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Pd(II)-Catalyzed Aminotetrazole Directed *Ortho*-Selective Halogenation of Arenes

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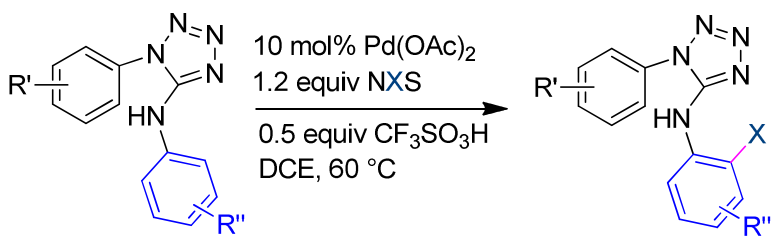


ABSTRACT: A Pd(II)-catalyzed *ortho*-selective halogenation of *N*-aryl ring of *N*,1-diaryl-1*H*-tetrazol-5-amine has been described employing *N*-halosuccinimide as a halogen source *via* C-H bond activation. The present work features 5-aminotetrazole, as a directing group, for the chemo- and regioselective C-H halogenation of arenes. The kinetic isotope study (k_{H}/k_{D} = 2.9) suggests that the cleavage of the C-H bond takes place in the rate determining step. The scope and mechanism of the protocol have been demonstrated.

INTRODUCTION

The recent advances in transition-metal-catalysis have led to the development of effective methods for the direct functionalization of C-H bonds.[1] In these reactions, the incorporation of a directing group in the substrate has been found to be effective for the selective activation of a particular C-H bond (Figure 1).[2] In this context, considerable effort has been made on the search of effective directing groups for the selective C-H functionalization processes.[3-9]

N-Aryl-5-aminotetrazole is an essential structural motif in many compounds that are important in biological and medicinal sciences. For example, the compounds having *N*-aryl-5-aminotetrazole core structure exhibit anti-inflammatory,[10a] anti-asthmatic,[10b-c] anti-viral,[10d] anti-neoplastic,[10e] cognition disorder[10f] and antibiotic[10g] properties. In particular, *N*-(2-halophenyl)-1*H*-tetrazol-5-amines are known to exhibit herbicidal and anti-allergic properties.[11] However, these compounds could not be obtained by desulfurization[12] techniques as shown in Scheme 1. In addition, the classical methods used for the synthesis of *N*-(2-halophenyl)-1-phenyl-1*H*-tetrazol-5-amines often suffer due to limited substrate scope along with the requirement of harsh reaction conditions.[11] The development of a straightforward protocol for the direct *ortho*-halogenation of the *N*-aryl ring of the *N*-aryl-5-aminotetrazole is thus highly desirable.

Furthermore, aryl halides are extremely valuable starting materials for synthetic elaboration. For example, they find widespread applications as precursors for the synthesis of organometallic reagents.[13a] In recent decades, aryl halides are used as substrates to construct carbon-carbon and carbon-heteroatom bonds via transition metal catalyzed cross-coupling reactions.[13b-c] In addition, they serve as a prominent structural motif in biologically active molecules.[14] However, the classical methods used for the arene halogenation often suffer due to over halogenation and low regioselectivity.[15] Thus, considerable efforts have been recently made for the development of new methods for the regioselective C-H halogenation of arenes employing directing groups in the presence of transition metal catalysis.[3] Palladium based catalytic systems have been studied for the halogenation of arenes employing carboxylic acid, amide, nitrile and pyridine as the directing groups,[3a-f] while the rhodium based systems have been demonstrated with amides and esters.[3g] Herein, we report a Pd-catalyzed 5-aminotetrazole directed chemo- and *ortho*-selective halogenation of arenes utilizing *N*-halosuccinimide as a halogen source. This protocol is simple, general and effective at moderate temperature to afford the target products in moderate to high yield.

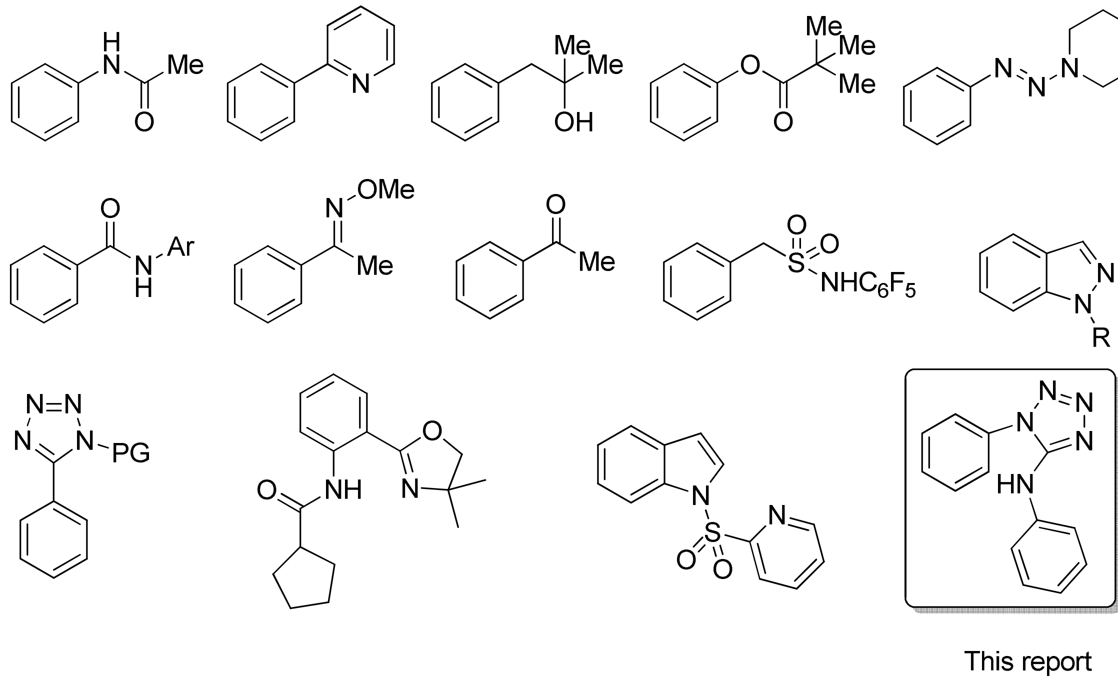
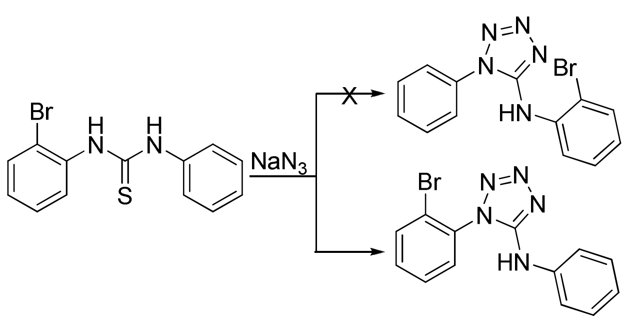


Figure 1. Examples of different diverse directing groups for C-H activation reactions.



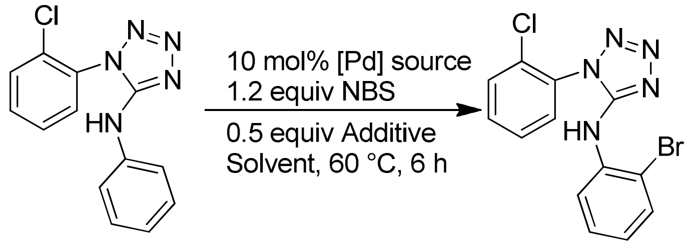
Scheme 1.

RESULTS AND DISCUSSION

First, the optimization of the reaction conditions for bromination was carried out using 1-(2-chlorophenyl)-*N*-phenyl-1*H*-tetrazol-5-amine **1a** as a model substrate with *N*-bromosuccinimide (NBS) as a bromine source using different Pd-sources, solvents and additives at varied temperatures (Table 1). To our delight, the reaction proceeded selectively to brominate the *ortho*-position of the *N*-aryl ring in high yield. Among the set of additives examined, CF_3SO_3H gave the desired product **2a** in 92% yield (entry 3), while CF_3CO_2H (TFA) and *p*-TsOH (PTSA) were found to be less effective in affording the target product in 50-60% yield. In case of the solvents, 1,2-dichloroethane (DCE) gave the best results, whereas 1,2-dimethoxyethane (DME) and CH_3CO_2H gave inferior results, while CH_3CN and toluene were failed to produce the desired product. The catalytic activity of different Pd-sources was evaluated, and $Pd(OAc)_2$ was found to be superior to $PdCl_2$ and $Pd(PPh_3)_2Cl_2$. Lowering the amount of the Pd-source and the temperature led to afford the target product **2a** in <72% yield. Control experiments without the Pd-source gave **2a** in 10% yield along with unreacted starting material **1a**.

Having these optimal conditions in hand, the scope of the protocol was studied for the bromination of a wide range of *N*,1-diaryl-1*H*-tetrazol-5-amine derivatives (Table 2). The substrates **1c-f** having 4-Cl, 4-F, 4-^{i}Pr and 4-Me substituents on both the aryl rings readily proceeded reaction to afford the target products **2c-f** in 84%, 82%, 88% and 91% yields, respectively. The substrate bearing 2,4-diMe substituents **1h** required slightly longer reaction time to give the desired product **2h** in 63% yield. While the unsymmetrical substrates **1j-n** bearing electron donating and -withdrawing groups underwent reaction to produce the target *ortho*-brominated products **2j-n** in 74-92% yields. In case of the substrates having 3-Me and 3,4-diMe groups on the aryl rings, a mixture of 2-bromo and 2,6-dibromo compounds **2b** and **2b'**, and **2i** and **2i'** was obtained in 78% and 90% yields, respectively. Likewise, the symmetrical substrate bearing 4-OMe group on the aryl rings **1g** gave a mixture of *ortho*-brominated products **2g** and **2g'** in 88% yield.

Table 1. Optimization of the Reaction Conditions[a]

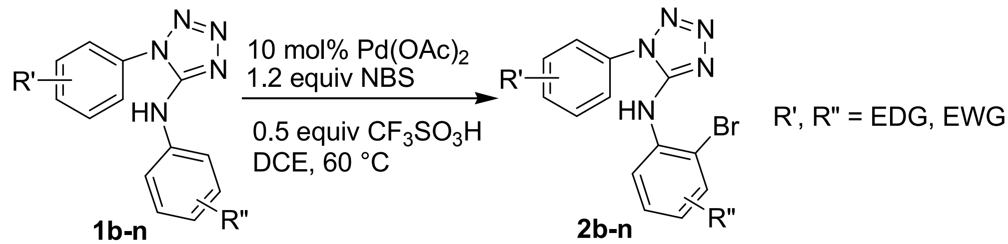


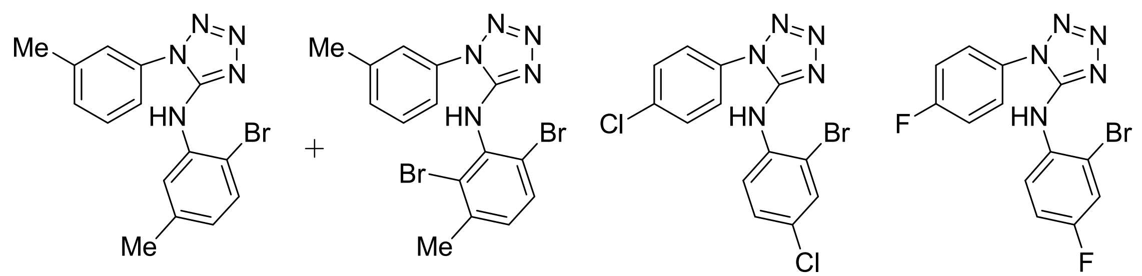
1a **2a**

Entry	Catalyst	Additive	Solvent	Yield (**2a**) (%)[b]
1	$Pd(OAc)_2$	TFA	DCE	60
2	$Pd(OAc)_2$	PTSA	DCE	50
3	$\mathbf{Pd(OAc)_2}$	$\mathbf{CF_3SO_3H}$	**DCE**	**92**
4	$Pd(OAc)_2$	CF_3SO_3H	CH_3CN	0
5	$Pd(OAc)_2$	CF_3SO_3H	toluene	0
6	$Pd(OAc)_2$	CF_3SO_3H	DME	40
7	$Pd(OAc)_2$	CF_3SO_3H	CH_3CO_2H	60
8	$PdCl_2$	CF_3SO_3H	DCE	47
9	$Pd(PPh_3)_2Cl_2$	CF_3SO_3H	DCE	55
10[c]	$Pd(OAc)_2$	CF_3SO_3H	DCE	72
11[d]	$Pd(OAc)_2$	CF_3SO_3H	DCE	43
12	-	CF_3SO_3H	DCE	10

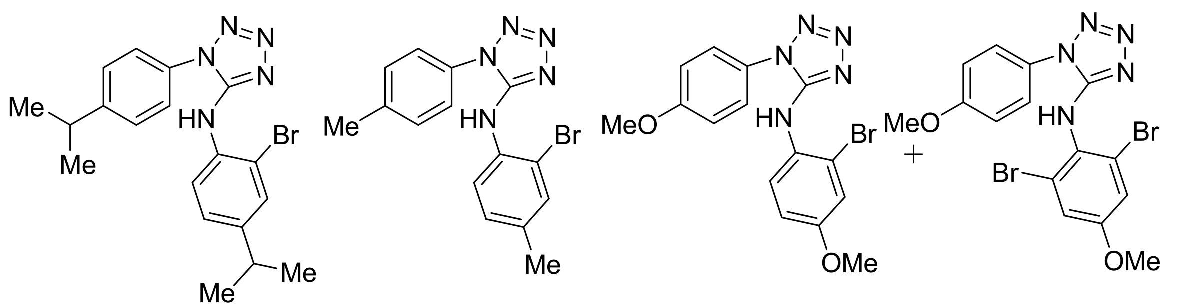
[a] Reaction conditions: substrate **1a** (1 mmol), Pd-source (10 mol %), NBS (1.2 mmol), additive (0.5 mmol), solvent (2 mL), 60 °C, 6 h. [b] Determined by 400 MHz ^1H NMR. [c] Temperature (40 °C) was used. [d] Pd-source (5 mol %) was used.

Table 2. ***Ortho*****-Bromination of *N*-Aryl Ring of *N*,1-Diaryl-1*H*-tetrazol-5-amine**[a]

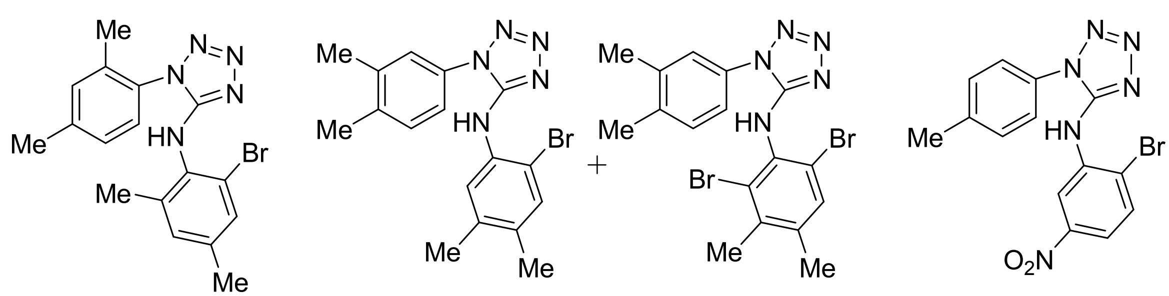




2b 6 h, 78%, 3.2:1 **2b'** **2c**, 6 h, 84% **2d**, 10 h, 82%

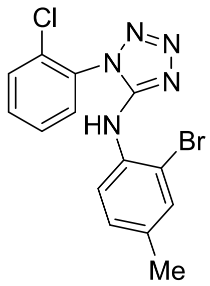


2e, 10 h, 88% **2f**, 10 h, 91% **2g** 6 h, 88%, 1:1 **2g'**

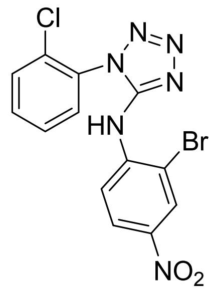


2h, 8 h, 63% **2i** 6 h, 90%, 2.5:1 **2i'** **2j**, 8 h, 79%

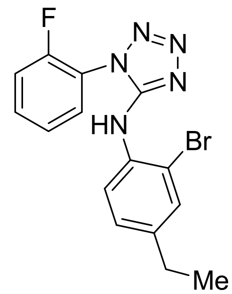
Table 2 Continues...



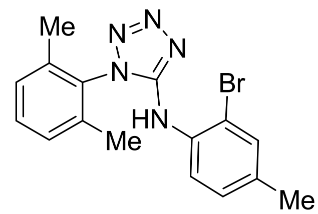
2k, 6 h, 92%



2l, 8 h, 74%



2m, 8 h, 79%



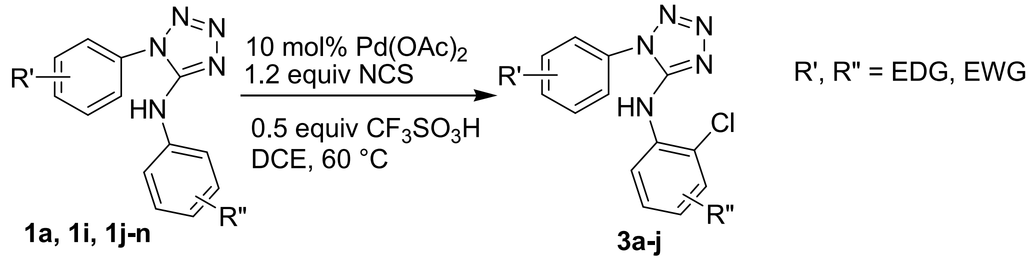
2n, 8 h, 89%

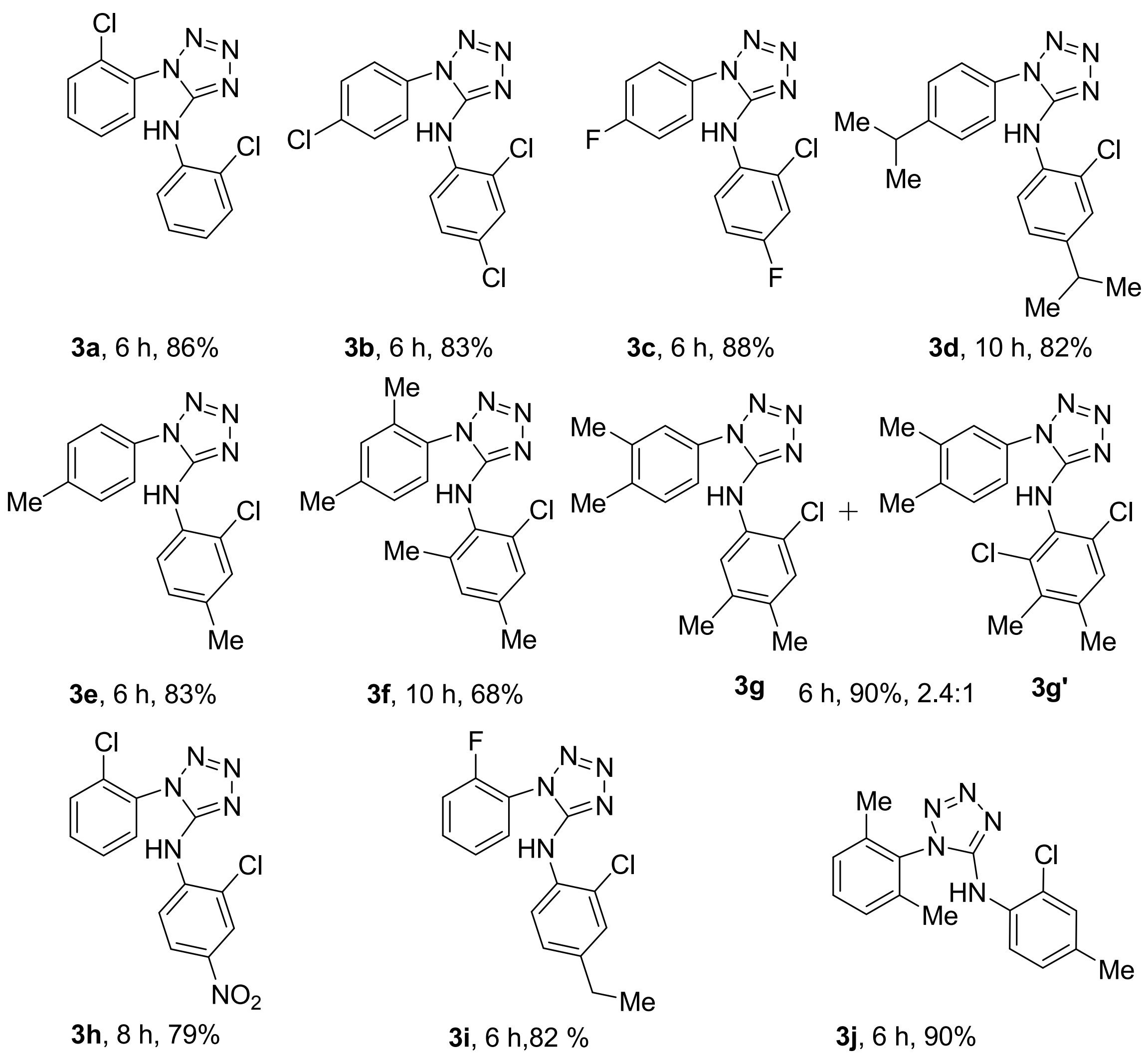
[a] Substrate (1 mmol), $Pd(OAc)_2$ (10 mol %), NBS (1.2 mmol), CF_3SO_3H (0.5 mmol), DCE (2 mL), 60 °C, 6-10 h.

Next, the chlorination of the substituted *N*-aryl-1-aryl-1*H*-tetrazol-5-amine derivatives was studied employing *N*-chlorosuccinimide (NCS) as a halogen source (Table 3). The symmetrically substituted substrates with 4-Cl, 4-F, 4-^{i}Pr, 4-Me and 2,4-diMe groups on the aryl rings proceeded reaction to give the corresponding *ortho*-chlorinated products **3b-f** in 68-88% yields. Similarly, the unsymmetrical substrates **1a** and **1l-n** readily underwent reaction to afford the target products **3a** and **3h-j** in 86% and 79-90% yields, respectively, while the substrate **1i** led to the formation of a mixture of 2-chloro- and 2,6-dichlorinated products **3g** and **3g'** in 90% yield.

Finally, the iodination of *N*-aryl-1-aryl-1*H*-tetrazol-5-amines was investigated in the presence of *N*-iodosuccinimide (NIS) as a halogen source (Table 4). The reactions of *N*,1-diaryl-1*H*-tetrazol-5-amines having 4-F, 4-^{i}Pr, 4-Me, 2,4 diMe and 3,4-diMe groups both on the aryl rings were studied. As above, the reactions occurred to give the corresponding *ortho*-iodinated products **4a-e** in 73-93% yields, while the substrate **1k** and **1n** with unsymmetrical substituents gave the target products **4f** and **4g** in 89% and 90% yields, respectively. In these substrates, the reactions were selective affording mono iodinated compounds as the sole products.

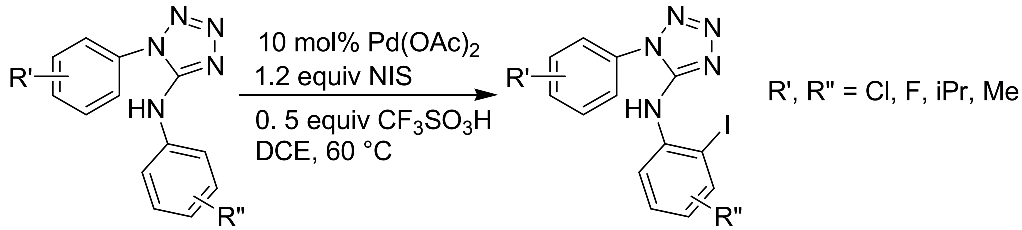
Table 3. *Ortho*-Chlorination of *N*-Aryl Ring of *N*,1-Diaryl-1*H*-tetrazol-5-amine[a]



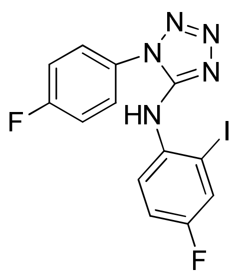


[a] Substrate (1 mmol), $Pd(OAc)_2$ (10 mol %), *N*-chlorosuccinimide (NCS) (1.2 mmol), CF_3SO_3H (0.5 mmol), DCE (2 mL), 60 °C, 6-10 h.

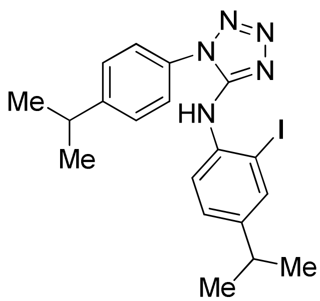
Table 4. *Ortho*-Iodination of *N*-Aryl Ring of *N*,1-Diaryl-1*H*-tetrazol-5-amine[a]



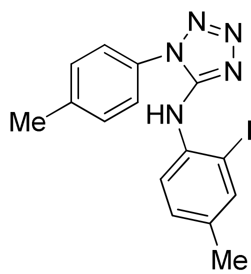
1d-f, h, i, k → **4a-g**



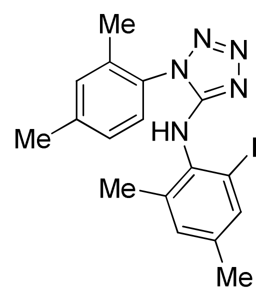
4a, 6 h, 90%



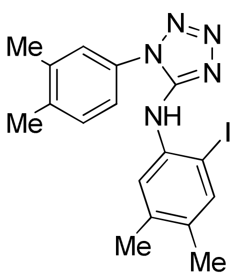
4b, 6 h, 87%



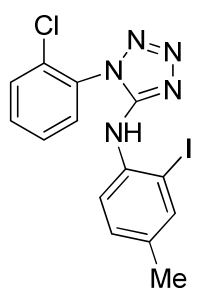
4c, 6 h, 93%



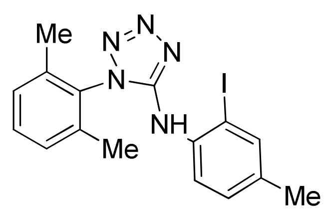
4d, 10 h, 73%



4e, 6 h, 86%



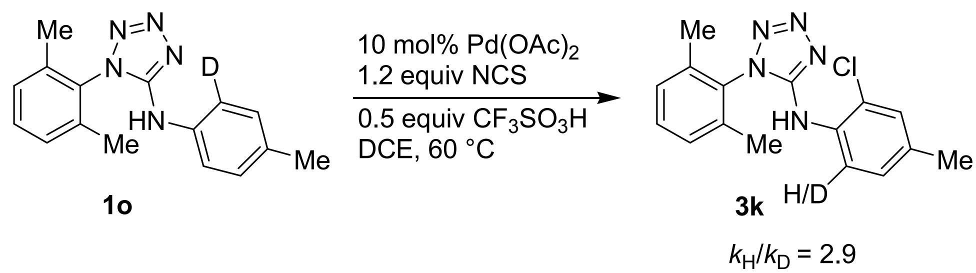
4f, 6 h, 89%



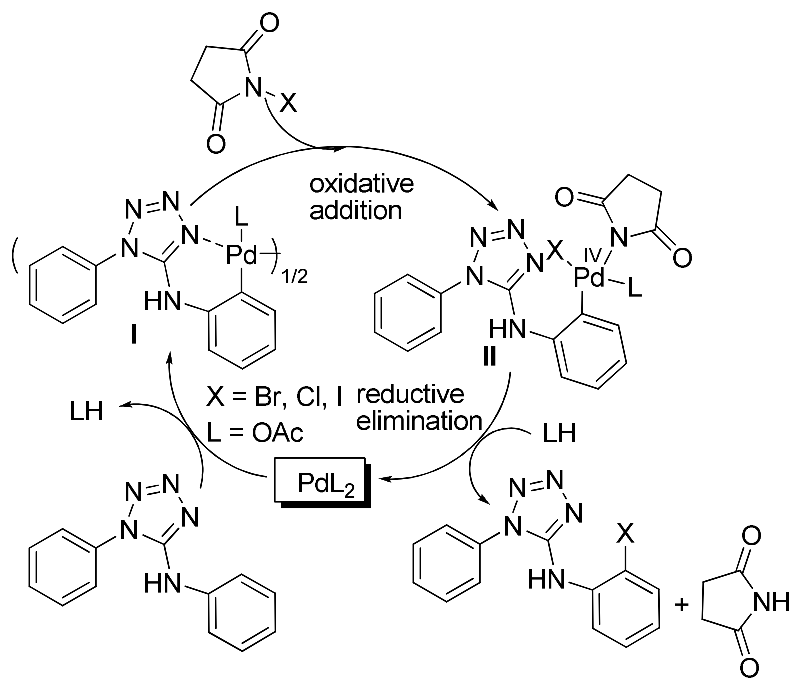
4g, 6 h, 90%

[a] Substrate (1 mmol), $Pd(OAc)_2$ (10 mol %), *N*-iodosuccinimide (NIS) (1.2 mmol), CF_3SO_3H (0.5 mmol), DCE (2 mL), 60 °C, 6-10 h.

Recrystallization of **4b** in CH_3CN gave a single crystal whose structure was confirmed by X-ray analysis (see Supporting Information). These results suggest that protocol is general and can be used for the *ortho*-selective bromination, chlorination and iodination of arenes employing *N*-halosuccinimide as a halogen source. It is noteworthy that the halogenation selectively takes place on the *N*-aryl ring without affecting the 1-aryl system.



Scheme 2. Kinetic Isotope Study.



Scheme 3. Plausible Catalytic Cycle.

To reveal the nature of the C-H bond cleavage, the kinetic isotope effect was investigated for the halogenation of *N*-(2-deutero-4-methylphenyl)-1-(2,6-dimethylphenyl)-1*H*-tetrazol-5-amine **1o** (Scheme 2). The observed results ($k_H/k_D = 2.9$) indicate that the cleavage of *ortho* C-H bond is involved in the rate determining step (see the Supporting Information).[16e] Thus, the reaction of 5-aminotetrazole with $Pd(OAc)_2$ may give a six membered cyclopalladated intermediate **I** *via* amino-tetrazole chelation assisted C-H bond activation (Scheme 3).[16,3d] The intermediate **I** may then undergo oxidative addition with NXS to yield Pd(IV)[16d,e] complex **II**, which may complete the catalytic cycle *via* reductive elimination[16,3d] of the halogenated products and regeneration of the Pd(II) species. The function of the CF_3SO_3H may be presumably to protonate the carbonyl of the NXS that could lead to more effective X^- source.[3c,f] In addition, CF_3SOH may tune the electrophilicity of Pd(II) that could improve the C-H activation process.[16d]

CONCLUSIONS

In summary, Pd(II)-catalyzed 5-aminotetrazole assisted *ortho*-selective direct halogenation of *N*-aryl ring of *N*,1-diaryl-1*H*-tetrazol-5-amine derivatives has been described utilizing *N*-halosuccinimide as a halogenating agent *via* C-H bond activation at moderate temperature. The reaction is chemo- and regioselective and the halogenated products can be obtained in moderate to high yield.

EXPERIMENTAL SECTION

General Procedure for the Pd(II)-Catalyzed Halogenation of Aminotetrazoles. CF_3SO_3H (0.5 mmol) was added to a stirred solution of aminotetrazole **1** (1 mmol), $Pd(OAc)_2$ (10 mol %) and NXS (1.2 mmol) in DCE (2 mL) under air. The mixture was stirred at 60 °C for the appropriate time and the progress of the reaction was monitored by TLC using ethyl acetate and hexane as eluent. After completion, the reaction mixture was cooled to room temperature and treaed with saturated $NaHCO_3$ (5 mL). The resulting solution was extracted with ethyl acetate (3 x 10 mL) and washed with brine (2 x 5 mL). Drying (Na_2SO_4) and evaporation of the solvent gave a residue that was purified on silica gel column chromatography using hexane and ethyl acetate as eluent to afford analytically pure substituted *N*-(2-haloaryl)aminotetrazoles.

***N*-(2-Bromophenyl)-1-(2-chlorophenyl)-1*H*-tetrazol-5-amine 2a.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.71; 294 mg, 84% yield; white solid; mp 96-97 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (d, *J* = 8.8 Hz, 1H), 7.80 (d, *J* = 6.8 Hz, 2H), 7.50-7.47 (m, 2H), 7.37-7.33 (m, 2H), 7.13 (s, 1H), 7.04-7.00 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.9, 134.6, 134.1, 131.7, 129.2, 128.4, 125.9, 124.9, 124.4, 124.1, 121.7, 120.2, 119.2; FT-IR (KBr) 3445, 3387, 2956, 2926, 1714, 1603, 1567, 1517, 1487, 1380, 1111, 1072, 827, 751 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{13}H_9ClBrN_5H$ 351.9781, found 351.9789.

***N*-(2-Bromo-5-methylphenyl)-1-*m*-tolyl-1*H*-tetrazol-5-amine 2b and *N*-(2,6-dibromo-3-methylphenyl)-1-*m*-tolyl-1*H*-tetrazol-5-amine 2b'.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.68; white solid; 283 mg, 78% yield; mp 101-102 °C; both isomers are reported together (ratio: 3.2:1 as determined by NMR);^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1H, major isomer), 8.30 (d, *J* = 9.2 Hz, 1H, minor isomer), 7.64 (s, 1H, major isomer), 7.57-7.50 (m, 4H, 2H major + 2H minor isomers), 7.41-7.36 (m, 6H, 3H major + 3H minor isomers), 7.16 (br s, 1H), 2.56 (s, 3H, minor isomer), 2.47 (s, 6H, 3H major + 3H minor isomers), 2.40 (s, 3H, major isomer);^{13}C NMR (75 MHz, $CDCl_3$) δ 150.8, 150.7, 141.3, 139.2, 137.7, 135.4, 134.8, 134.7, 132.3, 132.2, 131.5, 130.5, 125.0, 124.9, 121.2, 121.1, 120.3, 118.0, 117.2, 114.9, 108.9, 24.6, 23.0, 21.4; FT-IR (KBr) 3365, 3086, 2918, 2857, 1958, 1598, 1559, 1522, 1493, 1449, 1385, 1313, 1124, 1089, 1046, 875, 795, 692 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{15}H_{14}BrN_5H$ 344.0505, found 344.0504; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{15}H_{13}Br_2N_5H$ 423.9689, found 423.9685.

***N*-(2-Bromo-4-chlorophenyl)-1-(4-chlorophenyl)-1*H*-tetrazol-5-amine 2c.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.70; white solid; 320 mg, 84% yield; mp 175-176 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.48 (d, *J* = 8.8 Hz, 1H), 7.65 (d, *J* = 8.4 Hz, 2H), 7.57-7.53 (m, 3H), 7.39 (dd, J = 8.8, 2.4 Hz. 1H), 7.13 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.8, 137.3, 133.4, 131.3, 131.0, 129.5, 129.2, 129.0, 128.7, 125.8, 122.2, 120.0; FT-IR (KBr) 3434, 3364, 2923, 2846, 1733, 1602, 1561, 1399, 1259, 1086, 1034, 814, 735 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{13}H_8BrCl_2N_5H$ 383.9413, found 383.9427.

***N*-(2-Bromo-4-fluorophenyl)-1-(4-fluorophenyl)-1*H*-tetrazol-5-amine 2d.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.62; white solid; 287 mg, 82% yield; mp 171-172 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47-8.44 (m, 1H), 7.61-7.57 (m, 2H), 7.39-7.33 (m, 2H), 7.30-7.27 (m, 1H), 7.16-7.11 (m, 1H), 6.97 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 164.1, 161.6, 159.4, 156.9, 153.1, 151.7, 132.6, 128.5, 126.6, 126.5, 122.4, 122.3, 119.5, 119.2, 117.2, 117.0, 115.3, 115.1, 114.6, 114.5; FT-IR (KBr) 3423, 3385, 2961, 2926, 2254, 1618, 1578, 1508, 1260, 1237, 1157, 1024, 809, 760 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{13}H_8F_2BrN_5H$ 352.0004, found 352.0000.

***N*-(2-Bromo-4-isopropylphenyl)-1-(4-isopropylphenyl)-1*H*-tetrazol-5-amine 2e.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.64; thick colorless liquid; 352 mg, 88% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, J = 8.4 Hz, 1H), 7.50-7.45 (m, 4H), 7.35-7.34 (d, J = 2.0 Hz, 1H), 7.23 (dd, J = 8.4, 2.0 Hz, 1H), 7.10 (br s, 1H), 3.03-2.99 (m, 1H), 2.85-2.82 (m, 1H), 1.30 (d, J = 6.8 Hz, 6H), 1.20 (d, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.5, 151.0, 145.1, 133.5, 130.2, 130.0, 128.5, 126.8, 124.1, 119.2, 112.1, 33.9, 33.2, 23.8, 23.7; FT-IR (KBr) 3372, 2961, 2928, 2870, 1598, 1556, 1523, 1460, 1388, 1364, 1316, 1238, 1117, 1084, 1058, 1013, 838, 710 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{19}H_{22}BrN_5H$ 402.1113, found 402.1119.

***N*-(2-Bromo-4-methylphenyl)-1-*p*-tolyl-1*H*-tetrazol-5-amine 2f.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.72; white solid; 313 mg, 91% yield; mp 152-153 °C; ^{1}H NMR

(400 MHz, $CDCl_3$) δ 8.35 (d, *J* = 8.4 Hz, 1H), 7.47-7.42 (m, 4H), 7.32 (s, 1H), 7.19 (dd, *J* = 8.4, 1.6 Hz, 1H), 7.09 (br s, 1H), 2.47 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.2, 141.1, 134.2, 133.4, 132.6, 131.3, 130.1, 129.6, 124.3, 119.0, 112.0, 21.4, 20.5; FT-IR (KBr) 3381, 3085, 2917, 1599, 1566, 1525, 1318, 1235, 1179, 1083, 1038, 816, 720 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{15}H_{14}BrN_5H$ 344.0505, found 344.0504.

***N*-(2-Bromo-4-methoxyphenyl)-1-(4-methoxyphenyl)-1*H*-tetrazol-5-amine 2g and *N*-(2,6-dibromo-4-methoxyphenyl)-1-(4-methoxyphenyl)-1*H*-tetrazol-5-amine 2g'.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.48; white solid; 366 mg, 88% yield; mp 147-148 °C; both isomers are reported together (ratio: 1:1 as determined by NMR); ^1H NMR (400 MHz, $CDCl_3$) δ 8.68 (s, 1H), 8.32 (d, *J* = 9.2 Hz, 1H), 7.49-7.46 (m, 5H), 7.13-7.06 (m, 4H), 7.02 (s, 1H), 6.95 (dd, *J* = 9.2, 2.8 Hz, 1H), 6.80 (br s, 1H), 3.89 (s, 6H), 3.84 (s, 3H), 3.77 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 161.2, 161.1, 155.6, 151.6, 151.1, 151.0, 128.5, 128.2, 126.2, 124.9, 124.7, 122.6, 120.9, 120.4, 120.2, 115.7, 115.6, 114.8, 113.6, 112.7, 56.7, 55.8; FT-IR (KBr) 3434, 3393, 2925, 2851, 1603, 1523, 1486, 1263, 1209, 1086, 1021, 824, 801, 746 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd $C_{15}H_{14}BrN_5O_2H$ 376.0404, found 376.0404; $[M+H]^+$ calcd for $C_{15}H_{13}Br_2N_5O_2H$ 455.9416, found 455.9420.

***N*-(2-Bromo-4,6-dimethylphenyl)-1-(2,4-dimethylphenyl)-1*H*-tetrazol-5-amine 2h.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.50; white solid; 234 mg, 63% yield; mp 98-99 °C; ^1H NMR (400 MHz, $CDCl_3$) δ 7.29-7.20 (m, 4H), 7.02 (s, 1H), 5.73 (br s, 1H), 2.43 (s, 3H), 2.29 (s, 6H), 2.20 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.8, 141.6, 138.8, 137.6, 135.9, 132.5, 132.0, 131.2, 130.7, 128.6, 128.2, 126.9, 122.0, 21.2, 20.6, 18.9, 17.3; FT-IR (KBr) 3370, 3247, 2959, 2923, 1714, 1587, 1515, 1476, 1381, 1293, 1227, 1102, 1087, 1027, 818, 734 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{17}H_{18}BrN_5H$ 372.0818, found 372.0820.

***N*-(2-Bromo-4,5-dimethylphenyl)-1-(3,4-dimethylphenyl)-1*H*-tetrazol-5-amine 2i and *N*-(2,6-dibromo-3,4-dimethylphenyl)-1-(3,4-dimethylphenyl)-1*H*-tetrazol-5-amine 2i'.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.71; white solid; 354 mg, 90% yield; mp 116-117 °C; both isomers are reported together (ratio: 2.5:1 as determined by NMR); ^{1}H NMR (400 MHz, $CDCl_3$)δ 8.26 (s, 1H, major isomer), 8.24 (s, 1H, minor isomer), 7.40 (s, 1H, minor isomer), 7.38-7.37 (m, 2H, major isomer), 7.34-7.30 (m, 2H, 1H major + 1H minor isomers), 7.27 (s, 1H, major isomer), 7.19 (d, *J* = 8.4 Hz, 1H, minor isomer), 7.09 (br s, 1H), 2.38 (s, 15H, 6H major + 9H minor isomers), 2.32 (s, 3H minor isomer), 2.29 (s, 3H major isomer), 2.21 (s, 3H, major isomer); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.2, 151.0, 139.5, 137.7, 136.6, 133.8, 133.3, 132.8, 132.6, 132.4, 131.5, 130.2, 130.1, 129.4, 125.1, 121.3, 120.0, 116.0, 115.6, 108.6, 20.8, 20.3, 19.9, 19.87, 19.7, 19.0; FT-IR (KBr) 3376, 2971, 2920, 1594, 1558, 1518, 1451, 1396, 1245, 1114, 1087, 1026, 874, 832, 723cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{17}H_{18}BrN_5H$ 372.0818, found 372.0807; $[M+H]^+$ calcd for $C_{17}H_{17}Br_2N_5H$ 453.9866, found 453.9862.

***N*-(2-Bromo-5-nitrophenyl)-1-*p*-tolyl-1*H*-tetrazol-5-amine 2j.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.54; 295 mg, 79% yield; thick yellow liquid; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (d, *J* = 8.4 Hz, 1H), 7.56-7.47 (m, 6H), 2.50 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6) δ 150.8, 150.6, 141.5, 137.9, 131.3, 129.5, 129.2, 124.2, 121.9, 119.0, 103.9, 21.4; FT-IR (KBr) 3427, 2912, 2247, 1635, 1605, 1525, 1344, 1116, 1024, 998, 823, 764 cm^{-1}. HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{14}H_{11}BrN_6O_2Na$ 397.0030, found 397.0025.

***N*-(2-Bromo-4-methylphenyl)-1-(2-chlorophenyl)-1*H*-tetrazol-5-amine 2k.** Analytical TLC on silica gel, 1:4 ethyl acetate/ hexane R_f = 0.70; white solid; 337 mg, 92% yield; mp 158-159 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (d, *J* = 8.4 Hz, 1H), 7.75 (dd, *J* = 8.4, 0.8 Hz, 1H), 7.42

(s, 1H), 7.30-7.22 (m, 3H), 7.12 (br s, 1H), 6.97-6.93 (m, 1H), 2.44 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.8, 141.3, 134.6, 131.5, 129.1, 128.4, 127.1, 126.3, 123.8, 122.6, 121.5, 119.0, 23.6; FT-IR (KBr) 3381, 3104, 2921, 1898, 1605, 1567, 1515, 1314, 1093, 1034, 823, 736 cm^{-1}. HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{14}H_{11}BrClN_5H$ 363.9959, found 363.9957.

***N*-(2-Bromo-4-nitrophenyl)-1-(2-chlorophenyl)-1*H*-tetrazol-5-amine 2l.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.42; white solid; 293 mg, 74% yield; mp 116-117 °C; ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO-d_6) δ 8.36 (d, J = 2.4 Hz, 1H), 8.29 (d, J = 9.2 Hz, 1H), 8.19-8.16 (m, 2H), 7.67- 7.61 (m, 3H), 7.56 (dd, J = 7.6, 1.6 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$ + DMSO-d_6) δ 150.6, 141.8, 141.2, 132.4, 130.5, 130.4, 128.8, 128.7, 128.1, 127.5, 123.7, 117.8, 111.1; FT-IR (KBr) 3445, 3109, 2928, 2258, 1605, 1520, 1412, 1339, 1283, 1115, 1025, 1001, 827, 742 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{13}H_8BrClN_6O_2H$ 394.9653, found 394.9658.

***N*-(2-Bromo-4-ethylphenyl)-1-(2-fluorophenyl)-1*H*-tetrazol-5-amine 2m.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.50; white solid; 285 mg, 79% yield; mp 106-107 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 8.4 Hz, 1H), 7.64-7.56 (m, 2H), 7.43-7.35 (m, 2H), 7.32 (s, 1H), 6.93 (br s, 1H), 2.59 (q, J = 7.6 Hz, 2H), 1.19 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.4, 154.8, 152.0, 141.0, 133.8, 133.4, 133.23, 133.2, 131.6, 129.4, 129.0, 128.4, 128.3, 126.09, 126.1, 125.0, 122.9, 120.3, 120.2, 120.0, 119.4, 117.8, 117.6, 112.4, 28.6, 15.5; FT-IR (KBr) 3383, 3074, 2966, 2931, 2863, 1599, 1563, 1522, 1461, 1390, 1316, 1258, 1228, 1085, 1041, 979, 877, 824, 757, 663 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{15}H_{13}BrFN_5H$ 362.0411, found 362.0413.

***N*-(2-Bromo-4-methylphenyl)-1-(2,6-dimethylphenyl)-1*H*-tetrazol-5-amine 2n.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.55; white solid; 318 mg, 89% yield; mp 134-

135 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.0 Hz, 1H), 7.32-7.28 (m, 1H), 7.18-7.16 (m, 3H), 7.07 (d, *J* = 8.4 Hz, 1H), 6.47 (br s, 1H), 2.16 (s, 3H), 1.95 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 136.6, 134.3, 133.1, 132.4, 131.5, 129.4, 129.3, 119.2, 112.1, 20.3, 17.4; FT-IR (KBr) 3483, 3367, 3137, 3953, 2921, 2863, 2754, 2360, 1590, 1566, 1493, 1404, 1310, 1243, 1170, 1119, 1144, 1043, 891, 814, 775, 596 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{16}H_{16}BrN_5H$ 360.0643, found 360.0644

***N*,1-Bis(2-chlorophenyl)-1*H*-tetrazol-5-amine 3a.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.66; white solid; 264 mg, 86% yield; mp 81-82 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 8.8 Hz, 1H), 7.70 (d, *J* = 7.6 Hz, 1H), 7.63-7.59 (m, 1H), 7.57-7.53 (m, 2H), 7.35-7.31(m, 2H), 7.01-6.97 (m, 1H), 6.82 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.8, 134.6, 133.0, 131.4, 131.3, 129.6, 129.4, 129.1, 128.9, 128.2, 124.0, 121.8, 119.2; FT-IR (KBr) 3433, 2925, 2857, 2318, 1742, 1603, 1568, 1465, 1448, 1265, 1089, 1028, 795, 744 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{13}H_9Cl_2N_5H$ 306.0308, found 306.0307.

1-(4-Chlorophenyl)-*N*-(2,4-dichlorophenyl)-1*H*-tetrazol-5-amine 3b. Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.50; white solid; 212 mg, 63% yield; mp 180-181 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (d, *J* = 8.4 Hz, 1H), 7.68-7.66 (m, 2H), 7.59-7.55 (m, 2H), 7.47-7.40 (m, 1H), 7.35-7.27 (m, 1H), 7.10 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 151.1, 135.9, 133.8, 131.0, 130.5, 130.2, 128.7, 128.5, 127.7, 125.4, 121.3; FT-IR (KBr) 3459, 3375, 3096, 2915, 1652, 1652, 1599, 1559, 1511, 1491, 1467, 1275, 1260, 1093, 1048, 859, 831, 764, 749 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{13}H_8Cl_3N_5H$ 339.9918, found 339.9907.

***N*-(2-Chloro-4-fluorophenyl)-1-(4-fluorophenyl)-1*H*-tetrazol-5-amine 3c.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.61; white solid; 270 mg, 88% yield; mp 101-102 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46-8.41 (m, 1H), 7.60-7.56 (m, 2H), 7.38-7.33 (m, 2H), 7.15-

7.06 (m, 2H), 6.92 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 164.0, 161.4, 159.3, 156.8, 153.0, 151.7, 131.4, 128.5, 126.5, 126.4, 125.0, 124.8, 122.62, 122.6, 117.0, 116.8, 116.4, 116.2, 114.8, 114.5, 114.3; FT-IR (KBr) 3398, 3325, 2981, 2394, 1685, 1612, 1578, 1502, 1365, 1260, 1242, 1162, 1023, 826, 793 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{13}H_8F_2ClN_5H$ 308.0509, found 308.0509.

***N*-(2-Chloro-4-isopropylphenyl)-1-(4-isopropylphenyl)-1*H*-tetrazol-5-amine 3d.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.60; thick colorless liquid; 291 mg, 82% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 8.0 Hz, 1H), 7.50-7.45 (m, 4H), 7.19-7.16 (m, 2H), 7.06 (br s, 1H), 3.05-2.98 (m, 1H), 2.87-2.80 (m, 1H), 1.30 (d, *J* = 7.2 Hz, 6H), 1.21 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.7, 151.1, 144.8, 132.4, 130.2, 128.6, 126.8, 126.2, 124.1, 119.1, 33.9, 33.3, 23.8, 23.7; FT-IR (KBr) 3388, 3043, 2961, 2928, 2870, 1908, 1599, 1556, 1523, 1461, 1416, 1390, 1317, 1240, 1117, 1143, 1085, 1051, 1013, 980, 909, 837, 780, 723, 676 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{19}H_{22}ClN_5H$ 356.1636, found 356.1637.

***N*-(2-Chloro-4-methylphenyl)-1-*p*-tolyl-1*H*-tetrazol-5-amine 3e.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.70; white solid; 249 mg, 83% yield; mp 137-138 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, *J* = 8.0 Hz, 1H), 7.46-7.41 (m, 4H), 7.16-7.13 (m, 2H), 7.04 (br s, 1H), 2.47 (s, 3H), 2.29 (s, 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ 151.2, 141.2, 133.8, 132.3, 131.3, 130.1, 129.5, 129.0, 124.3, 121.4, 119.0, 21.5, 20.7; FT-IR (KBr) 3397, 3085, 2922, 2851, 1619, 1604, 1561, 1525, 1380, 1316, 1234, 1087, 1046, 817 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{15}H_{14}ClN_5H$ 300.1010; found 300.1007.

***N*-(2-Chloro-4,6-dimethylphenyl)-1-(2,4-dimethylphenyl)-1*H*-tetrazol-5-amine 3f.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.48; white solid; 222 mg, 68% yield; mp 102-103 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.28-7.26 (m, 2H), 7.22 (s, 1H), 7.07 (s, 1H), 6.98 (s, 1H), 5.72 (br s, 1H), 2.43 (s, 3H), 2.28 (s, 6H), 2.19 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.9, 141.7, 138.4, 137.5, 136.0, 132.6, 130.9, 130.6, 128.6, 128.3, 127.7, 126.9, 21.3, 20.9, 18.7, 17.4; FT-IR (KBr) 3158, 3065, 2968, 2923, 1587, 1512, 1478, 1312, 1285, 1227, 1114, 1085, 1027, 850, 816 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{17}H_{18}ClN_5H$ 328.1323, found 328.1323.

***N*-(2-Chloro-4,5-dimethylphenyl)-1-(3,4-dimethylphenyl)-1*H*-tetrazol-5-amine 3g and *N*-(2,6-dichloro-3,4-dimethylphenyl)-1-(3,4-dimethylphenyl)-1*H*-tetrazol-5-amine 3g'.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.70; white solid; 304 mg, 90% yield; mp 130-131 °C; both isomers are reported together (ratio: 2.4:1 as determined by NMR); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.24 (s, 1H, major isomer), 8.21 (s, 1H, minor isomer), 7.38 (s, 1H, minor isomer), 7.36 (d, *J* = 11.6 Hz, 1H, major isomer), 7.29 (dd, *J* = 8.0, 2.4 Hz, 2H, major isomer), 7.20 (s, 1H, minor isomer), 7.14 (d, *J* = 8.4 Hz, 1H, minor isomer), 7.10 (s, 1H, major isomer), 7.02 (br s, 1H), 2.36 (s, 12H, 6H major + 6H minor isomers), 2.30 (3H, minor isomer), 2.28 (3H, major isomer), 2.27 (3H, minor isomer), 2.19 (3H, major isomer); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.1, 151.0, 139.6, 137.0, 134.8, 132.6, 132.3, 132.2, 132.1, 131.5, 130.2, 130.15, 129.5, 128.7, 125.2, 122.1, 121.2, 120.0, 118.3, 115.8, 20.4, 19.9, 19.8, 19.7, 19.0, 16.9; FT-IR (KBr) 3158, 3065, 2968, 2923, 1587, 1512, 1478, 1312, 1285, 1227, 1114, 1085, 1027, 850, 816, 732 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{17}H_{18}ClN_5H$ 328.1323; found 328.1318; $[M+H]^+$ calcd for $C_{17}H_{17}Cl_2N_5H$ 362.0934; found 362.0927.

***N*-(2-Chloro-4-nitrophenyl)-1-(2-chlorophenyl)-1*H*-tetrazol-5-amine 3h.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.20; white solid; 276 mg, 79% yield; mp 135-136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.75 (d, *J* = 9.2 Hz, 1H), 8.29-8.24 (m, 2H), 7.75-7.56 (m, 4H), 7.19 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6) δ 151.0, 142.3, 140.4, 133.0, 131.2, 130.9, 129.3, 128.8, 124.8, 124.0, 121.5, 118.0; FT-IR (KBr) 3439, 3112, 2932, 2249, 1624, 1524, 1409, 1337, 1279, 1125, 1045, 1003, 810, 725, 649 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{13}H_8Cl_2N_6O_2H$ 351.0159, found 351.0157.

***N*-(2-chloro-4-ethylphenyl)-1-(2-fluorophenyl)-1*H*-tetrazol-5-amine 3i.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.50; white solid; 259 mg, 82% yield; mp 113-114 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, J = 8.4 Hz, 1H), 7.61-7.55 (m, 2H), 7.46-7.36 (m, 2H), 7.15-7.12 (m, 2H), 6.91 (br s, 1H), 2.59 (q, J = 7.6 Hz, 2H), 1.19 (t, J = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.3, 154.8, 152.0, 140.6, 133.2, 133.1, 132.3, 128.4, 128.3, 127.7, 126.13, 126.1, 121.9, 120.4, 120.3, 119.4, 117.8, 117.6, 28.1, 15.5; FT-IR (KBr) 3444, 3066, 2970, 2871, 1602, 1522, 1503, 1464, 1390, 1318, 1257, 1230, 1131, 1021, 874, 755, 708 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{15}H_{13}ClFN_5H$ 318.0916, found 318.0912.

***N*-(2-Chloro-4-methylphenyl)-1-(2,6-dimethylphenyl)-1*H*-tetrazol-5-amine 3j.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.50; white solid; 281 mg, 90% yield; mp 130-131 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.36 (d, J = 8.0 Hz, 1H), 7.46-7.42 (m, 1H), 7.31-7.28 (m, 2H), 7.18-7.16 (m, 2H), 6.49 (br s, 1H), 2.30 (s, 3H), 2.08 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.9, 136.8, 134.0, 132.1, 131.6, 129.5, 129.4, 128.8, 121.6, 119.4, 20.5, 17.4; FT-IR (KBr) 3141, 3056, 2924, 2886, 1701, 1657, 1611, 1556, 1501, 1478, 1445, 1379, 1305, 1263, 1242, 1208, 1161, 785 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{16}H_{16}ClN_5H$ 314.1167, found 314.1168.

***N*-(4-Fluoro-2-iodophenyl)-1-(4-fluorophenyl)-1*H*-tetrazol-5-amine 4a.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.66; white solid; 360 mg, 90% yield; mp 173-174 °C; ^{1}H NMR (400 MHz, $CDCl_3$ + DMSO) δ 8.35-8.31 (m, 1H), 7.63-7.59 (m, 2H), 7.48 (dd, J = 8.0, 3.2 Hz, 1H), 7.37-7.33 (m, 2H), 7.17-7.12 (m, 1H), 6.83 (br s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$

+ DMSO-d_6) δ 163.3, 160.8, 159.4, 156.9, 152.1, 135.7, 128.3, 126.3, 126.2, 125.0, 124.8, 123.8, 116.3, 116.1, 115.3, 115.1, 93.0; FT-IR (KBr) 3427, 2255, 2128, 1645, 1578, 1522, 1509, 1234, 1048, 1025, 103, 825, 764, 632 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{13}H_8F_2IN_5H$ 399.9865, found 399.9856.

***N*-(2-Iodo-4-isopropylphenyl)-1-(4-isopropylphenyl)-1*H*-tetrazol-5-amine 4b.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.50; white solid; 388 mg, 87% yield; mp 109-110 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (d, *J* = 7.6 Hz, 1H), 7.49 (d, *J* = 1.6 Hz, 1H),7.47-7.37 (m, 4H), 7.17 (dd, *J* = 8.4, 1.4 Hz, 1H), 6.87 (br s, 1H), 2.95-2.90 (m, 1H), 2.74-2.69 (m, 1H), 1.21 (d, *J* = 6.8 Hz, 6H), 1.12 (d, *J* = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.8, 151.6, 145.9, 136.7, 136.3, 130.2, 128.6, 127.9, 124.6, 119.1, 88.6, 34.0, 33.2, 23.92, 23.9; FT-IR (KBr) 3492, 337, 2960, 2868, 1593, 1557, 1523, 1483, 1460, 1410, 1388, 1314, 1261,1084, 1058, 1031, 1013, 837, 749 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{19}H_{22}IN_5H$ 448.0993, found 448.0997.

***N*-(2-Iodo-4-methylphenyl)-1-*p*-tolyl-1*H*-tetrazol-5-amine 4c.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.73; white solid; 364 mg, 93% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (d, *J* = 8.4 Hz, 1H), 7.55 (s, 1H), 7.49-7.42 (m, 4H), 7.21 (d, *J* = 8.4 Hz, 1H), 6.92 (br s, 1H), 2.47 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$)δ 151.5, 141.1, 139.1, 136.0, 134.8, 131.2, 130.5, 130.0, 124.5, 118.7, 88.3, 21.4, 20.3; FT-IR (KBr) 3456, 3352, 2922, 2846, 1722, 1594, 1559, 1523, 1478, 1380, 1305, 1085, 1035, 818, 740 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{15}H_{14}IN_5H$ 392.0367, found 392.0368.

***N*-(2-Iodo-4,6-dimethylphenyl)-1-(2,4-dimethylphenyl)-1*H*-tetrazol-5-amine 4d**. Analytical TLC on silica gel,1:4 ethyl acetate/hexane R_f = 0.53; brown liquid; 307 mg, 73% yield; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (s, 1H), 7.32 (d, *J* = 8.0 Hz, 1H), 7.26 (s, 1H), 7.21 (d, *J* = 6.4 Hz, 1H), 7.04 (s, 1H), 5.55 (br s, 1H), 2.42 (s, 3H), 2.28 (s, 3H), 2.23 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.6, 141.8, 139.5, 137.3, 136.9, 136.1, 134.8, 132.7, 132.4, 128.5, 128.3, 127.0, 99.7, 21.4, 20.5, 19.5, 17.7; FT-IR (KBr) 3389, 3054, 2922, 2851, 1599, 1565, 1520, 1453, 1386, 1245, 1113, 1087, 1022, 877, 819, 639 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{17}H_{18}IN_5H$ 420.0680, found 420.0682.

***N*-(2-Iodo-4,5-dimethylphenyl)-1-(3,4-dimethylphenyl)-1*H*-tetrazol-5-amine 4e.** Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.71; white solid; 362 mg, 86% yield; mp 153-154 °C;^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.47 (s, 1H), 7.37-7.33 (m, 3H), 6.91 (br s, 1H), 2.36 (s, 6H), 2.27 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 151.3, 139.6, 139.0, 138.8, 136.1, 133.7, 131.5, 130.1, 125.3, 121.8, 120.0, 84.1, 20.0, 19.9, 19.8, 18.8; FT-IR (KBr) 3359, 3054, 2950, 2919, 2851, 1589, 1557, 1518, 1450, 1393, 1245, 1084, 873, 831 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{17}H_{18}IN_5H$ 420.0680, found 420.0685.

1-(2-Chlorophenyl)-*N*-(2-iodo-4-methylphenyl)-1*H*-tetrazol-5-amine 4f. Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.72; white solid; 364 mg, 89% yield; mp 108-109 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44-8.42 (m, 1H), 8.07 (d, *J* = 8.4 Hz, 1H), 7.46 (d, *J* = 2.4 Hz, 1H), 7.35-7.30 (m, 2H), 7.18 (br s, 1H), 7.12 (dd, *J* = 8.4, 2.4 Hz, 1H), 7.02 (td, *J* = 8.0, 1.6 Hz, 1H), 2.52 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 150.6, 144.9, 141.0, 134.5, 132.5, 129.1, 128.3, 125.0, 123.9, 122.5, 121.5, 119.0, 103.2, 28.4; FT-IR (KBr) 3467, 3387, 2922, 2840, 1603, 1566, 1520, 1470, 1374, 1317, 1088, 1017, 576 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{14}H_{11}ClIN_5H$ 411.9820, found 411.9831.

1-(2,6-Dimethylphenyl)-*N*-(2-iodo-4-methylphenyl)-1*H*-tetrazol-5-amine 4g: Analytical TLC on silica gel, 1:4 ethyl acetate/hexane R_f = 0.50; white solid; 364 mg, 90% yield; mp 156-157 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.8 Hz, 1H), 7.42 (d, *J* = 1.2 Hz, 1H), 7.34-7.30 (m, 1H), 7.20 (d, J = 7.6 Hz, 2H), 7.12 (dd, J = 8.4, 1.2 Hz, 1H), 6.36 (br s, 1H), 2.16 (s, 3H), 1.98 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.1, 138.9, 136.8, 135.7, 134.8, 131.6, 130.4, 129.5, 129.4, 118.7, 88.3, 20.2, 17.5; FT-IR (KBr) 3343, 3201, 2920, 2858, 1596, 1588, 1561, 1525, 1486, 1473, 1445, 1376, 1308, 1236, 1169, 1087, 984, 868, 811, 777, 730 cm^{-1}; HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{16}H_{16}IN_5H$ 406.0523, found 406.0524.

ASSOCIATED CONTENT

Supporting Information

General information, procedure for the preparation of deuterated aniline, isotopic kinetic study, crystal structure and data, and NMR (^{1}H and ^{13}C) spectra of **2a-n, 3a-j, 4a-g, 1o and 3o**. This material is available free of charge via the internet at http://pubs.acs.org.

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