorobenzene, may be involved in this reaction (Table 2). The tetrazole **1a** in reactions with mesitylene and durene did not give appropriate hydroarylation products (entries 8, 9), apparently, due to steric hindrance from the side of the methyl groups of these arenes. Oligomeric products were obtained in these cases.

Table 2 Hydroarylation of 5-Styryltetrazoles **1a–e** with Arenes under Superelectrophilic Activation with Brønsted (TfOH, FSO_3H) or Lewis ($AlCl_3$, $AlBr_3$) Acids Leading to Compounds **2a–s**



Entry	Starting materials		Reaction conditions[a]	Reaction product			
	Tetrazole	R^2 in arene		**2**	R^1	R^2	Yield (%)
1	**1a**, R^1 = H	H	E	unreacted initial **1a**			
2			A	**2a**	H	H	70
3			B				95
4			C				90
5			G				98
6		1,3-Me_2	A	**2b**	H	2,4-Me_2	73
7		1,4-Me_2	A	**2c**	H	2,5-Me_2	80
8		1,3,5-Me_3	A	oligomers			
9		1,2,4,5-Me_4	A	oligomers			
10		*t*-Bu	A	**2a**	H	H	46
				2d	H	4-*t*-Bu	14
11		1,2-Cl_2	A[b]	**2e**	H	3,4-Cl_2	27
				2f	H	2,3-Cl_2	30
12			G	**2e**	H	3,4-Cl_2	96
13		MeO	A[c]	**2g**	H	4-MeO	62
				2h	H	2-MeO	24
14		1,2-$(MeO)_2$	A[d]	**2i**	H	3,4-$(MeO)_2$	66
				2j	H	2,3-$(MeO)_2$	10
15	**1b**, R^1 = Me	H	A	**2a**	H	H	59
				2k	Me	H	29
16			D	**2k**	Me	H	67

Table 2 (continued)

Entry	Starting materials		Reaction conditions[a]	Reaction product			
	Tetrazole	R^2 in arene		**2**	R^1	R^2	Yield (%)
17	**1c**, R^1 = *t*-Bu	H	A	**2a**	H	H	46
18			B	**2a**	H	H	58
19		1,3-Me_2	A[e]	**2b**	H	2,4-Me_2	63
				2l	H	3,5-Me_2	21
20		MeO	D	**2m**	*t*-Bu	4-MeO	15
				2g	H	4-MeO	8
21	**1d**, R^1 = Cl	MeO	A	**2n**	Cl	H	48
22		1,2-Cl_2	A	**2o**	Cl	3,4-Cl_2	86
23		MeO	A[f]	**2p**	Cl	4-MeO	72
				2q	Cl	2-MeO	11
24	**1e**, R^1 = OMe	H	E	oligomers			
25			A	**2a**	H	H	51
26			B	**2g**	OMe	H	44
27			C	**2a**	H	H	74
				2g	OMe	H	24
28			F	**2g**	OMe	H	73
29			D	**2g**	OMe	H	85
30		1,3-Me_2	A	**2r**	OMe	2,4-Me_2	21
31		MeO	A	**2s**	OMe	4-MeO	35

[a] A: TfOH, r.t., 3 h; B: $AlCl_3$, CH_2Cl_2, r.t., 3 h; C: $AlBr_3$, r.t., 3 h; D: FSO_3H, CH_2Cl_2, –80 °C, 4 h; E: H_2SO_4 96%, r.t., 3 h; F: TfOH, CH_2Cl_2, 0 °C, 4 h; G: TfOH, 120 °C, 5 min, microwave irradiation.
[b] Ratio of isomers **2e**/**2f** is 1:1.
[c] Ratio of isomers **2g**/**2h** is 2.6:1.
[d] Ratio of isomers **2i**/**2j** is 6.6:1.
[e] Ratio of isomers **2b**/**2l** is 3:1.
[f] Ratio of isomers **2p**/**2q** is 6.5:1.

Tetrazoles **1b**, **1e** having electron-donating methyl and methoxyl groups in the aromatic ring in the reaction with benzene under the action of TfOH or $AlBr_3$ at room temperature, in addition to the target substances **2k** and **2g**, also give **2a** (entries 15, 25, 27). The latter is formed as the product of an exchange of aryl groups for the phenyl. Similar exchanges were observed by us previously in hydroarylation reactions of amides of cinnamic acids.[14p] We managed to completely suppress the exchange by decreasing the reaction temperature in CF_3SO_3H to 0 °C (entry 28) or in FSO_3H to –80 °C (entries 16, 29).

In the reaction of the *tert*-butyl-substituted tetrazole **1c** with arenes in TfOH (entries 17, 19) and $AlCl_3$ (entry 18) or when tetrazole **1a** interacts with *tert*-butylbenzene (entry 10) at room temperature, the formation of products **2a**,**b**,**l**, not containing the *tert*-butyl substituent was observed. In this case, *ipso*-substitution of the *tert*-butyl group by a proton under superacidic conditions takes place. We were able to suppress this process partially at a low temperature of –80 °C in FSO_3H (entry 20).

Some individual aromatic substrates gave regioisomeric reaction products. Thus, in some cases, reactions with anisole (**2g** + **2h**, entry 13), veratrole (**2i** + **2j**, entry 14), *meta*-xylene (**2b** + **2l**, entry 19), and 1,2-dichlorobenzene (**2e** + **2f**, entry 11) gave substitution products at various positions of the aromatic ring of these arenes. This indicates the high reactivity of intermediate dications **B** (see Scheme 2).

As a whole, this reaction is an efficient hydroarylation method of the C=C bond of 5-styryltetrazoles **1** and in the majority of cases leads to the target products in good yields of 60–95%. Transformations of substances **1** in superacids proceed regioselectively only at the C=C bond and does not affect the tetrazole cycle.

Despite the advantages of the method proposed by us, it is obvious that an important task is the minimization of the reaction time. To intensify chemical processes microwave (MW) activation is widely used.[19] We checked the possibility of conducting the studied hydroarylation reaction in TfOH under the conditions of microwave irradiation. Truly,

microwave irradiation allows a sharp reduction in the reaction time to 5 minutes at 120 °C for the interaction of tetrazole **1a** with benzene and 1,2-dichlorobenzene to form substances **2a** (yield of 98%) and **2e** (yield of 96%) (entries 5, 12). Under thermal conditions, these reactions proceeded in 3 hours at room temperature (entries 2, 11).

In summary, we developed an efficient method of the synthesis of 5-(2,2-diarylethyl)-2-methyl-2*H*-tetrazoles based on reactions of 5-(2-arylethenyl)-2-methyl-2*H*-tetrazoles with arenes under the superelectrophilic activation with Brønsted or Lewis acids.

The NMR spectra of solutions of compounds in $CDCl_3$ were recorded on a Bruker AM-500 spectrometer at 25 °C (at 500 and 125 MHz for ^1H and ^{13}C NMR spectra, respectively). The residual proton solvent peak $CDCl_3$ (δ = 7.26) for ^1H NMR spectra, and the carbon signal of $CDCl_3$ (δ = 77.0) for ^{13}C NMR spectra were used as references. IR spectra of compounds in KBr were taken with Shimadzu IR Affinity-1 spectrometer in region 400–4000 cm^{-1} with resolution 4 cm^{-1}, Happ-Genzel apodization, 20 scans. HRMS was carried out at an instrument Bruker MicroTOF (ESI). GC-MS: data were obtained at a machine G2570A GC/MSD Agilent Technologies 6850c with a column HP-5MS (3 m × 0.25 mm), a thickness of the stationary phase 0.25 μm. Microwave reactions were carried out at a machine DISCOVER SP. The preparative reactions were monitored by TLC on silica gel plates (Silufol UV-254) using UV light for detection. Column chromatography was performed on silica gel Chemapol 40/100 (0.04–0.10 mm) eluting with petroleum ether–Et_2O mixtures.

All computations has been carried out at the DFT/HF hybrid level of theory using Becke's three-parameter hybrid exchange functional in combination with the gradient-corrected correlation functional of Lee, Yang, and Parr (B3LYP) by using GAUSSIAN 2003 program packages.[20] The geometries optimization were performed using the 6-311+G(2d,2p) basis set. The Hessian matrix was calculated analytically for the optimized structures in order to prove the location of correct minima (no imaginary frequencies) and to estimate the thermodynamic parameters.

Starting 5-(2-arylethenyl)-2-methyl-2*H*-tetrazoles **1a–e** were synthesized and characterized by us previously.[21]

5-(2,2-Diarylethyl)-2-methyl-2*H*-tetrazoles 2 from Tetrazoles 1 and Arenes in TfOH; General Procedure (Table 2)

Tetrazole **1** (0.25 mmol) was added to a mixture of arene (0.3 mmol) and TfOH (1 mL) at r.t. (or other temperature as indicated in Table 2). The mixture was stirred at r.t. for 3 h (or other times and temperatures as indicated in Table 2). Then the mixture was poured into water (20 mL), sat. aq $NaHCO_3$ solution was added to pH 8–9, and reaction product was extracted with $CHCl_3$ (3 × 30 mL). The combined extracts were dried (Na_2SO_4), the solvent was distilled off under reduced pressure, and the residue was subjected to chromatographic separation (silica gel, gradient petroleum ether–Et_2O).

In the same manner, reactions were carried out in TfOH (1 mL) at 0 °C, or FSO_3H (1 mL) at –80 °C (see Table 2), CH_2Cl_2 (1 mL) was added for better solubility of benzene.

5-(2,2-Diarylethyl)-2-methyl-2*H*-tetrazoles 2 from Tetrazoles 1 and Benzene under the Action of $AlCl_3$ or $AlBr_3$; General Procedure (Table 2)

Tetrazole **1** (0.27 mmol) was added to a solution of AlX_3 (X = Cl, Br) (1.34 mmol) in benzene (4 mL) at r.t. The mixture was stirred at r.t. for 3 or 4 h (as indicated in Table 2). Then the mixture was poured into water (20 mL), sat. aq $NaHCO_3$ solution was added to pH 8–9, and reaction product was extracted with $CHCl_3$ (3 × 30 mL). The combined extracts were dried (Na_2SO_4), the solvent was distilled off under reduced pressure, and the residue was subjected to chromatographic separation (silica gel, petroleum ether–Et_2O).

Yields of compounds **2a–r** are given in Table 2.

Properties of 2-methyl-5-(2,2-diphenylethyl)-2*H*-tetrazole (**2a**), 2-methyl-5-[2-(2,4-dimethylphenyl)-2-phenylethyl]-2*H*-tetrazole (**2b**), 2-methyl-5-[2-(2,5-dimethylphenyl)-2-phenylethyl]-2*H*-tetrazole (**2c**), 5-[2-(4-methoxyphenyl)-2-phenylethyl]-2-methyl-2*H*-tetrazole (**2g**), 5-[2-(2-methoxyphenyl)-2-phenylethyl]-2-methyl-2*H*-tetrazole (**2h**), 5-[2-(3,4-dimethoxyphenyl)-2-phenylethyl]-2-methyl-2*H*-tetrazole (**2i**), 5-[2-(2,3-dimethoxyphenyl)-2-phenylethyl]-2-methyl-2*H*-tetrazole (**2j**) were previously reported.[10]

5-[2-(4-*tert*-Butylphenyl)-2-phenylethyl]-2-methyl-2*H*-tetrazole (2d)

Obtained as an oily yellow mixture with compound **2a**; yield: 23 mg (14%).

IR (KBr) (for mixture of isomers): 2925, 2855, 1600, 1495, 1449, 1388, 1278, 1200, 1077, 1035, 778, 705, 611 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$, from the spectrum of the mixture): δ = 1.30 (s, 9 H, 3 CH_3), 3.60 (d, *J* = 8.2 Hz, 2 H, CH_2), 4.20 (s, 3 H, CH_3), 4.64 (t, *J* = 8.2 Hz, 1 H, CH), 7.17–7.31 (m, 9 H_{arom}).

^{13}C NMR (125 MHz, $CDCl_3$, from the spectrum of the mixture): δ = 31.6, 34.8, 39.1, 49.2, 126.2, 126.5, 127.8, 128.4, 128.6, 141.5, 143.3, 165.1.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{20}H_{25}N_4$: 321.2074; found: 321.2071.

5-[2-(3,4-Dichlorophenyl)-2-phenylethyl]-2-methyl-2*H*-tetrazole (2e)

White solid; yield: 80 mg (96%); mp 120–121 °C.

IR (KBr): 2922, 1722, 1592, 1562, 1493, 1470, 1445, 1396, 1309, 1155, 1030, 822, 702, 565 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 3.58 (d, *J* = 8.0 Hz, 2 H, CH_2), 4.23 (s, 3 H, CH_3), 4.65 (t, *J* = 8.0 Hz, 1 H, CH), 7.10–7.33 (m, 8 H_{arom}).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 31.3, 39.2, 48.3, 126.6, 127.2, 127.7, 127.8, 128.2, 128.5, 129.9, 130.4, 140.4, 143.4, 165.1.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{16}H_{15}N_4Cl_2$: 333.0668; found: 333.0670.

5-[2-(2,3-Dichlorophenyl)-2-phenylethyl]-2-methyl-2*H*-tetrazole (2f)

Obtained as an oily yellow mixture with compound **2e**; yield: 27 mg (30%).

IR (KBr) (for mixture of isomers): 2924, 2953, 1676, 1602, 1499, 1468, 1255, 1171, 1028, 742, 699 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$, from the spectrum of the mixture): δ = 3.50–3.52 (m, 2 H, CH_2), 4.16 (s, 3 H, CH_3), 4.52–4.59 (m, 1 H, CH), 7.05–7.33 (m, 8 H_{arom}).

^{13}C NMR (125 MHz, $CDCl_3$, from the spectrum of the mixture): δ = 31.6, 39.1, 49.2, 126.5, 127.0, 127.6, 127.8, 128.5, 128.8, 130.5, 132.4, 142.2, 143.3, 164.5.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{15}N_4Cl_2$: 333.0668; found: 333.0670.

2-Methyl-5-[2-(4-methylphenyl)-2-phenylethyl]-2*H*-tetrazole (2k)

Colorless oil; yield: 30 mg (67%).

IR (KBr): 2960, 2861, 1602, 1494, 1463, 1382, 1276, 1123, 1073, 1037, 820, 744, 703 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.29 (s, 3 H, CH_3), 3.63 (d, *J* = 8.2 Hz, 2 H, CH_2), 4.21 (s, 3 H, CH_3), 4.69 (t, *J* = 8.2 Hz, 1 H, CH), 6.98–6.99 (m, 1 H_{arom}), 7.06–7.08 (m, 2 H_{arom}), 7.14–7.16 (m, 2 H_{arom}), 7.17–7.18 (m, 2 H_{arom}), 7.27 (s, 2 H_{arom}).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 20.9, 31.6, 39.2, 49.3, 126.4, 127.8, 128.4, 129.0, 130.8, 133.0, 135.8, 140.0, 165.3.

GC-MS: *m*/*z* (%) = 278 [M]$^+$ (20), 181 (100), 165 (30), 115 (5).

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{19}N_4$: 279.1604; found: 279.1593.

2-Methyl-5-[2-(3,5-dimethylphenyl)-2-phenylethyl]-2*H*-tetrazole (2l)

Obtained as an yellow oily mixture with compound **2b**; yield: 20 mg (21%).

IR (KBr) (for mixture of isomers): 2920, 1602, 1495, 1450, 1387, 1193, 1033, 850, 705 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$, from the spectrum of the mixture): δ = 2.26 (s, 6 H, 2 CH_3), 3.57 (d, *J* = 8.2 Hz, 2 H, CH_2), 4.20 (s, 3 H, CH_3), 4.55 (t, *J* = 8.2 Hz, 1 H, CH), 6.90 (s, 8 H_{arom}).

^{13}C NMR (100 MHz, $CDCl_3$, from the spectrum of the mixture): δ = 21.3, 31.6, 39.1, 49.4, 125.6, 126.4, 126.5, 127.8, 128.1, 128.2, 128.4, 137.8, 143.3, 165.3.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{18}H_{21}N_4$: 293.1761; found: 293.1783.

5-[2-(4-*tert*-Butylphenyl)-2-(4-methoxyphenyl)ethyl]-2-methyl-2*H*-tetrazole (2m)

Obtained as an yellow oily mixture with compound **2g**; yield: 26 mg (15%).

IR (KBr) (for mixture of isomers): 2961, 1610, 1512, 1464, 1303, 1249, 1180, 1113, 1033, 837, 701 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$, from the spectrum of the mixture): δ = 1.27 (s, 9 H, 3 CH_3), 3.58–3.60 (m, 2 H, CH_2), 3.75 (s, 3 H, OCH_3), 4.20 (s, 3 H, CH_3), 4.64 (t, *J* = 8.2 Hz, 1 H, CH), 7.16–7.19 (m, 4 H_{arom}), 7.25–7.26 (m, 4 H_{arom}).

^{13}C NMR (125 MHz, $CDCl_3$, from the spectrum of the mixture): δ = 31.3, 34.3, 39.2, 48.3, 55.1, 113.8, 125.4, 126.4, 127.2, 128.7, 135.4, 140.8, 149.1, 165.4.

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{21}H_{27}N_4O$: 351.2179; found: 351.2180.

5-[2-(4-Chlorophenyl)-2-phenylethyl]-2-methyl-2*H*-tetrazole (2n)

Colorless solid; yield: 36 mg (48%); mp 91–92 °C.

IR (KBr): 2960, 1602, 1464, 1382, 1286, 1125, 1074, 744 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.59 (d, *J* = 8.2 Hz, 2 H, CH_2), 4.21 (s, 3 H, CH_3), 4.67 (t, *J* = 8.2 Hz, 1 H, CH), 7.18–7.25 (m, 8 H_{arom}), 7.27–7.29 (m, 1 H_{arom}).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 31.5, 39.2, 48.9, 126.7, 127.7, 128.6, 128.7, 129.2, 132.3, 141.7, 142.9, 164.9.

GC-MS: *m*/*z* (%) = 298 [M]$^+$ (16), 201 (100), 165 (55).

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{16}ClN_4$: 299.1058; found: 299.1058.

5-[2-(4-Chlorophenyl)-2-(3,4-dichlorophenyl)ethyl]-2-methyl-2*H*-tetrazole (2o)

Yellow oil; yield: 44 mg (86%).

IR (KBr): 2961, 2862, 1600, 1464, 1382, 1275, 1124, 1073, 1040, 743 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.55 (d, *J* = 8.2 Hz, 2 H, CH_2), 4.23 (s, 3 H, CH_3), 4.63 (t, *J* = 8.2 Hz, 1 H, CH), 7.08 (d, *J* = 8.4 Hz, 1 H_{arom}), 7.16 (d, *J* = 8.4 Hz, 2 H_{arom}), 7.25 (d, *J* = 8.4 Hz, 2 H_{arom}), 7.30 (s, 1 H_{arom}), 7.33 (d, *J* = 8.3 Hz, 1 H_{arom}).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 31.3, 39.3, 48.0, 127.1, 128.9, 129.0, 129.8, 130.6, 130.9, 132.7, 132.9, 140.6, 143.1, 164.3.

GC-MS: *m*/*z* (%) = 366 [M]$^+$ (14), 269 (100), 233 (12), 199 (65), 163 (14).

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{16}H_{14}Cl_3N_4$: 367.0279; found: 367.0274.

5-[2-(4-Chlorophenyl)-2-(4-methoxyphenyl)ethyl]-2-methyl-2*H*-tetrazole (2p)

Obtained as an yellow oily mixture with compound **2q**; yield: 59 mg (72%).

IR (KBr) (for mixture of isomers): 2927, 2837, 1610, 1512, 1492, 1408, 1250, 1180, 1092, 1033, 825, 785 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$, from the spectrum of the mixture): δ = 3.55 (d, *J* = 8.2 Hz, 2 H, CH_2), 3.75 (s, 3 H, OCH_3), 4.20 (s, 3 H, CH_3), 4.61 (t, *J* = 8.2 Hz, 1 H, CH), 7.14–7.22 (m, 8 H_{arom}).

^{13}C NMR (125 MHz, $CDCl_3$, from the spectrum of the mixture): δ = 31.7, 39.2, 48.1, 55.2, 114.0, 128.2, 128.6, 129.1, 132.1, 135.0, 142.1, 158.3, 165.0.

GC-MS: *m*/*z* (%) = 328 [M]$^+$ (5), 231 (100), 196 (5), 181 (5), 165 (5), 153 (12).

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{18}ClN_4O$: 329.1164; found: 329.1169.

5-[2-(4-Chlorophenyl)-2-(2-methoxyphenyl)ethyl]-2-methyl-2*H*-tetrazole (2q)

Obtained as an yellow oily mixture with compound **2p**; yield: 9 mg (11%).

IR (KBr) (for mixture of isomers): 2927, 2837, 1610, 1512, 1492, 1408, 1250, 1180, 1092, 1033, 825, 785 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.68 (d, *J* = 8.2 Hz, 2 H, CH_2), 3.80 (s, 3 H, OCH_3), 4.20 (s, 3 H, CH_3), 4.94 (t, *J* = 8.2 Hz, 1 H, CH), 6.79–6.81 (m, 8 H_{arom}).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 31.7, 39.2, 48.1, 55.2, 114.0, 128.2, 128.6, 129.1, 132.1, 135.0, 142.1, 158.3, 165.0.

GC-MS: *m*/*z* (%) = 328 [M]$^+$ (13), 297 (28), 231 (81), 165 (40), 152 (11), 125 (100).

HRMS: *m*/*z* [M + H]$^+$ calcd for $C_{17}H_{18}ClN_4O$: 329.1164; found: 329.1169.

5-[2-(4-Methoxyphenyl)-2-(2,4-dimethylphenyl)ethyl]-2-methyl-2*H*-tetrazole (2r)

Colorless oil; yield: 17 mg (21%).

IR (KBr): 2936, 2838, 1606, 1512, 1452, 1352, 1292, 1249, 1177, 1030, 834, 768 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 2.25 (s, 6 H, 2 CH_3), 3.56 (d, *J* = 8.0 Hz, 2 H, CH_2), 3.75 (s, 3 H, OCH_3), 4.21 (s, 3 H, CH_3), 4.56 (t, *J* = 8.0 Hz, 1 H, CH), 6.78–6.80 (m, 3 H_{arom}), 6.88–6.91 (m, 2 H_{arom}), 7.17 (d, *J* = 8.0 Hz, 2 H_{arom}).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 21.3, 31.8, 39.2, 48.7, 55.2, 113.8, 125.5, 125.9, 128.0, 128.1, 128.8, 135.6, 137.9, 143.7, 158.0, 165.5.

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{19}H_{23}N_4O$: 323.1866; found: 323.1877.

5-[2,2-Bis(4-methoxyphenyl)ethyl]-2-methyl-2*H*-tetrazole (2s)

White solid; yield: 28 mg (35%); mp 94–95 °C.

IR (KBr): 2937, 2836, 1607, 1582, 1512, 1464, 1302, 1250, 1179, 1115, 1028, 835, 806, 767 cm^{-1}.

^1H NMR (500 MHz, $CDCl_3$): δ = 3.56 (d, *J* = 8.2 Hz, 2 H, CH_2), 3.74 (s, 6 H, OCH_3), 4.20 (s, 3 H, CH_3), 4.59 (t, *J* = 8.2 Hz, 1 H, CH), 6.79 (d, *J* = 8.7 Hz, 4 H_{arom}), 7.16 (d, *J* = 8.7 Hz, 4 H_{arom}).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 32.0, 39.1, 48.0, 55.1, 113.8, 128.6, 135.9, 158.0, 165.3.

GC-MS: *m*/*z* (%) = 324 $[M]^+$ (10), 227 (100), 196 (5), 181 (6), 165 (8).

HRMS: *m*/*z* $[M + H]^+$ calcd for $C_{18}H_{21}N_4O_2$: 325.1659; found: 325.1654.

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0036-1588884.

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