Microwave-Assisted Stille Reactions as a Powerful Tool for Building Polyheteroaryl Systems Bearing a (1*H*)-1,2,4-Triazole Moiety

C. Cebrián,[a] A. de Cózar,[a] P. Prieto,*[a] A. Díaz-Ortiz,*[a] A. de la Hoz,[a] J. R. Carrillo,[a] A. M. Rodriguez,[a] F. Montilla[b]

[a] Facultad de Química, Universidad de Castilla-La Mancha, 13071, Ciudad Real, Spain
Fax +926-295318; E-mail: MariaPilar.Prieto@uclm.es

[b] Facultad de Ciencias, Universidad de Alicante, Apdo. de Correos 99, 03080, Alicante, Spain

Received 29 September 2009

Abstract: Stille couplings and the combination of Stille/Heck cross-coupling reactions provide useful access to tricyclic systems with valuable material properties from 3,5-dibromo-1,2,4-triazoles. The reactions can all be dramatically improved under microwave irradiation.

Key words: Stille reaction, microwave, (1*H*)-1,2,4-triazole, 1,2,3-triazole, electropolymerization

Research on the electrochemistry of new monomers and the electrosynthesis of electronically conducting polymers (ECPs) has been of great interest in the last few decades.[1] Most of the classical conducting polymers are based on polyaniline (PANI)[2] or heterocycles such as polypyrrole (PPy),[3] or polythiophene (PTh).[4]

A new synthetic approach to these materials involves the insertion of a functional species between two polymerizable moieties, for example, between two thiophene or pyrrole rings.[5] In this respect, the (1*H*)-1,2,4-triazole moiety could be a convenient functional group for insertion. This unit is of current interest owing to its widely reported properties and applications, such as in new materials,[6] in medicinal chemistry[7] and as a ligand.[8]

Many ECPs have been prepared through chemical methods – most involving organometallic coupling reactions, which are a powerful tool in organic synthesis.[9]

Microwave-assisted organic synthesis (MAOS)[10] is a relatively new technique in synthetic chemistry. Homogeneous transition-metal catalyzed reactions, which typically require long reaction times, represent one of the most important and best studied reaction types in MAOS, as evidenced by the numerous recent scientific publications, reviews and patents published in this field.[11] In this sense, Stille protocols are amongst the most versatile and well-investigated microwave-assisted cross-coupling reactions in modern organic synthesis and constitute a convenient C–C bond-forming tool.[12] The utility of the Stille reaction is widely recognized by the synthetic community. This is due to the growing availability of the organostannane derivatives[13] and their stability to air and moisture. In addition, the process is compatible with virtually any functional group, thereby eliminating the need for protection/deprotection strategies, which are a necessity with most organometallic reactions. The process is often regiospecific with regards to the newly formed C–C σ-bond and is particularly effective for transformations of highly functionalized molecules.[14]

However, to the best of our knowledge, reports related to the Stille reaction of (1*H*)-1,2,4-triazoles have not been published to date. Indeed, cross-coupling reactions on azoles with three heteroatoms are very rare and are limited to a few examples.[15]

As a new synthetic approach for building polyheteroaryl systems bearing a 1,2,4-triazole moiety, we report here the first Stille cross-coupling reaction of 3,5-dibromo-1-methyl-1*H*-1,2,4-triazole (**1**) with a range of stannyl derivatives under microwave irradiation in solvent-free conditions. Our aim was to develop a general procedure for the preparation of compounds with potential applications in different fields, such as electrochemistry, new materials or medicinal chemistry. The different reactivity of positions 3 and 5 of compound **1** led to a wide range of mono- and disubstituted, symmetric or asymmetric products.

On using either $PdCl_2(PPh_3)_2$/LiCl[16] or $PdCl_2(PPh_3)_2$/CuI[17] as the catalytic system, dibromotriazole **1** reacted with stannyl derivatives **2** (1.3 equiv) under microwave irradiation at 110 °C for 15 minutes to afford the 5-monosubstituted 1,2,4-triazoles **4** as the sole or main product with good yields. The results are summarized in Table 1.[18]

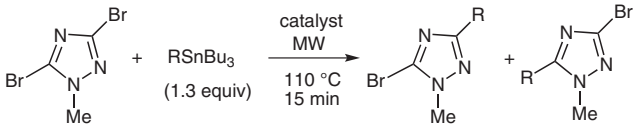
As one would expect, the higher reactivity of the 5-position of 1,2,4-triazoles explains the formation of product **4**. Only in the case of the highly reactive thiophene derivative **2a** was a small amount of the 3-substituted product **3a** obtained.

Experimental results showed that $PdCl_2(PPh_3)_2$/LiCl was the best catalytic system for five-membered heterocyclic and aryl stannanes (Table 1, entries 1 and 2). In contrast, $PdCl_2(PPh_3)_2$/CuI gave higher yields of products with six-membered heterocyclic stannanes (Table 1, entries 7 and 8).

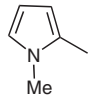
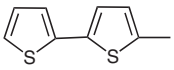
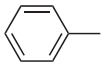
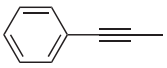
In order to evaluate the influence of microwave irradiation, we also performed the reaction between **1** and **2a** in an oil bath under similar reaction conditions (time and temperature); in this case, compounds **3a** and **4a** were obtained in 5% and 44% yield, respectively. When the reaction time was extended to 60 minutes the yields only improved to 7 and 57%, respectively. In the case of stan-

SYNLETT 2010, No. 1, pp 0055–0060
Advanced online publication: 02.12.2009
DOI: 10.1055/s-0029-1218533; Art ID: D27898ST

Table 1 Reactions between 3,5-Dibromo-1-methyl-(1*H*)-1,2,4-triazole (**1**) and Organostannanes **2**



1 2 3 4

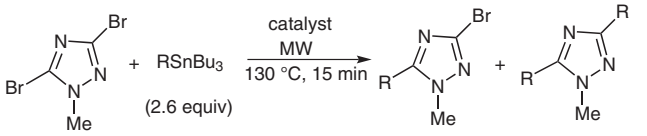
Entry	R	Catalytic system	Product [yield (%)]
1	 **2a**	$PdCl_2(PPh_3)_2$ + LiCl	**3a** (13) + **4a** (84)
2	 **2a**	$PdCl_2(PPh_3)_2$ + CuI	**3a** (8) + **4a** (60)
3	 **2b**	$PdCl_2(PPh_3)_2$ + LiCl	**4b** (88)
4	 **2c**	$PdCl_2(PPh_3)_2$ + LiCl	**4c** (77)
5	 **2d**	$PdCl_2(PPh_3)_2$ + LiCl	**4d** (82)
6	 **2e**	$PdCl_2(PPh_3)_2$ + LiCl	**4e** (60)
7	 **2f**	$PdCl_2(PPh_3)_2$ + LiCl	**4f** (41)
8	 **2f**	$PdCl_2(PPh_3)_2$ + CuI	**4f** (79)
9	 **2g**	$PdCl_2(PPh_3)_2$ + CuI	**4g** (58)

nyl derivative **2e**, the product yield decreased to 21% with classical heating. Microwave irradiation therefore represents the best heating source for performing these reactions and allows the synthesis of the 5-monosubstituted-1,2,4-triazoles **4** within 15 minutes in good yields.

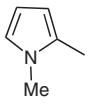
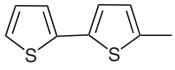
As a new application of this approach, we carried out these reactions under microwave irradiation with 2.6 equivalents of the organostannane derivative **2** in order to obtain symmetrical disubstituted systems bearing a (1*H*)-1,2,4-triazole moiety. The results are collected in Table 2.[19]

These outcomes show that the five-membered, disubstituted heterocyclic systems can be synthesized in good to excellent yields (65–98%). It is noteworthy that six-membered, disubstituted heterocyclic systems could not be obtained under either of the proven reaction conditions,

Table 2 Reactions between 3,5-Dibromo-1-methyl-(1*H*)-1,2,4-triazole (**1**) and Organostannanes **2**



1 2 4 5

Entry	R	Catalytic system	Product [yield (%)]
1	 **2a**	$PdCl_2(PPh_3)_2$ + LiCl	**5a** (98)
2	 **2b**	$PdCl_2(PPh_3)_2$ + LiCl	**4b** (12) + **5b** (85)
3	 **2c**	$PdCl_2(PPh_3)_2$ + LiCl	**5c** (65)
4	 **2f**	$PdCl_2(PPh_3)_2$ + CuI	**4f**[a]
5	 **2g**	$PdCl_2(PPh_3)_2$ + CuI	**4g**[a]
6	 **2g**	$PdCl_2(PPh_3)_2$ + LiCl	**4g**[a]

[a] Only the 5-monosubstituted product **4** was obtained.

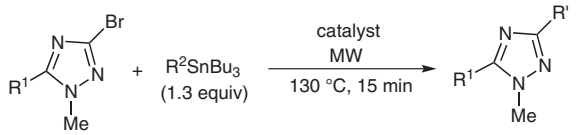
probably due to the low reactivity of the 3-position, and only the 5-monosubstituted product **4** was obtained.

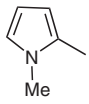
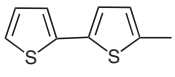
However, the different reactivities of the 3- and 5-positions of the dibromo derivative **1** allowed us to introduce different substituents into the triazole moiety. Thus, starting from 5-monosubstituted triazoles **4**, Stille reactions were performed with several organostannanes under microwave irradiation using different catalytic systems. The availability and easy access to the organostannane derivatives allowed the preparation of a wide range of polyheteroaryl systems bearing a (1*H*)-1,2,4-triazole moiety in a few minutes and in good yields. This approach represents a general procedure for building this type of compound. The main results are summarized in Table 3.[20]

However, as observed previously, the low reactivity of six-membered heterocyclic organostannanes and the 3-position of the 1,2,4-triazole unit, hampered our efforts to introduce a six-membered heterocyclic system in this position of the triazole moiety (Table 3, entry 3).

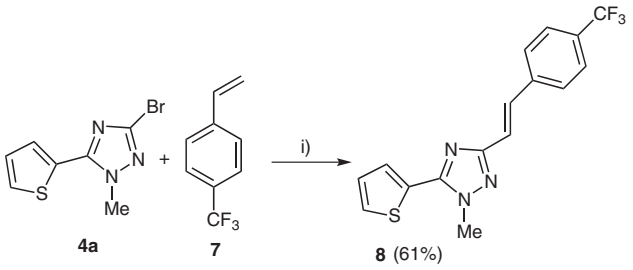
Recently, we reported the first microwave-assisted Heck reaction on a (1*H*)-1,2,4-triazole moiety as a new synthetic methodology for the preparation of alkenyl-(1*H*)-1,2,4-triazoles.[15f] As shown in Scheme 1, we carried out a com-

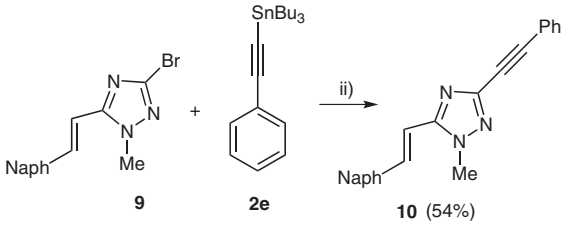
Table 3 Reactions between Monosubtitued Triazole Derivatives **4** and Organostannanes **2**



Entry	R^1	R^2	Product [yield (%)]
1	 **4a**	 **2b**	**6a** (68)[a]
2	 **4a**	 **2c**	**6b** (72)[a]
3	 **4a**	 **2g**	–[a,b]
4	 **4g**	 **2a**	**6c** (83)[b]

[a] Reaction conditions: $PdCl_2(PPh_3)_2$, LiCl.
[b] Reaction conditions: $PdCl_2(PPh_3)_2$, CuI.

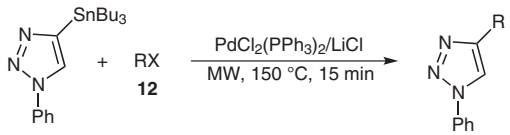


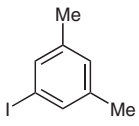
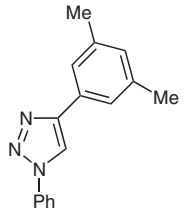
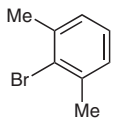
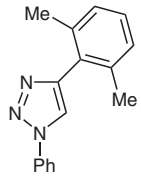
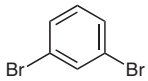
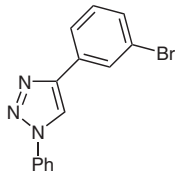
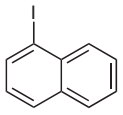
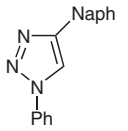
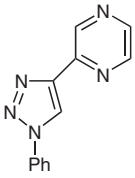
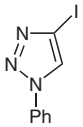
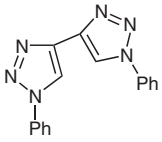
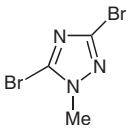
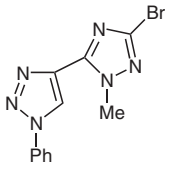


Scheme 1 Reagents and conditions: (i) Herrmann palladacycle, [(*t*-Bu)$_3$PH]BF$_4$, Cy$_2$NMe, bmimPF$_6$, MW, 170 °C, 35 min; (ii) $PdCl_2(PPh_3)_2$, LiCl, MW, 130 °C,15 min.

bination of Stille/Heck cross-coupling reactions in order to develop a new synthetic approach to highly conjugated compounds with valuable properties as materials. In the first case, we used Stille product **4a** and performed a Heck reaction with the styrene derivative **7** to obtain the disubstituted triazole **8** in 61% yield. Furthermore, Heck product **9** was reacted with the stannyl derivative **2e** to give compound **10** in 54% yield. Both reactions were performed under microwave irradiation in solvent-free conditions. The properties of these systems are currently under evaluation.

Table 4 Reactions between 1-Phenyl-4-(tributylstannyl)-1*H*-1,2,3-triazole (**11**) and Halo Derivatives **12**



Entry	RX	Product	Yield (%)
1	 **12a**	 **13a**	54
2	 **12b**	 **13b**	77
3	 **12c**	 **13c**	96
4	 **12d**	 **13d**	50
5	 **12e**	 **13e**	91
6	 **12f**	 **13f**	49
7	 **1**	 **13g**	76

Finally, we applied the synthetic approach developed here to the preparation of new biheteroaryl systems bearing a 1,2,3-triazole moiety. 1-Phenyl-4-(tributylstannyl)-1*H*-1,2,3-triazole (**11**) was reacted with different aryl or heteroaryl halides using Stille conditions under microwave irradiation to prepare new 1,2,3-triazole derivatives within 15 minutes in good yields (49–96%). The wide availability of aryl and heteroaryl halides makes this synthetic method widely applicable. Some of these compounds, bearing two triazole rings, are currently being tested as new ligands. The products synthesized are collected in Table 4.[21]

When the reaction was performed using the dihalogenated compounds **12c** or **1**, only the monosubstitued derivative was obtained (Table 4, Entries 3 and 7). In the case of **1**, the reactivity of the 5-position explains the formation of product **13g**.

In conclusion, we describe the first microwave-assisted Stille reaction involving a (1*H*)-1,2,4-triazole moiety. This methodology represents a general method for the preparation of a wide range of symmetrical and non-symmetrical 3,5-disubstituted (1*H*)-1,2,4-triazole derivatives in a few minutes and with good to excellent yields. The combined Heck/Stille cross-coupling reaction expands the applicability of this synthetic approach and allows the preparation of highly conjugated systems bearing a (1*H*)-1,2,4-triazole unit. Finally, we employed Stille conditions in the reaction of 1-phenyl-4-(tributylstannyl)-1*H*-1,2,3-triazole with halo derivatives in order to obtain new biheteroaryl systems in good yields. The availability of the reagents, short reaction times and good yields of the methods described here allow the easy preparation of a wide range of products with potential properties as new materials and in medicinal chemistry. The potential applications of these new compounds are currently under investigation in our laboratory.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

Acknowledgment

Financial support from the DGCYT of Spain through project CTQ2007-60037/BQU and from the Consejería de Educación y Ciencia, JCCM through projects PBI08-0259-7224, PCI08-0040 and PII2I09-0100-9633 is gratefully acknowledged.

References and Notes

(1) (a) Skotheim, T. A.; Reynolds, J. R. In *Conjugated Polymers. Theory, Synthesis, Properties, and Characterization*, 3rd ed.; CRC Press: Boca Raton, **2006**, Chap. 13 and 18. (b) Heinze, J. In *Organic Electrochemistry*; Lund, H.; Hammerich, O., Eds.; Marcel Dekker: New York, **2000**, .
(2) Diaz, A. F.; Logan, J. A. *J. Electroanal. Chem.* **1980**, *111*, 111.
(3) Diaz, A. F.; Kanazawa, K. K.; Gardini, G. P. *J. Chem. Soc., Chem. Commun.* **1979**, 635.
(4) Tourillon, G.; Garnier, F. *J. Electroanal. Chem.* **1982**, *135*, 173.
(5) (a) Groenendaal, L.; Zotti, G.; Aubert, P.-H.; Waybright, S. M.; Reynolds, J. R. *Adv. Mater.* **2003**, *15*, 855. (b) Reeves, B. D.; Grenier, C. R. G.; Argun, A. A.; Cirpan, A.; McCarley, T. D.; Reynolds, J. R. *Macromolecules* **2004**, *37*, 7559. (c) Zotti, G.; Zecchin, S.; Schiavon, G.; Verdelli, B.; Berlin, A.; Grimoldi, S. *Macromol. Chem. Phys.* **2004**, *205*, 2026.
(6) Wu, P. L.; Feng, X. J.; Tam, H. L.; Wong, M. S.; Cheah, K. W. *J. Am. Chem. Soc.* **2009**, *131*, 886.
(7) (a) Hanna, N. B.; Dimitrijevich, S. D.; Larson, S. B.; Robins, R. K.; Revankar, G. R. *J. Heterocycl. Chem.* **1988**, *25*, 1857. (b) Baldwin, J. J.; Novello, F. C. US Patent 3 892 762, **1976**.
(8) Kitchem, J. A.; Noble, A.; Brandt, C. D.; Moubaraki, B.; Murray, K. S.; Brooker, S. *Inorg. Chem.* **2008**, *47*, 9450.
(9) Nicolaou, K. C.; Bulger, P. G.; Sarlah, D. *Angew. Chem. Int. Ed.* **2005**, *44*, 4442.
(10) (a) de la Hoz, A.; Díaz-Ortiz, A.; Moreno, A.; Langa, F. *Eur. J. Org. Chem.* **2000**, 3659. (b) *Microwaves in Organic Synthesis*, 2nd ed.; Loupy, A., Ed.; Wiley-VCH: Weinheim, **2006**. (c) *Microwave-Assisted Organic Synthesis*; Lidström, P.; Tierney, J. P., Eds.; Blackwell Scientific: Oxford, **2004**, 320. (d) Kappe, C. O.; Stadler, A. *Microwaves in Organic and Medicinal Chemistry*; Wiley-VCH: Weinheim, **2005**. (e) de la Hoz, A.; Díaz-Ortiz, A.; Moreno, A. *Chem. Soc. Rev.* **2005**, *34*, 164. (f) Bogdal, D.; Loupy, A. *Org. Process Res. Dev.* **2008**, *12*, 710. (g) Kappe, C. O. *Chem. Soc. Rev.* **2008**, *37*, 1127. (h) Polshettiear, V.; Varma, R. *Chem. Soc. Rev.* **2008**, *37*, 1546.
(11) (a) Lahred, M.; Moberg, C.; Hallberg, A. *Acc. Chem. Res.* **2002**, *35*, 717. (b) Kappe, C. O. *Curr. Opin. Chem. Biol.* **2002**, *4*, 314. (c) Hayes, B. L. *Aldrichimica Acta* **2004**, *37*, 66. (d) Nilsson, K.; Olofsson, M.; Lahred, M. *Top. Curr. Chem.* **2006**, *266*, 103. (e) Appunnutah, P.; Van der Eycken, E. *Eur. J. Org. Chem.* **2008**, 1133; and references therein.
(12) (a) Kotha, S.; Lahiri, K.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633; and references therein. (b) Suenneman, H. W.; de Meijere, A. *Angew. Chem. Int. Ed.* **2004**, *43*, 895. (c) Kappe, C. O.; Dallinger, D. *Nat. Rev. Drug Discovery* **2006**, *5*, 51; and references therein.
(13) Pereyre, M.; Quintard, J. P.; Rahm, A. *Tin in Organic Synthesis*; Butterworths: London, **1987**.
(14) (a) Nicolaou, K. C.; Sorensen, E. J. *Classics in Total Synthesis*; VCH: Weinheim, **1996**. (b) Nicolaou, K. C.; Snyder, S. A. *Classics in Total Synthesis II*; Wiley-VCH: Weinheim, **2003**.
(15) (a) Schnürch, M.; Flasik, R.; Khan, A.; Spina, M.; Milhovilovix, M.; Stannetty, P. *Eur. J. Org. Chem.* **2006**, 3286. (b) Schöter, S.; Stock, C.; Bach, T. *Tetrahedron* **2005**, *61*, 2245. (c) Deng, J.; Wu, Y.; Chen, Q. *Synthesis* **2005**, 2730. (d) Maes, W.; Verstappen, B.; Dehaen, W. *Tetrahedron* **2006**, *62*, 2677. (e) Chuprakov, S.; Chernyak, N.; Dudnik, A.; Gevrogyan, V. *Org. Lett.* **2007**, *9*, 2333. (f) Chiong, H. A.; Daugulis, O. *Org. Lett.* **2007**, *9*, 1449. (g) Díaz-Ortiz, A.; Prieto, P.; de Cózar, A.; Cebrián, C.; Moreno, A.; de la Hoz, A. *Aus. J. Chem.* **2009**, in press. (h) Huang, J.; Macdonald, S. J. F.; Harrity, J. P. A. *Chem. Commun.* **2009**, 436. (i) Huang, J.; Macdonald, S. J. F.; Cooper, A. W. J.; Fisher, G.; Harrity, J. P. A. *Tetrahedron Lett.* **2009**, *50*, 5539.
(16) Olofsson, K.; Kim, S. Y.; Lahred, M.; Curran, D. P.; Hallberg, A. *J. Org. Chem.* **1999**, *64*, 4539.
(17) Heguaburu, V.; Sá, M. M.; Scharpiro, V.; Pandolfi, E. *Tetrahedron Lett.* **2008**, *49*, 6787.

(18) **General Procedure**: A mixture of 3,5-dibromo-1-methyl-1*H*-1,2,4-triazole (**1**; 200 mg, 0.83 mmol), stannyl derivative (**2**; 1.08 mmol), $PdCl_2(PPh_3)_2$ (12 mg, 0.017 mmol) and LiCl (106 mg, 2.49 mmol) or CuI (15.8 mg, 0.083 mmol) was irradiated under argon in a Discover™ (CEM) focused microwave reactor at 110 °C for 15 min. The crude products **3a** and **4a–g** were purified by flash chromatography on silica gel (hexane–EtOAc).

5-Bromo-1-methyl-3-(thiophen-2-yl)-1*H*-1,2,4-triazole (3a): Mp 54–55 °C; ^{1}H NMR ($CDCl_3$): δ = 7.58 (dd, *J* = 3.7, 1.2 Hz, 1 H, H-3′), 7.28 (dd, *J* = 5.1, 1.2 Hz, 1 H, H-5′), 7.02 (dd, *J* = 5.1, 3.7 Hz, 1 H, H-4′), 3.84 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 159.0, 132.8, 129.7, 127.7, 126.8, 126.5, 36.5 (CH_3).

3-Bromo-1-methyl-5-(thiophen-2-yl)-1*H*-1,2,4-triazole (4a): Mp 67–68 °C; ^{1}H NMR ($CDCl_3$): δ = 7.54–7.62 (m, 2 H, H-3″, H-5″), 7.19 (dd, *J* = 5.1, 3.7 Hz, 1 H, H-4″), 4.06 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 151.1, 138.7, 129.4, 129.0, 128.0, 127.9, 37.4 (CH_3).

3-Bromo-1-methyl-5-(1-methyl-1*H*-pyrrol-2-yl)-1*H*-1,2,4-triazole (4b): Mp 41–42 °C; ^{1}H NMR ($CDCl_3$): δ = 6.74 (t, *J* = 1.8 Hz, 1 H, H-5″), 6.41 (dd, *J* = 4.0, 1.5 Hz, 1 H, H-3″), 6.14 (dd, *J* = 3.7, 2.6 Hz, 1 H, H-4″), 4.06 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 149.9, 138.3, 126.8, 118.3, 113.1, 108.2, 37.1 (CH_3), 36.0 (CH_3).

5-(2,2′-Bithiophen-5-yl)-3-bromo-1-methyl-1*H*-1,2,4-triazole (4c): Mp 152–154 °C; ^{1}H NMR ($CDCl_3$): δ = 7.61 (d, *J* = 3.9 Hz, 1 H, H-3), 7.31 (dd, *J* = 5.1, 1.1 Hz, 1 H, H-3′), 7.27 (dd, *J* = 3.8, 1.1 Hz, 1 H, H-5′), 7.20 (d, *J* = 3.9 Hz, 1 H, H-4), 7.05 (dd, *J* = 5.1, 3.8 Hz, 1 H, H-4′); ^{13}C NMR ($CDCl_3$): δ = 150.7, 141.7, 138.7, 135.7, 129.5, 128.1, 125.9, 125.9, 125.0, 124.1, 35.5 (CH_3).

3-Bromo-1-methyl-5-phenyl-1*H*-1,2,4-triazole (4d): Mp 120–121 °C; ^{1}H NMR ($CDCl_3$): δ = 7.59–7.61 (m, 2 H, *o*-PhH), 7.44–7.46 (m, 3 H, *m*-PhH, *p*-PhH), 3.91 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 156.6, 139.1, 130.7, 129.0, 128.7, 126.7, 37.3 (CH_3).

3-Bromo-1-methyl-5-(phenylethynyl)-1*H*-1,2,4-triazole (4e): Mp 119–120 °C; ^{1}H NMR ($CDCl_3$): δ = 7.52–7.55 (m, 2 H, *o*-PhH), 7.28–7.94 (m, 3 H, *m*-PhH, *p*-PhH), 3.97 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 147.7, 140.3, 132.1, 132.0, 129.2, 128.7, 128.4, 121.7, 97.4, 89.5, 36.5 (CH_3).

2-(3-Bromo-1-methyl-1*H*-1,2,4-triazol-5-yl)pyridine (4f): Mp 78–80 °C; ^{1}H NMR ($CDCl_3$): δ = 8.68 (dd, *J* = 4.8, 1.8 Hz, 1 H, H-6), 8.20 (dd, *J* = 7.7, 1.1 Hz, 1 H, H-3), 7.85 (td, *J* = 7.7, 1.8 Hz, 1 H, H-4), 7.37 (ddd, *J* = 7.7, 4.8, 1.1 Hz, 1 H, H-5), 4.36 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 153.4, 148.9, 146.8, 138.3, 137.1, 124.5, 124.0, 39.3 (CH_3).

2-(3-Bromo-1-methyl-1*H*-1,2,4-triazol-5-yl)pyrazine (4g): Mp 131–133 °C; ^{1}H NMR ($CDCl_3$): δ = 9.45 (s, 1 H, H-3), 8.67, 8.64 (2 × s, 2 H, H-5 and H-6), 4.34 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 151.1, 145.2, 154.1, 143.1, 142.5, 138.8, 39.3 (CH_3).

(19) **General Procedure**: A mixture of 3,5-dibromo-1-methyl-1*H*-1,2,4-triazole (**1**; 200 mg, 0.83 mmol), stannyl derivative (**2**; 2.16 mmol, 2.6 equiv), $PdCl_2(PPh_3)_2$ (24 mg, 0.033 mmol) and LiCl (106 mg, 2.49 mmol) was irradiated under argon in a Discover™ (CEM) focused microwave reactor at 130 °C for the appropriate time. The crude products **5a–c** were purified by flash chromatography on silica gel (hexane–EtOAc).

1-Methyl-3,5-di(thiophen-2-yl)-1*H*-1,2,4-triazole (5a): Mp 107–108 °C; ^{1}H NMR ($CDCl_3$): δ = 7.71 (dd, *J* = 3.7, 1.1 Hz, 1 H, H-3′), 7,54 (dd, *J* = 3.7, 1.1 Hz, 1 H, H-3″), 7.53 (dd, *J* = 5.1, 1.1 Hz, 1 H, H-5″), 7.34 (dd, *J* = 4.8, 1.1 Hz, 1 H, H-5′), 7.18 (dd, *J* = 5.1, 3.7 Hz, 1 H, H-4″), 7.10 (dd, *J* = 5.1, 3.7 Hz, 1 H, H-4′), 4.07 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 157.3, 150.0, 133.5, 128.9, 128.7, 128.6, 127.9, 127.6, 126.3, 126.2, 37.1 (CH_3).

1-Methyl-3,5-bis(1-methyl-1*H*-pyrrol-2-yl)-1*H*-1,2,4-triazole (5b): Mp 78–79 °C; ^{1}H NMR ($CDCl_3$): δ = 6.74 (t, *J* = 2.0 Hz, 1 H, H-5″), 6.73 (dd, *J* = 2.0, 1.0 Hz, 1 H, H-5′), 6.62 (t, *J* = 2.0 Hz, 1 H, H-3′), 6.43 (dd, *J* = 4.4, 2.4 Hz, 1 H, H-3″), 6.17 (dd, *J* = 4.0, 2.4 Hz, 1 H, H-4″), 6.10 (dd, *J* = 3.4, 2.9 Hz, 1 H, H-4′), 3.94 (s, 3 H, CH_3), 3.91 (s, 3 H, CH_3), 3.85 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 155.9, 148.0, 126.1, 125.0, 124.8, 119.8, 112.3, 110.3, 108.0, 107.7, 36.7 (CH_3), 36.6 (CH_3), 36.1 (CH_3).

3,5-Di(2,2′-bithiophen-5-yl)-1-methyl-1*H*-1,2,4-triazole (5c): Mp 146–148 °C; ^{1}H NMR ($CDCl_3$): δ = 7.61 (d, *J* = 3.8 Hz, 1 H, H-3″), 7.45 (d, *J* = 3.8 Hz, 1 H, H-3), 7.22–7.31 (m, 5 H, H-4, H-3′, H-5′, H-3‴, H-5‴), 7.17 (d, *J* = 3.8 Hz, 1 H, H-4″), 7.07 (dd, *J* = 4.9, 3.8 Hz, 1 H), 7.03 (t, *J* = 4.3 Hz, 1 H, H-4′ and H-4‴); ^{13}C NMR ($CDCl_3$): δ = 156.9, 149.7, 140.8, 138.2, 137.2, 136.1, 131.9, 129.0, 128.1, 127.9, 127.2, 126.9, 125.6, 124.8, 124.7, 124.2, 124.1, 124.0, 37.3 (CH_3).

(20) **General Procedure**: A mixture of 5-monosubstituted triazole **4** (1 equiv), stannyl derivative (**2**; 1.3 equiv), $PdCl_2(PPh_3)_2$ (0.02 equiv) and LiCl (3 equiv) or CuI (0.1 equiv) was irradiated at the appropriate temperature and for the appropriate time under argon in a Discover™ (CEM) focused microwave reactor. The crude products **6a–c** were purified by flash chromatography on silica gel (hexane–EtOAc).

1-Methyl-3-(1-methyl-1*H*-pyrrol-2-yl)-5-(thiophen-2-yl)-1*H*-1,2,4-triazole (6a): Mp 88–89 °C; ^{1}H NMR ($CDCl_3$): δ = 7.53 (dd, *J* = 3.7, 1.5 Hz, 1 H, H-3″), 7.52 (dd, *J* = 5.1, 1.1 Hz, 1 H, H-5″), 7.18 (dd, *J* = 5.1, 3.7 Hz, 1 H, H-4″), 6.81 (dd, *J* = 3.7, 1.8 Hz, 1 H, H-5′), 6.70 (t, *J* = 2.2 Hz, 1 H, H-3′), 6.17 (dd, *J* = 3.7, 2.6 Hz, 1 H, H-4′), 4.08 (s, 3 H, CH_3), 4.00 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 156.3, 149.1, 129.5, 128.5, 128.2, 127.8, 125.2, 124.4, 110.8, 107.8, 37.0 (CH_3), 36.5 (CH_3).

3-(2,2′-Bithiophen-5-yl)-1-methyl-5-(thiophen-2-yl)-1*H*-1,2,4-triazole (6b): Mp 124–126 °C; ^{1}H NMR ($CDCl_3$): δ = 7.62 (d, *J* = 3.8 Hz, 1 H, H-4″), 7.57 (dd, *J* = 3.7, 1.1 Hz, 1 H, H-3‴), 7.55 (dd, *J* = 5.1, 1.1 Hz, 1 H, H-5‴), 7.24–7.23 (m, 2 H, H-3′, H-5′), 7.20 (dd, *J* = 5.1, 3.7 Hz, 1 H, H-4‴), 7.07 (dd, *J* = 3.8 Hz, 1 H, H-3″), 7.03 (dd, *J* = 3.8, 4.9 Hz, 1 H, H-4′), 4.09 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 156.9, 150.1, 138.2, 137.2, 131.9, 128.9, 128.8, 128.7, 127.9, 126.9, 124.7, 124.4, 124.0, 37.2 (CH_3).

2-[1-Methyl-3-(thiophen-2-yl)-1*H*-1,2,4-triazol-5-yl]pyrazine (6c): Mp 139–140 °C; ^{1}H NMR ($CDCl_3$): δ = 9.55 (d, *J* = 1.7 Hz, 1 H, H-3 Py), 8.64–8.67 (m, 2 H, H-5, H-6 Py), 7.75 (dd, *J* = 3.7, 1.1 Hz, H-3 thioph), 7.37 (dd, *J* = 5.1, 1.1 Hz, 1 H, H-5 thioph), 7.13 (dd, *J* = 5.1, 3.7 Hz, 1 H, H-4 thioph), 4.37 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 157.5, 150.1, 145.4, 144.7, 143.5, 143.0, 133.5, 127.7, 126.5, 126.3.

(21) **General Procedure**: A mixture of 1-phenyl-4-(tributylstannyl)-1*H*-1,2,3-triazole (**11**; 100 mg, 0.23 mmol), halogenated derivative **12** (0.25 mmol), $PdCl_2(PPh_3)_2$ (3 mg, 0.004 mmol) and LiCl (29.3 mg, 0.69 mmol) was irradiated at the appropriate temperature and for the appropriate time under argon in a Discover™ (CEM) focused microwave reactor. The crude products **13a–g** were purified by flash chromatography (hexane–EtOAc).

4-(3,5-Dimethylphenyl)-1-phenyl-1*H*-1,2,3-triazole (13a): Mp 115–116 °C; ^{1}H NMR ($CDCl_3$): δ = 8.1 (s, 1 H, H-5), 7.8 (d, *J* = 7.3 Hz, 2 H, *o*-PhH), 7.5 (m, 4 H, Ph′H), 7.4 (t, *J* = 7.3 Hz, 1 H, *p*-Ph′H), 7.0 (s, 1 H, *p*-PhH), 2.2 (s, 6 H, 2 × CH_3); ^{13}C NMR ($CDCl_3$): δ = 148.6, 138.5, 137.1, 130.1,

129.9, 128.7, 123.6, 120.5, 117.5, 21.3 (CH_3).

4-(2,6-Dimethylphenyl)-1-phenyl-1*H*-1,2,3-triazole (13b): Colorless oil; ^{1}H NMR ($CDCl_3$): δ = 7.9 (s, 1 H, H-5), 7.8 (d, *J* = 7.1 Hz, 2 H, *o*-PhH), 7.5 (t, *J* = 6.9 Hz, 2 H, *m*-PhH), 7.4 (t, *J* = 7.3 Hz, 1 H, *p*-PhH), 7.2–7.1 (m, 3 H, PhH′), 2.3 (s, 6 H, 2 × CH_3); ^{13}C NMR ($CDCl_3$): δ = 146.2, 137.9, 137.1, 129.8, 129.6, 123.6, 120.3, 117.5, 20.8 (CH_3).

4-(3-Bromophenyl)-1-phenyl-1*H*-1,2,3-triazole (13c): Yellow oil; ^{1}H NMR ($CDCl_3$): δ = 8.2 (s, 1 H), 8.0 (m, 1 H), 7.8–7.7 (m, 3 H), 7.6–7.5 (m, 4 H), 7.3 (t, *J* = 7.3 Hz, 1 H, *p*-PhH); ^{13}C NMR ($CDCl_3$): δ = 147.0, 136.9, 132.3, 131.3, 130.5, 129.8, 128.9, 128.8, 124.4, 123.0, 120.6, 117.9.

4-(Naphthalen-1-yl)-1-phenyl-1*H*-1,2,3-triazole (13d): Mp 106–107 °C; ^{1}H NMR ($CDCl_3$): δ = 8.5–8.4 (m, 1 H, H-Naph), 8.2 (s, 1 H, H-5), 7.9–7.8 (m, 5 H), 7.6–7.4 (m, 6 H); ^{13}C NMR ($CDCl_3$): δ = 147.6, 137.1, 133.9, 131.2, 129.9, 129.8, 129.2, 128.8, 128.5, 127.7, 127.4, 126.7, 126.1, 125.4, 120.6.

2-(1-Phenyl-1*H*-1,2,3-triazol-4-yl)pyrazine (13e): Colorless oil; ^{1}H NMR ($CDCl_3$): δ = 9.5 (s, 1 H, H-Py), 8.6 (s, 1 H, H-5), 8.6–8.5 (m, 2 H, H-Py), 7.8 (d, *J* = 7.3 Hz, 2 H, *o*-PhH), 7.5 (t, *J* = 7.3 Hz, 2 H, *m*-PhH), 7.4 (t, *J* = 7.3 Hz, 1 H, *p*-PhH); ^{13}C NMR ($CDCl_3$): δ = 146.6, 145.7, 144.1, 143.9, 142.3, 136.7, 129.9, 129.2, 120.9, 120.6.

1,1′-Diphenyl-1*H*,1′*H*-4,4′-bi(1,2,3-triazole) (13f): Mp 118–119 °C; ^{1}H NMR ($CDCl_3$): δ = 8.6 (s, 1 H), 8.0 (s, 1 H), 7.7 (d, *J* = 7.3 Hz, 4 H, *o*-PhH), 7.5 (t, *J* = 7.3 Hz, 4 H, *m*-PhH), 7.4 (d, *J* = 7.3 Hz, 2 H, *p*-PhH). ^{13}C NMR ($CDCl_3$): δ = 137.0, 134.4, 129.7, 128.7, 121.6, 120.6.

4-(3-Bromo-1-methyl-1*H*-1,2,4-triazol-5-yl)-1-phenyl-1*H*-1,2,3-triazole (13g): Mp 104–105 °C; ^{1}H NMR ($CDCl_3$): δ = 8.5 (s, 1 H, H-5), 7.7 (d, *J* = 7.3 Hz, 2 H, *o*-PhH), 7.5 (t, *J* = 8 Hz, 2 H, *m*-PhH), 7.4 (d, *J* = 7.1 Hz, 1 H, *p*-PhH), 4.3 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$): δ = 147.5, 138.9, 137.7, 136.3, 130.1, 129.6, 122.6, 120.6, 38.3 (CH_3).