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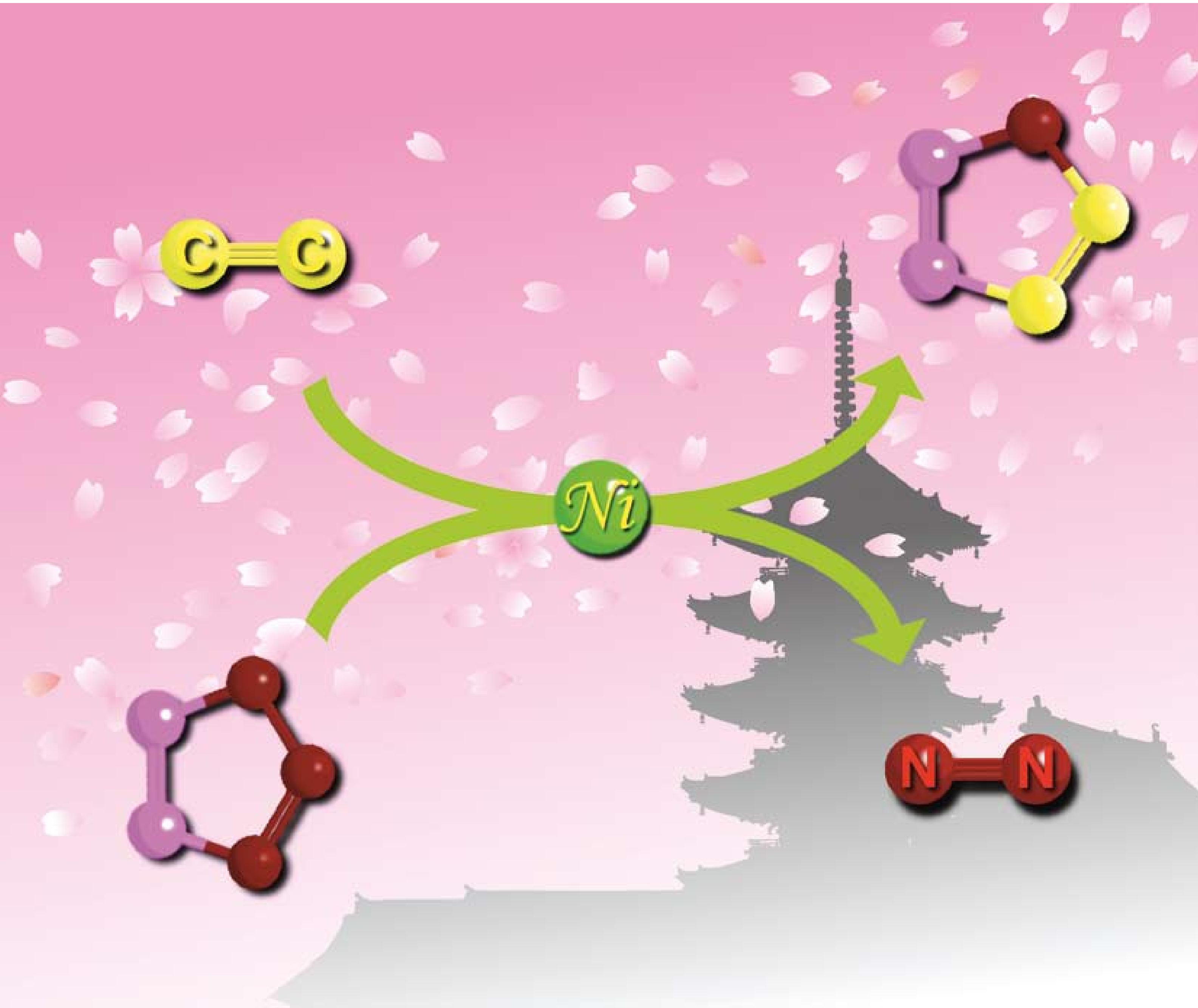

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FEATURE ARTICLE
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Nickel-catalysed denitrogenative alkyne insertion reactions of *N*-sulfonyl-1,2,3-triazoles†

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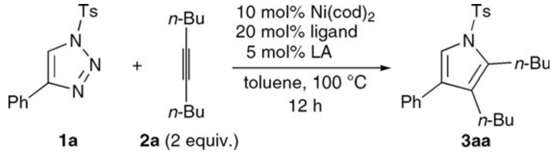
_N_-Sulfonyl-1,2,3-triazoles reacted with alkynes in the presence of a nickel(0)/phosphine catalyst to give substituted pyrroles, with the extrusion of molecular nitrogen; the triazole moiety isomerised to an α-imino diazo species, and the denitrogenative addition to nickel(0) was followed by the insertion of alkynes and reductive elimination.

The development of efficient methods for the synthesis of heterocyclic compounds is highly valuable,[1] particularly in the field of medicinal chemistry, because most biologically active compounds contain heterocyclic cores. Recently, transition metal-catalysed denitrogenative reactions of triazole derivatives, forming new heterocyclic systems, have been reported, in which diazo compounds were generated *in situ* by ring–chain tautomerisation, and subsequently converted to a reactive metal-carbenoid species. 7-Halo-substituted pyridotriazoles[2] and *N*-sulfonyl-1,2,3-triazoles[3] react with alkynes and nitriles in the presence of a rhodium catalyst, forming indolizines, imidazopyridines and imidazoles, respectively. Benzotriazoles have also been utilised in palladium-catalysed reactions with alkynes to provide indoles.[4] On the other hand, we have found that nickel-catalysed denitrogenative alkyne insertion reactions of 1,2,3-benzotriazin-4(3*H*)-ones give a wide range of substituted 1(2*H*)-isoquinolines in high yields.[5] We then envisaged that an analogous denitrogenative reaction of *N*-sulfonyl-1,2,3-triazoles with alkynes could be feasible, if the diazo tautomers could add to nickel(0) with extrusion of molecular nitrogen, providing a reactive nickel-carbenoid species.[6] We report herein nickel-catalysed denitrogenative alkyne insertion reactions of *N*-sulfonyl-1,2,3-triazoles, which present a new approach to the preparation of substituted pyrroles.[7]

The starting materials, 4-substituted 1-(*N*-tosyl)-1,2,3-triazoles, could be readily prepared by a copper-catalysed azide/alkyne cycloaddition.[8] When 4-phenyl-1-(*N*-tosyl)-1,2,3-triazole (**1a**) was treated with dec-5-yne (**2a**, 2 equiv.), Ni(cod)$_2$ (10 mol%) and PMe$_3$ (20 mol%) in toluene at 100 °C for 12 h, only a trace of the desired pyrrole, **3aa**, was obtained (Table 1, entry 1). However, the use of sterically-hindered phosphine ligands increased the yield up to 51% (Table 1, entries 2–4). Next, the effect of Lewis acid (LA) catalysts as additives was examined (Table 1, entries 5–8).[9] It was found that the reaction in the presence of AlPh$_3$ (5 mol%) gave **3aa** in 73% isolated yield.

Table 1 Optimisation study of the formation of pyrrole **3aa**

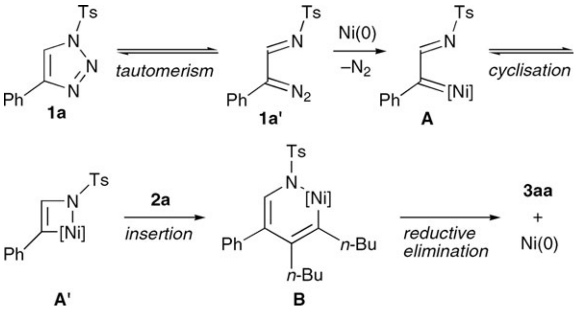


Entry	Ligand	Lewis acid	Yield (%)[a]
1	PMe$_3$	—	2
2	PCy$_3$	—	8
3	P(*t*-Bu)$_3$	—	13
4	P(*n*-Bu)Ad$_2$	—	51
5	P(*n*-Bu)Ad$_2$	BPh$_3$	49
6	P(*n*-Bu)Ad$_2$	ZnPh$_2$	62
7	P(*n*-Bu)Ad$_2$	AlMe$_3$	38
8	P(*n*-Bu)Ad$_2$	AlPh$_3$	81 (73)

[a] Determined by ^{1}H NMR using CHCl$_2$CHCl$_2$ as an internal standard. Isolated yields are given in parentheses.

A possible reaction pathway for the production of **3aa** from **1a** and **2a** is depicted in Scheme 1. Initially, a ring–chain tautomerisation of *N*-sulfonyl-1,2,3-triazole **1a** occurs to generate α-imino diazo compound **1a′**,[10] although the equilibrium lies far to the left. Diazo compound **1a′** adds to nickel(0), with release of molecular nitrogen, to give nickel-carbenoid **A**, which then cyclises to form azanickelacycle **A′**. Subsequent insertion of alkyne **2a** into the Ni–C bond leads to six-membered ring nickelacycle **B**. Finally, reductive elimination affords **3aa**, regenerating the nickel(0) catalyst. Possible effects of the LA catalysts may be (1) promoting the formation of α-imino diazo species **1a′**, and/or (2) accelerating the reductive elimination,[11] although we have no experimental results to support either of these postulates.

Under optimised reaction conditions, a variety of *N*-sulfonyltriazoles, **1b–j**, reacted with **2a** to furnish substituted



Scheme 1 Proposed reaction pathway.

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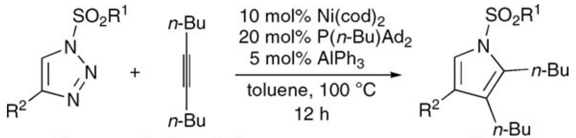
Table 2 The Nickel(0)-catalysed alkyne insertion reactions of **1** with **2a**

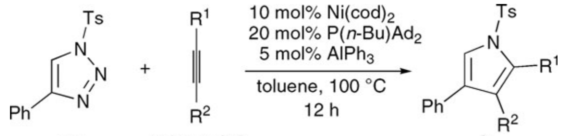


1 + **2a** (2 equiv.) → **3**

Entry	1	R^1	R^2	3	Yield (%)[a]
1	**1b**	Ph	Ph	**3ba**	65
2	**1c**	4-F-C_6H_4	Ph	**3ca**	46
3	**1d**	4-MeO-C_6H_4	Ph	**3da**	56[b]
4	**1e**	2-Naphthyl	Ph	**3ea**	58[b]
5	**1f**	Tol	Tol	**3fa**	64
6	**1g**	Tol	4-CF_3-C_6H_4	**3ga**	64[c]
7	**1h**	Tol	4-MeO-C_6H_4	**3ha**	59[b]
8	**1i**	Tol	4-Ph-C_6H_4	**3ia**	54
9	**1j**	Tol	2-Naphthyl	**3ja**	58
10	**1k**	Tol	*n*-Hexyl	**3ka**	5

[a] Isolated yield. [b] $Ni(cod)_2$ (15 mol%) and P(*n*-Bu)Ad_2 (30 mol%) were used. [c] 110 °C.

Table 3 Denitrogenative alkyne insertion reactions of **1a** with **2**



1a + **2** (2 equiv.) → **3**

Entry	2	R^1	R^2	3	Yield (%)[a]
1	**2b**	*n*-Pr	*n*-Pr	**3ab**	68
2	**2c**	Ph	Ph	**3ac**	31
3	**2d**	Me	*i*-Pr	**3ad**	68 (50 : 50)
4	**2e**	Me	$SiMe_3$	**3ae**	48 (58 : 42)[b]
5	**2f**	Bpin	*n*-Bu	**3af**	37 (57 : 43)[b]

[a] Isolated yield. The ratio of the regioisomers is shown in parentheses. [b] $Ni(cod)_2$ (15 mol%) and P(*n*-Bu)Ad_2 (30 mol%) were used.

pyrroles **3ba–ja** in yields ranging from 46 to 65% (Table 2, entries 1–9‡). However, the reaction of alkyl-substituted triazole **1k** proceeded sluggishly to form the desired product, **3ka**, in only 5% yield (Table 2, entry 10).

Various alkynes, **2**, were subjected to the denitrogenative insertion reaction with **1a** (Table 3). Symmetrical alkynes such as 4-octyne (**2b**) and diphenylethyne (**2c**) reacted to give **3ab** and **3ac** in 68 and 31% yields, respectively (Table 3, entries 1 and 2). The reaction of unsymmetrical alkynes gave a mixture of regioisomers (Table 3, entries 3–5). Terminal alkynes such as oct-1-yne and phenylethyne failed to participate in the reaction, presumably due to a rapid self-oligomerisation reaction.

In summary, we have demonstrated that the nickel-catalysed denitrogenative alkyne insertion reactions of *N*-sulfonyltriazoles provide a new synthetic route to substituted pyrroles from readily available starting materials. In these reactions, the triazole moiety is effectively activated by the combined use of nickel and a LA catalyst.

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Notes and references

‡ **General procedure**: In a glove box, **1** (0.20 mmol) and $AlPh_3$ (2.6 mg, 10 μmol) were charged into an oven-dried 4 mL vial equipped with a stirring bar. A solution of $Ni(cod)_2$ (5.5 mg, 20 μmol) and P(*n*-Bu)Ad_2 (14.3 mg, 40 μmol) in toluene (2 mL), and **2** (0.40 mmol), were added. The vial was then capped with a Teflon film and removed from the glove box. The reaction mixture was heated at 100 °C for 12 h. After this time, the reaction mixture was cooled to room temperature and stirred in open air for 30 min. The resulting mixture was passed through a pad of Florisil and eluted with ethyl acetate. The filtrate was concentrated under reduced pressure. The residue was purified by preparative thin layer chromatography (hexane/dichloromethane) to give product **3**.

1 For recent reviews, see: (*a*) D. M. D'Souza and T. J. J. Müller, *Chem. Soc. Rev.*, 2007, **36**, 1095; (*b*) M. Álvarez-Corral, M. Muñoz-Dorado and I. Rodríguez-García, *Chem. Rev.*, 2008, **108**, 3174; (*c*) N. T. Patil and Y. Yamamoto, *Chem. Rev.*, 2008, **108**, 3395.
2 (*a*) S. Chuprakov, F. W. Hwang and V. Gevorgyan, *Angew. Chem., Int. Ed.*, 2007, **46**, 4757; (*b*) For the related rhodium-catalysed cyclopropanation of pyridotriazoles, see: S. Chuprakov and V. Gevorgyan, *Org. Lett.*, 2007, **9**, 4463.
3 T. Horneff, S. Chuprakov, N. Chernyak, V. Gevorgyan and V. V. Fokin, *J. Am. Chem. Soc.*, 2008, **130**, 14972.
4 N. Shiraiwa, T. Nemoto, I. Nakamura and M. Terada, in *The 55th Symposium on Organometallic Chemistry*, The Kinki Chemical Society (Osaka, Japan), Osaka, Japan, September 28–30, 2008, P3A-11.
5 T. Miura, M. Yamauchi and M. Murakami, *Org. Lett.*, 2008, **10**, 3085.
6 For reactions of diazoalkanes with a nickel(0) catalyst, see: (*a*) A. Nakamura, T. Yoshida, M. Cowie, S. Otsuka and J. A. Ibers, *J. Am. Chem. Soc.*, 1977, **99**, 2108; (*b*) D. J. Mindiola and G. L. Hillhouse, *J. Am. Chem. Soc.*, 2002, **124**, 9976.
7 For recent reports on the synthesis of substituted pyrroles, see: (*a*) M. R. Rivero and S. L. Buchwald, *Org. Lett.*, 2007, **9**, 973; (*b*) M. Shindo, Y. Yoshimura, M. Hayashi, H. Soejima, T. Yoshikawa, K. Matsumoto and K. Shishido, *Org. Lett.*, 2007, **9**, 1963; (*c*) H. Dong, M. Shen, J. E. Redford, B. J. Stokes, A. L. Pumphrey and T. G. Driver, *Org. Lett.*, 2007, **9**, 5191; (*d*) C. V. Galliford and K. A. Scheidt, *J. Org. Chem.*, 2007, **72**, 1811; (*e*) V. Cadierno, J. Gimeno and N. Nebra, *Chem.–Eur. J.*, 2007, **13**, 9973; (*f*) S. Chiba, Y.-F. Wang, G. Lapointe and K. Narasaka, *Org. Lett.*, 2008, **10**, 313; (*g*) S. Cacchi, G. Fabrizi and E. Filisti, *Org. Lett.*, 2008, **10**, 2629; (*h*) Y. Lu and B. A. Arndtsen, *Angew. Chem., Int. Ed.*, 2008, **47**, 5430.
8 E. J. Yoo, M. Ahlquist, S. H. Kim, I. Bae, V. V. Fokin, K. B. Sharpless and S. Chang, *Angew. Chem., Int. Ed.*, 2007, **46**, 1730.
9 For LA-accelerated reactions involving nickel(0) species, see: (*a*) N. M. Brunkan, D. M. Brestensky and W. D. Jones, *J. Am. Chem. Soc.*, 2004, **126**, 3627; (*b*) H. P. Hratchian, S. K. Chowdhury, V. M. Gutiérrez-García, K. K. D. Amarasinghe, M. J. Heeg, H. B. Schlegel and J. Montgomery, *Organometallics*, 2004, **23**, 4636; (*c*) S. Ogoshi, M. Ueta, T. Arai and H. Kurosawa, *J. Am. Chem. Soc.*, 2005, **127**, 12810; (*d*) Y. Nakao, A. Yada, S. Ebata and T. Hiyama, *J. Am. Chem. Soc.*, 2007, **129**, 2428.
10 (*a*) P. Grünanger and P. V. Finzi, *Tetrahedron Lett.*, 1963, **4**, 1839; (*b*) R. E. Harmon, F. Stanley, Jr, S. K. Gupta and J. Johnson, *J. Org. Chem.*, 1970, **35**, 3444; (*c*) G. Himbert, D. Frank and M. Regit, *Chem. Ber.*, 1976, **109**, 370.
11 Q. Shen and J. F. Hartwig, *J. Am. Chem. Soc.*, 2007, **129**, 7734.