Organic & Biomolecular Chemistry

PAPER

View Article Online
View Journal | View Issue

Cite this: *Org. Biomol. Chem.*, 2014, **12**, 5954

Pyridine-phosphinimine ligand-accelerated Cu(I)-catalyzed azide–alkyne cycloaddition for preparation of 1-(pyridin-2-yl)-1,2,3-triazole derivatives†

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Received 6th June 2014,
Accepted 18th June 2014

DOI: 10.1039/c4ob01176g

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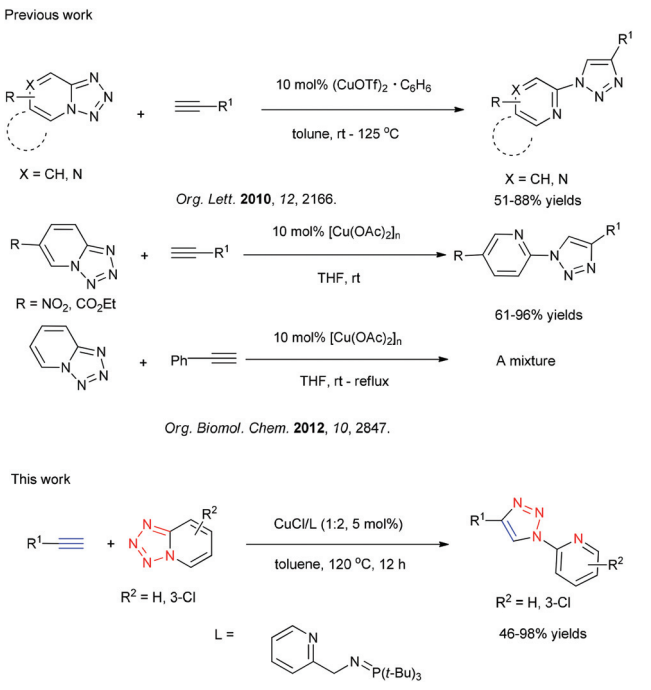
A series of phosphinimine ligands were designed and used in the Cu(I)-catalyzed azide–alkyne cycloaddition (CuAAC) reaction of tetrazolo[1,5-*a*]pyridines and alkynes for the first time. By optimizing the reaction conditions, an efficient catalytic system (CuCl/2-PyCH$_2$N=P^{t}Bu$_3$) was developed to give 1-(pyridin-2-yl)-1,2,3-triazole derivatives in moderate to excellent yields (46–98%).

Introduction

Several derivatives of 1-(pyridin-2-yl)-1,2,3-triazole have been used as ligands[1] in coordination chemistry and have exhibited a wide range of biological activities.[2] These compounds were usually prepared by base-promoted substitution between 1,2,3-triazole and 2-halopyridine[2b,3] or by 1,3-dipolar cycloaddition[1c,2d,4] and other procedures.[5] As we know, Cu-catalyzed azide–alkyne cycloaddition (CuAAC) has proven to be the most efficient method to construct the 1,2,3-triazole ring.[6] The combination of $CuSO_4$ and sodium ascorbate as a precatalyst system was discovered by Sharpless *et al.* and widely used in CuAAC reactions.[6a,b] Afterwards, it was reported that polydentate nitrogen ligands not only stabilize Cu(I) intermediates[7] but also accelerate the catalytic process,[8] for example, tris-[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]amine (TBTA) is the most widely used ligand,[6d] and this allowed the direct use of Cu(I) salts as catalysts in CuAAC reactions. Several other ligand systems have also shown to enhance the reaction rate of the CuAAC, such as simple monodentate phosphine complexes $Cu(P(OMe)_3)_3Br$,[9] $Cu(PPh_3)_3Br$[10] and $Cu(PPh_3)_2OAc$.[11] Monodentate phosphoramidite[12] and thioethers[13] have also been reported. Several Cu(I) complexes with N-heterocyclic carbene ligands have been described as CuAAC catalysts.[14] However, preparation of 1-(pyridin-2-yl)-1,2,3-triazole is not easy using CuAAC reactions. Up to now, only two reports dealing with the CuAAC methodology of tetrazolo[1,5-*a*]pyridines have been published (Scheme 1);[4e,g] however, the methods described in the literature[4e,g] provided low to moderate yields (especially unsubstituted tetrazoles) and the CuAAC methodology for tetrazoles bearing 8-substituted withdrawing groups was not mentioned. The reason why tetrazolo[1,5-*a*]pyridine derivatives are not active in traditional CuAAC reactions is that these azides exist in equilibrium between a closed form (tetrazole A), which is the main form at room temperature, and an open



Scheme 1 Synthesis of N-heterocycle-substituted 1,2,3-triazole.

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†Electronic supplementary information (ESI) available. CCDC 975322. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c4ob01176g

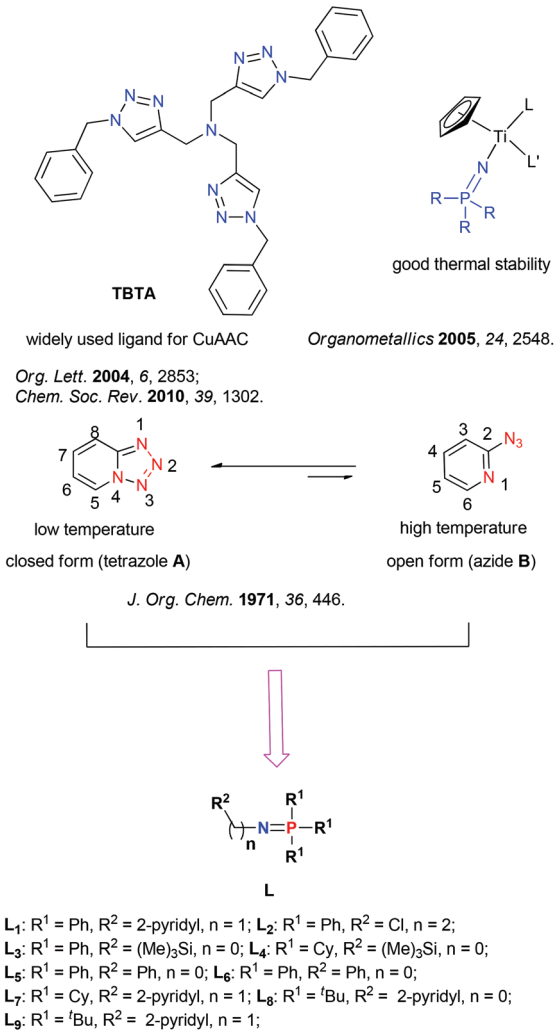
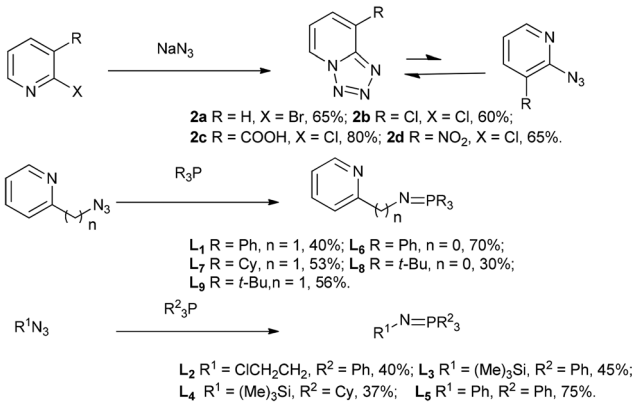


Fig. 1 Design of phosphinimine ligands for CuAAC.

form (azide B), which is a favorable form at high temperatures (Fig. 1).[4e] Investigation showed that the tetrazole–azide isomerization is mostly dependent upon the substituent and its position on the pyridine ring. The electron-withdrawing groups at the C-6 position of the tetrazole favors the open form B; in contrast, tetrazoles with withdrawing groups (NO_2, COOH, and Cl) at the C-8 position and the unsubstituted tetrazole mainly exist in the closed form A.[15]

To develop a general method to efficiently construct 1-(pyridin-2-yl)-1,2,3-triazole rings, a series of phosphinimine ligands which have exhibited good thermal stability in olefin polymerization[16] (Fig. 1) were investigated to accelerate Cu(I)-catalyzed 2-azidopyridine (open form, Scheme 2)–alkyne cycloaddition reaction at high temperatures according to the well-established nitrogen-based ligands[7] and phosphine-based ligands.[9–12] Furthermore, the catalytic activities of these ligands were screened with tetrazolo[1,5-*a*]pyridine and ferrocenyl acetylene as the substrates and TBTA was chosen as a reference for our study, and then the methodology was extended to synthesis of various 1-(pyridin-2-yl)-1,2,3-triazoles.



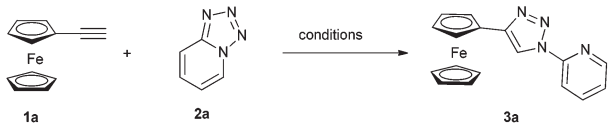
Scheme 2 Synthesis of substrates **2a–2d** and ligands L_1–L_2.

Results and discussion

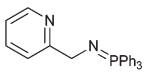
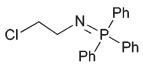
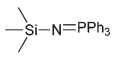
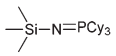
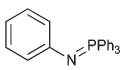
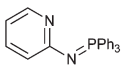
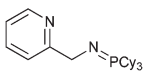
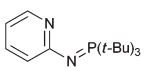
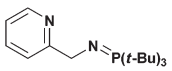
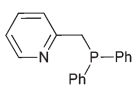
The substrates **2a–2d** were synthesized from 3-substituted-2-halopyridines as shown in Scheme 1. Compound **2a** was prepared by substitution between 2-bromopyridine and sodium azide in DMF at 125 °C, and compounds **2a–2d** were obtained by a similar method. The ligands L_1–L_{10} were prepared from azides and trisubstituted phosphines as shown in Scheme 2. The chlorination of pyridin-2-ylmethanol gave 2-(chloromethyl)pyridine, followed by oxidation of trisubstituted phosphines to give ligands L_1, L_7 and L_9.[17a] The ligands L_2–L_6 and L_8 were obtained by a similar method. The ligand L_{10} was synthesized by employing the published method.[17b]

For the preliminary study, we intended to synthesize 1-(pyridin-2-yl)-4-ferrocenyl-1,2,3-triazole using the most popular catalytic system $CuSO_4{\cdot}5H_2O$/NaAsc (Table 1, entry 1),[6a] but we did not obtain the desired product, and therefore tetrazolo-[1,5-*a*]pyridine and ferrocenyl acetylene were chosen as model substrates for the screening of the optimum CuAAC reaction conditions. As shown in Table 1, no expected **3a** was produced under catalysis of CuI at room temperature (entry 2). Then the reaction was carried out at 100 °C using different copper(I) halides as the catalysts[4e] (Table 1, entries 3–5); CuCl showed the highest catalytic activity to give **3a** in 53% yield (Table 1, entry 5). In consideration of the fact that ligands can enhance the CuAAC reaction rate,[7e] TBTA which is the most widely used ligand in CuAAC reaction was used as a ligand in the reaction, but it afforded the product **3a** in only 22% yield (Table 1, entry 6). At the same time, a series of phosphinimine ligands (Fig. 1) were synthesized and investigated.[7,12] To our delight, the same reaction gave **3a** in 68% yield using the previously reported phosphinimine ligand[17a,18] (Table 1, entry 7). Subsequently, the electronic and steric effect of other phosphinimine ligands (Table 1, entries 8–15) was evaluated. Gratifyingly, *N*-(tri-*tert*-butylphosphoranylidene)-2-pyridinylmethanamine (L_9) was the most effective ligand and the yield of the desired product **3a** reached 85% (Table 1, entry 15). However, when employing a N,P-ligand without the phosphinimine functional group, 2-(diphenylphosphinomethyl)pyridine (Table 1, entry 16), the yield of the product **3a** was only 32%. Lower yields were also

Table 1 Screening of the catalytic systems[a]



1a 2a 3a

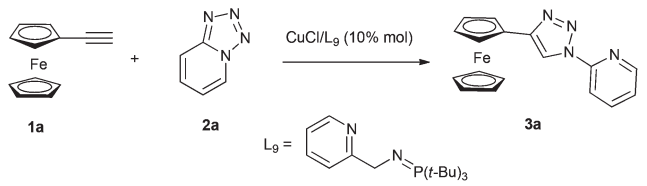
Entry	Catalyst (10 mol%)	Ligand (10 mol%)	Solvent (0.25 M)	t [°C]	Time [h]	Yield[b] [%]
1	$CuSO_4{\cdot}5H_2O$/NaVc	—	THF–H_2O	25	2	0
2	CuI	—	Toluene	25	16	0
3	CuI	—	Toluene	100	16	19
4	CuI	—	Toluene	100	16	42
5	CuBr	—	Toluene	100	16	53
6	CuCl	TBTA[c]	Toluene	100	16	22
7	CuCl		Toluene	100	16	68
8	CuCl		Toluene	100	16	Trace
9	CuCl		Toluene	100	16	54
10	CuCl		Toluene	100	16	53
11	CuCl		Toluene	100	16	61
12	CuCl		Toluene	100	16	55
13	CuCl		Toluene	100	16	70
14	CuCl		Toluene	100	16	75
15	**CuCl**		**Toluene**	**100**	**16**	**85**
16	CuCl		Toluene	100	16	32
17	CuCl	PPh_3	Toluene	100	16	61
18	CuCl	PCy_3	Toluene	100	16	64
19	CuCl	$P(t\text{-Bu})_3$	Toluene	100	16	70
20	CuCl		Toluene	100	16	46

[a] Reaction conditions: tetrazolo[1,5-*a*]pyridine (0.4 mmol), ferrocenyl acetylene (0.48 mmol), solvent (0.8 mL). [b] Isolated yield. [c] TBTA = tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]amine.

obtained using the monodentate PPh_3, PCy_3, $P(t\text{-Bu})_3$ and pyridine as the ligand respectively (Table 1, entries 17–20). The ligand ($\mathbf{L_9}$) containing the methylene group displayed better catalytic activity than the ligand ($\mathbf{L_8}$) (Table 1, entries 14–15). From the above results, it can be seen that the phosphinimine moiety and the methylene moiety play an important role in the cycloaddition reaction of tetrazolo[1,5-*a*]pyridine and ferrocenylacetylene, and the ligand ($\mathbf{L_9}$) was chosen as the best ligand.

In order to find the optimal conditions for our reaction, a small screening of reaction time, temperature, solvents, CuCl/ligand ratios and catalyst loadings was performed for the cycloaddition reaction of tetrazolo[1,5-*a*]pyridine and ferrocenylacetylene (Tables 2 and 3). Firstly, the reaction time was changed

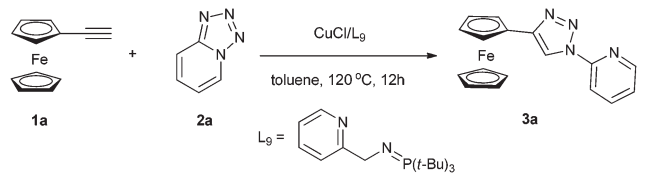
Table 2 Optimization of the reaction conditions[a]



Entry	Solvent (0.25 M)	t [°C]	Time [h]	Yield[b] [%]
1	Toluene	100	10	75
2	Toluene	100	12	85
3	Toluene	100	16	85
4	Toluene	100	20	75
5	Toluene	60	12	Trace
6	Toluene	80	12	28
7	Toluene	120	12	90
8	Toluene	140	12	70
9	Dioxane	120	12	13
10	DMSO	120	12	21
11	DMF	120	12	14

[a] Reaction conditions: 2-azidopyridine (0.4 mmol), ferrocenyl acetylene (0.48 mmol), CuCl/L (0.04 mmol), solvent (0.8 mL). [b] Isolated yield.

Table 3 Effects of the CuCl/ligand ratios and catalyst loadings[a]



Entry	Catalyst loading (mol%)	CuCl/ligand	Yield[b] [%]
1	10	1 : 1	90
2	10	1 : 2	95
3	10	1 : 3	86
4	10	1 : 4	36
5	5	1 : 2	95
6	2.5	1 : 2	91

[a] Reaction conditions: 2-azidopyridine (0.4 mmol), ferrocenyl acetylene (0.48 mmol), solvent (0.8 mL). [b] Isolated yield.

from 10 h to 20 h (Table 2, entries 1–4) and the reaction standing for 12 h afforded the compound **3a** in the best yield (Table 2, entry 2). Then when the reaction temperature was varied between 60 °C and 140 °C (Table 2, entries 5–8), it was found that the yield of compound **3a** was greatly affected by the temperature. For example, compound **3a** was readily prepared in good yield (85%) when the reaction was carried out at 100 °C for 12 h (Table 2, entry 2), whereas at 80 °C low yield (28%) of compound **3a** was obtained (Table 2, entry 6). The reaction gave compound **3a** in the best yield (90%) at 120 °C for 12 h (Table 2, entry 7), but the yield significantly reduced when the solvent was replaced by dioxane, DMSO or DMF (Table 2, entries 9–11). Subsequently, the CuCl/ligand ratios and catalyst loadings were screened (Table 3) and the optimal reaction conditions were obtained (Table 3, entry 5).

With the optimized results in hand, we tested the generality of cycloaddition reaction of substituted tetrazolo[1,5-*a*]pyridines and alkynes (Table 4). As shown in Table 4, the highly active catalyst (CuCl/L_9, 1 : 2) gave satisfying results with low-loading (5 mol%) for substituted tetrazolo[1,5-*a*]pyridine and aromatic alkyne cycloaddition reaction (Table 4, entries 1–9). Reaction of electron-rich aromatic alkynes and tetrazolo[1,5-*a*]-pyridines was efficient and gave products **3a–3d** in excellent yields (>95%, Table 4, entries 1–4). When the aromatic alkynes had a relatively low electron density in the aromatic rings, the reactions gave products **3e–3i** in moderate to good yields (52–81%, Table 4, entries 5–9). Then we tested the reaction activities of tetrazolo[1,5-*a*]pyridines and alkyl alkynes and the reactions gave products **3j–3n** in moderate yields (49–60%, Table 4, entries 10–14). Finally, we tried to challenge the CuAAC reactions of tetrazoles bearing 8-substituted withdrawing groups (NO_2, COOH, and Cl), which were difficult to carry out.[4e,g] To our delight, 8-chlorotetrazolo[1,5-*a*]pyridine could react with ferrocenyl acetylene or ethynylbenzene smoothly to give the product **3o** or **3p** in 46% and 48% yield, respectively (Table 4, entries 15–16). Unfortunately, we did not obtain the desired 1,2,3-triazole products by CuAAC reactions using tetrazolo[1,5-*a*]pyridine-8-carboxylic acid or 8-nitrotetrazolo[1,5-*a*]-pyridine as the substrate under the same reaction conditions. The possible reason was that these tetrazolo[1,5-*a*]pyridine derivatives may decompose at the reaction temperature (120 °C).[19]

In order to further confirm the structure of the synthesized 1,4-substituted-1,2,3-triazole derivatives, compound **3a** was cultivated in a mixture of dichloromethane and hexane to give an orange crystal suitable for X-ray single-crystal diffraction. The crystal structure is shown in Fig. 2.[20]

Experimental section

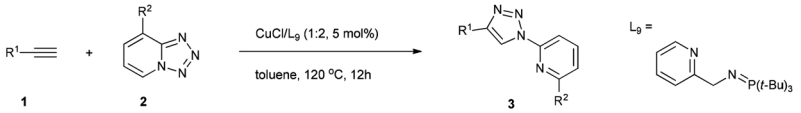
General experimental methods

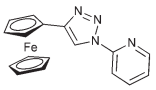
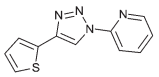
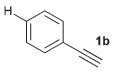
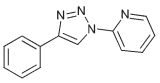
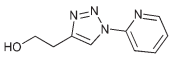
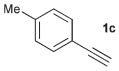
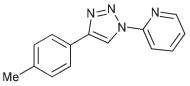
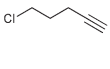
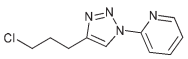
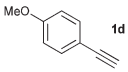
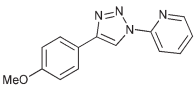
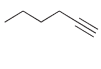
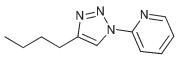
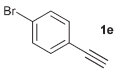
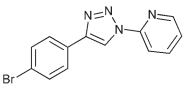
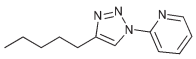
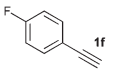
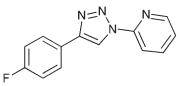
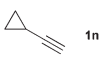
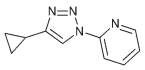
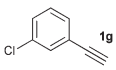
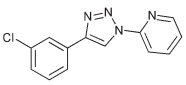
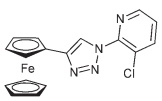
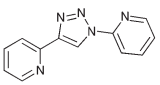
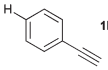
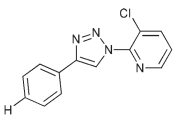
All NMR experiments were carried out on a 500 spectrometer using $CDCl_3$, DMSO-d_6 or C_6D_6 as the solvent with tetramethylsilane as the internal standard (^{31}P NMR with 85% H_3PO_4 as the internal standard). Chemical shift values (δ) are given in parts per million. Elemental analyses were determined on an elemental analyzer. HRMS data were obtained on an FTICR-MS instrument. The melting points were determined on an X-4 binocular microscope melting point apparatus and are uncorrected. CH_3CN, $CHCl_3$, dioxane, toluene, DMF and DMSO were dried according to the literature techniques.

Synthesis of ferrocenyl acetylene (1a). Ferrocenyl acetylene was synthesized according to the literature.[21] ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.60–4.30 (m, 2H), 4.33–4.09 (m, 7H), 2.73 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 82.6, 73.5, 71.7, 70.0, 68.7, 63.8.

Synthesis of tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]amine (TBTA). Tris[(1-benzyl-1*H*-1,2,3-triazol-4-yl)methyl]amine (TBTA) was synthesized according to the literature.[22] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (s, 3H), 7.39–7.29 (m, 9H), 7.25 (dd,

Table 4 Synthesis of 1-(pyridin-2-yl)-1,2,3-triazole derivatives[a]



Entry	R^1≡	R^2	Product	Yield[b] [%]	Entry	R^1≡	R^2	Product	Yield[b] [%]
1	 1a	H 2a	 **3a**	95	9	 1i	H 2a	 **3i**	77
2	 1b	H 2a	 **3b**	95	10	 1j	H 2a	 **3j**	55
3	 1c	H 2a	 **3c**	97	11	 1k	H 2a	 **3k**	49
4	 1d	H 2a	 **3d**	98	12	 1l	H 2a	 **3l**	54
5	 1e	H 2a	 **3e**	68	13	 1m	H 2a	 **3m**	55
6	 1f	H 2a	 **3f**	52	14	 1n	H 2a	 **3n**	60
7	 1g	H 2a	 **3g**	79	15[c]	 1a	H 2b	 **3o**	46
8	 1h	H 2a	 **3h**	81	16[c]	 1b	H 2b	 **3p**	48

[a] General reaction conditions: azide (0.4 mmol), alkyne (0.48 mmol), CuCl (0.02 mmol), ligand (0.04 mmol), toluene (0.8 mL), 120 °C, 12 h. [b] Isolated yield. [c] Reaction performed at 100 °C for 24 h.

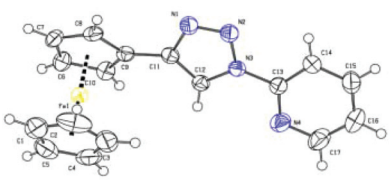


Fig. 2 ORTEP diagram of compound **3a**.

J = 7.8, 2.3 Hz, 6H), 5.50 (s, 6H), 3.70 (s, 6H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 144.3, 134.8, 129.1, 128.7, 128.0, 123.8, 100.0, 54.1, 47.1.

Synthesis of tetrazolo[1,5-*a*]pyridine derivatives (2a–2d)

Tetrazolo[1,5-a]pyridine ***2a***. 2-Bromopyridine (6.0 g, 38.2 mmol), NaN_3 (3.34 g, 51.4 mmol) and 18-crown-6 (1.0 g, 3.8 mmol) were added to DMF (60 mL), and then the mixture was heated for 48 h at 125 °C in the dark. The crude reaction mixture was concentrated *in vacuo* and recrystallized from ethanol to give compound **2a** as a colorless acicular crystal (3.5 g, 65% yield): mp 155–156 °C (lit.[19] 156–158 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.86 (d, J = 6.9 Hz, 1H), 8.07 (d, J = 9.0 Hz, 1H), 7.94–7.46 (m, 1H), 7.27 (t, J = 6.6 Hz, 1H).

8-Chlorotetrazolo[1,5-a]pyridine ***2b***. 2,3-Dichloropyridine (0.5 g, 3.2 mmol) and NaN_3 (0.5 g, 7.7 mmol) were added to a mixture of ethanol (5 mL) and water (45 mL), followed by addition of 10% HCl (5 mL). The mixture was heated to reflux for 48 h. The solvent was concentrated *in vacuo* and the residue was washed with water (20 mL). The crude product was purified by recrystallization from ethanol to give the product **2b** as a white solid (3.0 g, 60% yield): mp 106–107 °C (lit.[23a] 105–106 °C). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.80 (d, 1H), 7.73 (d, 1H), 7.23 (t, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.8, 130.9,

124.0, 123.0, 116.6. Anal. Calcd for $C_5H_3N_4Cl$: C, 38.86; H, 1.96; N, 36.25; Found: C, 38.72; H, 1.91; N, 35.91.

Tetrazolo[1,5-a]pyridine-8-carboxylic acid ***2c***. Compound **2c** was prepared using the same method as compound **2b**. This compound was obtained as a white solid (4.2 g, 80% yield).[23b] ^{1}H NMR (500 MHz, DMSO-d_6) δ 13.89 (s, 1H), 9.53 (d, J = 6.7 Hz, 1H), 8.40 (d, J = 7.0 Hz, 1H), 7.54 (t, J = 7.0 Hz, 1H).

8-Nitrotetrazolo[1,5-a]pyridine ***2d***. Compound **2d** was prepared using the same method as compound **2b**. This compound was obtained as a white solid (0.34 g, 65% yield): mp 179–181 °C.[15e] ^{1}H NMR (500 MHz, DMSO-d_6) δ 9.77 (d, 1H), 8.89 (d, 1H), 7.68 (t, 1H); ^{13}C NMR (126 MHz, DMSO-d_6) δ 143.8, 136.3, 133.5, 132.5, 116.7. Anal. Calcd for $C_5H_3N_5O_2$: C, 36.37; H, 1.83; N, 42.42; Found: C, 36.30; H, 1.75; N, 42.70.

Synthesis of ligands (L_1–L_{10})

(2-Pyridyl)-CH$_2$-N=PPh$_3$ ***L$_1$***. A mixture of $SOCl_2$ (7.4 mL) and $CHCl_3$ (20 mL) was slowly added to a stirred solution of 2-pyridylmethanol (6 mL, 62.2 mmol) in $CHCl_3$ (30 mL) which was cooled in an ice–salt bath. Then the reaction stood for 3 h at the same temperature. The solution was neutralized with saturated $NaHCO_3$ solution, and the organic layer was washed with H_2O and dried over anhydrous $MgSO_4$. After filtration the solvent was removed under vacuum to give a yellow oil (7.2 g, 91% yield) which was used in the next step without purification.

To a stirred solution of a freshly prepared 2-(chloromethyl)-pyridine (18.3 mmol, 3.0 g) in acetonitrile (100 mL) were added NaN_3 (4.3 g, 66 mmol) and NaI (1.0 g, 6.7 mmol). The stirred mixture was refluxed for 24 h and then cooled, and the solution was washed with H_2O. The product was extracted into $CHCl_3$, and the organic layer was dried over anhydrous $MgSO_4$. After filtration the solvent was removed under vacuum to give a yellow oil (5.9 g, 94% yield). The oil was not purified because of the risk of explosion.

A mixture of 2-(azidomethyl)pyridine (3.0 g, 22.8 mmol) and toluene (20 mL) was slowly added to a stirred solution of PPh_3 (3.0 g, 11.4 mmol) in toluene (30 mL). Then the mixture was heated to reflux for 8 h and then cooled. The solvent was removed under vacuum to give a pale yellow solid. The crude product was washed with CH_3CN at −40 °C to obtain the product $\mathbf{L_1}$ as a white solid (0.6 g, 40% yield).[17a] ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 (d, 1H), 7.95 (d, 1H), 7.74–7.60 (m, 7H), 7.53–7.46 (m, 3H), 7.46–7.35 (m, 6H), 7.11–6.89 (m, 1H), 4.51 (d, 2H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 165.8, 165.6, 148.1, 136.3, 132.5, 132.5, 131.8, 131.3, 131.3, 131.0, 128.5, 128.4, 121.3, 120.7, 51.2, 51.1. ^{31}P NMR (202 MHz, $CDCl_3$) δ 13.25.

3-Chloro-N-(triphenylphosphoranylidene)propan-1-amine ***L$_2$***. 1-Azido-2-chloroethane was prepared as a colorless oil (1.3 g, 53% yield) according to the literature.[24] Under argon 1-azido-2-chloroethane (1.2 g, 11.4 mmol) was slowly added to a solution of PPh_3 (3.0 g, 11.5 mmol) in toluene (5 mL), at the same time a large amount of gas emitted from the solution. After the addition was complete the reaction mixture was kept at 25 °C for 8 h. The solvent was removed under vacuum to give a pale yellow viscous oil which was washed with petroleum ether to give compound $\mathbf{L_2}$ as a white solid (1.5 g, 40% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (dd, J = 11.2, 7.5 Hz, 6H), 7.52 (t, J = 7.1 Hz, 3H), 7.45 (dd, J = 7.2, 5.6 Hz, 6H), 3.70 (t, J = 6.6 Hz, 2H), 3.23 (dt, J = 16.3, 6.3 Hz, 2H), 2.10–1.91 (m, 2H); ^{31}P NMR (202 MHz, $CDCl_3$) δ 11.85.

1,1,1-Trimethyl-N-(triphenylphosphoranylidene)silanamine ***L$_3$***. Compound $\mathbf{L_3}$ was prepared as a white solid (4.4 g, 45% yield) according to the literature.[25] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69–7.62 (m, 6H), 7.50–7.43 (m, 3H), 7.44–7.37 (m, 6H), −0.06 (s, 9H). ^{31}P NMR (202 MHz, $CDCl_3$) δ −1.41.

1,1,1-Trimethyl-N-(tricyclohexylphosphoranylidene)silanamine ***L$_4$***. Compound $\mathbf{L_4}$ was prepared as a white solid (3.8 g, 37% yield) according to the literature.[26] ^{1}H NMR (500 MHz, C_6D_6) δ 1.53–1.71 (m, 15H), 1.30–1.44 (m, 8H), 1.03–1.15 (m, 10H), 0.45 (s, 9H); ^{31}P NMR (202 MHz, C_6D_6) δ 17.63.

N-(Triphenylphosphoranylidene)aniline ***L$_5$***. Compound $\mathbf{L_5}$ was prepared as a white solid (1.7 g, 75% yield) according to the literature.[27] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (q, 6H), 7.52 (t, 3H), 7.45 (m, 6H), 7.02 (t, 2H), 6.82 (d, 1H), 6.41 (t, 1H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 151.2, 132.7, 131.8, 131.6, 130.8, 128.7, 123.5, 117.4.

N-(Triphenylphosphoranylidene)pyridin-2-amine ***L$_6$***. A mixture of 2-aziopyridine **2a** (0.6 g, 5 mmol) and PPh_3 (1.3 g, 5 mmol) were dissolved in DMF (20 mL). Then the mixture was stirred for 8 h at 110 °C and then cooled. The solvent was removed under vacuum to give a pale yellow solid. The crude product was washed with petroleum ether to give compound $\mathbf{L_6}$ as a white solid (1.24 g, 70% yield).[26] ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (m, 6H, Ph), 7.70 (d, 1H, Py, J = 10 Hz), 7.51–7.58 (m, 9H), 7.35 (t, 1H, Py, J = 10 Hz), 6.78 (t, 1H, Py, J = 10 Hz), 6.42 (d, 1H, Py, J = 5 Hz); ^{31}P NMR (202 MHz, $CDCl_3$) δ 12.26 (s, PPh_3).

(2-Pyridyl)-CH$_2$-N=PCy$_3$ ***L$_7$***. Compound $\mathbf{L_7}$ was prepared using the same method as compound $\mathbf{L_1}$. This compound was obtained as a white solid (0.73 g, 53% yield). ^{1}H NMR (500 MHz, C_6D_6) δ 8.38 (d, 1H, Py), 7.86 (d, 1H, Py), 7.61 (t, 1H, Py), 6.99 (t, 1H, Py), 4.48 (d, 2H, CH_2), 2.03–1.96 (m, 3H, PCy_3), 1.90–1.68 (m, 15H, PCy_3), 1.43–1.41 (m, 6H, PCy_3), 1.19–1.16 (m, 9H, PCy_3),; ^{31}P NMR (202 MHz, C_6D_6) δ 29.17 (s, PCy_3). Anal. Calcd for $C_{24}H_{39}N_2P$: C, 74.57; H, 10.17; N, 7.25; Found: C, 74.85; H, 10.32; N, 7.05.

N-(tri-tert-Butylphosphoranylidene)pyridin-2-amine ***L$_8$***. Compound $\mathbf{L_8}$ was prepared using the same method as compound $\mathbf{L_6}$. This compound was obtained as a white solid (0.14 g, 30% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.87 (d, 1H, Py, J = 15 Hz), 8.08 (d, 1H, Py, J = 10 Hz), 7.72 (t, 1H, Py, J = 10 Hz), 7.28 (d, 1H, Py, J = 15 Hz), 1.64 (s, 27H, P^tBu_3); ^{31}P NMR (202 MHz, $CDCl_3$) δ 70.72 (s, P^tBu_3). Anal. Calcd for $C_{17}H_{31}N_2P$: C, 69.35; H, 10.61; N, 9.51; Found: C, 69.61; H, 10.80; N, 9.77.

(2-Pyridyl)-CH$_2$-N=P^{t}Bu$_3$ ***L$_9$***. Compound $\mathbf{L_9}$ was prepared using the same method as compound $\mathbf{L_1}$. This compound was obtained as a white solid (0.68 g, 56% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.49 (d, 1H), 7.59–7.55 (m, 1H), 7.39 (d, 1H), 7.10–7.07 (m, 1H), 4.97 (s, 2H), 1.49–1.46 (s, 27 H); ^{13}C NMR (126 MHz, C_6D_6) δ 161.9, 149.4, 135.7, 128.4, 128.3, 128.2, 128.0, 128.0, 127.9, 123.1, 121.3, 68.1, 40.2, 39.9, 29.9; ^{31}P NMR (202 MHz, $CDCl_3$) δ 54.12. Anal. Calcd for $C_{18}H_{33}N_2P$:

C, 70.09; H, 10.78; N, 9.08; Found: C, 70.34; H, 10.42; N, 9.05.

2-((Diphenylphosphino)methyl)pyridine ***L*$_{10}$**. Compound $\mathbf{L_{10}}$ was prepared as a white solid (4.2 g, 56% yield) according to the literature.[28] ^{1}H NMR (500 MHz, $CDCl_3$, δ) 8.50 (d, J = 5.5 Hz, 1H), 7.48 (d, J = 1.8 Hz, 1H), 7.44–7.32 (m, 10H), 7.06 (t, J = 7.0 Hz, 1H), 6.97 (d, J = 8.7 Hz, 1H), 3.64 (s, 2H); ^{31}P NMR (202 MHz, $CDCl_3$) δ −10.34.

Representative procedure for the preparation of 1-(pyridin-2-yl)-1,2,3-triazole derivatives 3a–3p (Table 4, entry 1, as an example). Under a nitrogen atmosphere, a 25 mL Schlenk tube was charged with anhydrous toluene (0.80 mL), CuCl (2 mg, 0.02 mmol) and the ligand $\mathbf{L_9}$ (12.32 mg, 0.04 mmol). The mixture was stirred for 30 min at room temperature. Then tetrazolo[1,5-*a*]pyridine **2a** (48 mg, 0.4 mmol), ferrocenylacetylene (101 mg, 0.48 mmol) and anhydrous toluene (0.80 mL) were added into the Schlenk tube successively. Then the mixture was stirred for 12 h at 120 °C and cooled. Removal of the solvent yielded a residue, which was purified by flash column chromatography (silica gel, CH_2Cl_2–EtOAc–hexane = 1 : 1 : 5) to give compound **3a** as an orange solid (125.0 mg, 95% yield): mp 235–238 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.51 (d, J = 20.3 Hz, 2H), 8.24 (d, J = 8.2 Hz, 1H), 8.02–7.79 (m, 1H), 7.36 (dd, J = 6.8, 5.2 Hz, 1H), 4.85 (s, 2H), 4.37 (s, 2H), 4.13 (s, 5H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.2, 148.5, 147.5, 139.1, 123.4, 115.8, 113.8, 77.3, 77.0, 76.8, 69.7, 68.9, 66.9. Anal. Calcd for $C_{17}H_{14}FeN_4$: C, 61.84; H, 4.27; N, 16.97; Found: C, 61.75; H, 4.34; N, 16.89. ESI-MS calcd for $C_{17}H_{14}FeN_4$: 330.06, Found: $[M]^+$ 330.8.

Compound ***3b***.[4e] White solid (84.4 mg, 95% yield): mp 129–131 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.82 (s, 1H), 8.53 (d, J = 4.3 Hz, 1H), 8.26 (d, J = 8.2 Hz, 1H), 8.01–7.91 (m, 3H), 7.47 (t, J = 7.7 Hz, 2H), 7.37 (dd, J = 13.6, 6.2 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.2, 148.6, 139.2, 130.2, 128.9, 128.5, 125.9, 123.6, 116.8, 113.9, 77.3, 77.0, 76.8, 32.3. Anal. Calcd for $C_{13}H_{10}N_4$: C, 70.26; H, 4.54; N, 25.21; Found: C, 69.96; H, 4.35; N, 25.01. ESI-MS calcd for $C_{13}H_{10}N_4$: 222.09; Found: $[M + H]^+$ 223.03.

Compound ***3c***. White solid (91.6 mg, 97% yield): mp 119–121 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.79 (d, J = 14.9 Hz, 1H), 8.54 (s, 1H), 8.26 (d, J = 7.8 Hz, 1H), 7.94 (t, J = 7.8 Hz, 1H), 7.83 (t, J = 10.5 Hz, 2H), 7.37 (d, J = 5.5 Hz, 1H), 7.32–7.22 (m, 2H), 2.41 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.2, 148.5, 139.1, 138.4, 129.6, 127.4, 125.8, 123.5, 123.0, 116.4, 113.9, 21.4. Anal. Calcd for $C_{14}H_{12}N_4$: C, 71.17; H, 5.12; N, 23.71; Found: C, 70.97; H, 5.51; N, 23.52. ESI-MS calcd for $C_{14}H_{12}N_4$: 236.11; Found: $[M]^+$ 236.94.

Compound ***3d***. White solid (98.8 mg, 98% yield): mp 106–109 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 (s, 1H), 8.55 (s, 1H), 8.26 (d, J = 6.9 Hz, 1H), 7.94 (t, J = 7.7 Hz, 1H), 7.88 (d, J = 8.6 Hz, 2H), 7.37 (s, 1H), 7.01 (d, J = 8.6 Hz, 2H), 3.87 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 160.0, 148.7, 139.3, 127.4, 123.4, 123.0, 116.0, 114.5, 114.0, 55.5. Anal. Calcd for $C_{14}H_{12}N_4O$: C, 66.65; H, 4.79; N, 22.21; Found: C, 66.83; H, 4.59; N, 22.05. ESI-MS calcd for $C_{14}H_{12}N_4O$: 252.10; Found: $[M]^+$ 252.89.

Compound ***3e***. White solid (81.6 mg, 68% yield): mp 174–176 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.81 (s, 1H), 8.52 (d, J = 4.7 Hz, 1H), 8.24 (d, J = 8.2 Hz, 1H), 7.94 (td, J = 8.0, 1.7 Hz, 1H), 7.82 (d, J = 8.4 Hz, 2H), 7.59 (d, J = 8.4 Hz, 2H), 7.37 (dd, J = 7.3, 4.9 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.0, 148.6, 147.0, 139.2, 133.8, 132.0, 131.8, 129.2, 127.4, 123.7, 122.4, 116.9, 113.8. ESI-MS calcd for $C_{13}H_9BrN_4$: 300.00; Found: $[M + H]^+$ 301.53. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{13}H_9BrN_4$ 301.0089; Found: 301.0087.

Compound ***3f***. White solid (49.9 mg, 52% yield): mp 108–111 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.56 (s, 1H), 8.27 (d, J = 6.8 Hz, 1H), 8.01–7.86 (m, 3H), 7.39 (s, 1H), 7.17 (t, J = 8.6 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 148.1, 147.5, 138.2, 126.6, 125.4, 122.6, 115.5, 115.0, 114.8, 112.8, 76.3, 76.0, 75.7, 31.3. Anal. Calcd for $C_{13}H_9FN_4$: C, 64.99; H, 3.78; N, 23.32; Found: C, 65.21; H, 3.52; N, 22.99. ESI-MS calcd for $C_{13}H_9FN_4$: 240.08. Found: $[M]^+$ 240.95.

Compound ***3g***. White solid (80.9 mg, 79% yield): mp 137–14 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.82 (s, 1H), 8.52 (d, J = 4.3 Hz, 1H), 8.23 (d, J = 8.2 Hz, 1H), 7.98–7.90 (m, 2H), 7.81 (d, J = 7.6 Hz, 1H), 7.42–7.35 (m, 2H), 7.33 (d, J = 8.0 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.0, 148.6, 146.7, 139.2, 134.9, 132.0, 130.2, 128.4, 125.9, 123.9, 123.7, 117.2, 113.8. Anal. Calcd for $C_{13}H_9ClN_4$: C, 60.83; H, 3.53; N, 21.83; Found: C, 60.73; H, 3.23; N, 21.43. ESI-MS calcd for $C_{13}H_9ClN_4$: 256.05. Found: $[M + H]^+$ 257.11.

Compound ***3h***. White solid (72.3 mg, 81% yield): mp 132–134 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.18 (s, 1H), 8.66 (s, 1H), 8.55 (d, J = 3.8 Hz, 1H), 8.25 (d, J = 7.7 Hz, 2H), 7.94 (t, J = 7.6 Hz, 1H), 7.82 (t, J = 7.2 Hz, 1H), 7.41–7.32 (m, 1H), 7.27 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.0, 149.7, 149.1, 148.8, 148.6, 139.1, 136.9, 123.7, 123.1, 120.5, 119.4, 113.9. ESI-MS calcd for $C_{12}H_9N_5$: 223.09. Found: [M + H] 224.07. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{12}H_9N_5$ 224.0936; Found: 224.0928.

Compound ***3i***. White solid (70.2 mg, 77% yield): mp 129–134 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.71 (s, 1H), 8.51 (d, J = 4.2 Hz, 1H), 8.22 (d, J = 8.2 Hz, 1H), 7.92 (dd, J = 11.2, 4.4 Hz, 1H), 7.50 (d, J = 3.2 Hz, 1H), 7.42–7.31 (m, 2H), 7.17–7.05 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.0, 148.6, 143.3, 139.2, 132.5, 127.8, 125.5, 124.7, 123.7, 116.2, 113.9. ESI-MS calcd for $C_{11}H_8N_4S$: 228.05. Found: $[M + H]^+$ 229.11. HRMS (ESI-TOF) m/z: $[M + H]^+$ calcd for $C_{11}H_8N_4S$ 229.0548; Found: 229.0546.

Compound ***3j***. White solid (41.8 mg, 55% yield): mp 69–71 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (dd, J = 28.0, 10.2 Hz, 2H), 8.27–8.08 (m, 1H), 7.92 (s, 1H), 7.35 (s, 1H), 4.04 (s, 2H), 3.07 (s, 2H), 2.60 (s, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.3, 148.5, 139.1, 127.4, 123.5, 122.9, 119.4, 113.7, 61.5, 31.0. ESI-MS calcd for $C_9H_{10}N_4O$: 190.09. Found: $[M + H]^+$ 191.21. HRMS (ESI-TOF) m/z: $[M + Na]^+$ calcd for $C_9H_{10}N_4ONa$ 213.0752; Found: 213.0748.

Compound ***3k***. Colorless liquid (43.5 mg, 49% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.46 (d, J = 3.4 Hz, 1H), 8.35 (s, 1H), 8.15 (d, J = 8.0 Hz, 1H), 7.88 (t, J = 7.4 Hz, 1H), 7.37–7.27 (m, 1H), 3.60 (t, J = 6.2 Hz, 2H), 2.97 (t, J = 7.1 Hz,

2H), 2.31–2.11 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.2, 148.5, 146.9, 139.1, 123.4, 118.6, 113.7, 44.0, 31.8, 22.7. ESI-MS calcd for $C_{10}H_{11}ClN_4$: 222.07. Found: $[M + H]^+$ 223.52. HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{10}H_{11}ClN_4Na$ 245.0570; Found: 245.0586.

Compound ***3l***. Colorless liquid (43.6 mg, 54% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.48 (d, J = 4.0 Hz, 1H), 8.30 (s, 1H), 8.18 (d, J = 8.2 Hz, 1H), 7.89 (td, J = 8.2, 1.7 Hz, 1H), 7.31 (dd, J = 7.2, 5.0 Hz, 1H), 2.81 (t, J = 7.7 Hz, 2H), 1.76–1.68 (m, 2H), 1.44 (dd, J = 13.8, 6.3 Hz, 2H), 0.95 (t, J = 7.4 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.4, 148.9, 148.4, 139.0, 123.2, 118.0, 113.7, 31.4, 25.3, 22.3, 13.8. ESI-MS calcd for $C_{11}H_{14}N_4$: 202.12. Found: $[M + H]^+$ 203.47. HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{11}H_{14}N_4Na$ 225.1116; Found: 225.1114.

Compound ***3m***. Colorless liquid (47.5 mg, 55% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (s, 1H), 8.30 (s, 1H), 8.16 (d, J = 8.1 Hz, 1H), 7.88 (t, J = 7.7 Hz, 1H), 7.41–7.26 (m, 1H), 2.79 (t, J = 7.6 Hz, 2H), 1.83–1.64 (m, 2H), 1.40–1.33 (m, 4H), 0.89 (t, J = 6.8 Hz, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 149.4, 149.0, 148.4, 139.0, 123.3, 118.0, 113.7, 32.3, 32.2, 31.4, 29.0, 25.6, 22.4, 14.0. ESI-MS calcd for $C_{12}H_{16}N_4$: 216.14. Found: $[M + H]^+$ 217.44. HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{12}H_{16}N_4Na$ 239.1237; Found: 239.1266.

Compound ***3n***. Colorless liquid (44.6 mg, 60% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.42 (s, 1H), 8.20 (s, 1H), 8.11 (s, 1H), 7.83 (s, 1H), 7.26 (s, 1H), 2.06 (d, J = 54.7 Hz, 1H), 1.52–1.17 (m, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 150.9, 149.3, 148.4, 139.0, 123.3, 117.0, 113.7, 7.9, 6.8. ESI-MS calcd for $C_{10}H_{10}N_4$: 186.1. Found: $[M + H]^+$ 187.30. HRMS (ESI-TOF) *m*/*z*: $[M + Na]^+$ calcd for $C_{10}H_{10}N_4Na$ 209.0803; Found: 209.0793.

Compound ***3o***. Orange solid (67.0 mg, 46% yield): mp 245–247 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.52 (s, 1H), 8.03 (d, J = 30 Hz, 2H), 7.42 (s, 1H), 4.88 (s, 2H), 4.41 (s, 2H), 4.18 (s, 5H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 147.1, 146.6, 146.1, 140.9, 125.7, 125.3, 119.4, 77.4, 77.2, 76.9, 70.2, 69.4, 67.3. Anal. Calcd for $C_{17}H_{13}ClFeN_4$: C, 56.00; H, 3.59; N, 15.37; Found: C, 55.75; H, 3.91; N, 15.17. ESI-MS calcd for $C_{17}H_{13}ClFeN_4$: 364.02. Found: $[M]^+$ 364.7.

Compound ***3p***. White solid (49.2 mg, 48% yield): mp 140–142 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54 (d, J = 3.9 Hz, 1H), 8.40 (s, 1H), 8.02 (d, J = 7.9 Hz, 1H), 7.95 (d, J = 7.5 Hz, 2H), 7.45 (dt, J = 7.9, 6.1 Hz, 3H), 7.38 (t, J = 7.2 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 146.3, 146.0, 145.0, 139.8, 129.0, 127.9, 127.5, 125.0, 124.7, 124.3, 119.2, 76.3, 76.0, 75.8. Anal. Calcd for $C_{13}H_9ClN_4$: C, 60.83; H, 3.53; N, 21.83; Found: C, 60.58; H, 3.74; N, 21.64. ESI-MS calcd for $C_{13}H_9ClN_4$: 256.05. Found: $[M]^+$ 256.09.

Conclusions

In conclusion, we have presented an efficient and practical catalytic system for the synthesis of 1,4-substituted-1-(pyridin-2-yl)-1,2,3-triazoles. Under the optimal conditions, 5 mol% of CuCl and 10 mol% of 2-PyCH$_2$N=P^{t}Bu$_3$ (**L$_9$**) in toluene at 120 °C were used. Good to excellent yields were obtained by using electron-rich aromatic alkynes as the substrates, at the same time using electron-deficient aromatic alkynes and alkyl alkynes as the substrates afforded the desired products in moderate yields. More remarkably, 8-chlorotetrazolo[1,5-*a*]-pyridine which exists mainly in closed form equilibrium (Scheme 2) can react with ferrocenyl acetylene or ethynylbenzene smoothly to give the products in moderate yield.

Acknowledgements

This work was financially supported by the National Science Foundation of China (Nos. 21004032, 21364005, 21202079), the Key Project of Chinese Ministry of Education in China (no. 210077), Startup Foundation for Outstanding Young Scientists of Inner Mongolia University (Z20080213, no. 115110).

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