ORGANIC
LETTERS

2013
Vol. 15, No. 16
4182–4185

Diazo Compounds as Electrophiles To React with 1,4-Dilithio-1,3-dienes: Efficient Synthesis of 1-Imino-pyrrole Derivatives

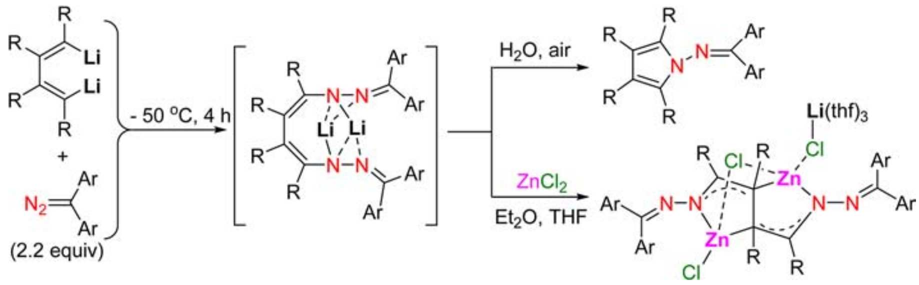
Ming Zhan,[†] Shaoguang Zhang,[†] Wen-Xiong Zhang,[†] and Zhenfeng Xi[*,†,‡]

Beijing National Laboratory for Molecular Sciences (BNLMS), Key Laboratory of Bioorganic Chemistry and Molecular Engineering of Ministry of Education, College of Chemistry, Peking University, Beijing 100871, China, and State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, CAS, Shanghai 200032, China

zfxi@pku.edu.cn

Received July 4, 2013

ABSTRACT



1-Imino-pyrrole and indole derivatives were synthesized in high yields from the reaction of diaryl diazomethanes with 1,4-dilithio-1,3-dienes. Diaryl diazomethanes reacted as electrophiles in this reaction. An unprecedented Zn-complex was formed via transmetalation of the above reaction intermediate with $ZnCl_2$ and was structurally characterized. The *trans*-μ_2-η^1:η^1 coordination mode in the solid state for this azaallylzinc compound was observed.

Diazo compounds are a class of important building blocks in synthetic chemistry.[1] Among various reaction patterns, diazo compounds are usually known to act as metal carbene precursors,[2] 1,3-dipoles,[3] and nucleophiles.[4] However, as demonstrated in Scheme 1, although it is fundamental and straightforward that diazo compounds behave as electrophiles to react with organometallic reagents, such a reaction type is very rare, mainly due to the high reactivity (instability) of the generated diazo organometallic intermediates.[5,6] Therefore, a way to stabilize such reactive species is highly demanded to synthetically utilize this fundamental reaction.

In recent years, we have studied the synthesis, reaction chemistry, and synthetic applications of 1,4-dilithio-1,3-

---

[†] Peking University.

[‡] Shanghai Institute of Organic Chemistry.

(1) For reviews on applications of diazo compounds, see: (a) Ye, T.; Mckervey, M. A. *Chem. Rev.* **1994**, *94*, 1091. (b) Doyle, M. P.; Mckervey, M. A.; Ye, T. *Modern Catalytic Methods for Organic Synthesis with Diazo Compounds*; Wiley: New York, 1998. (c) Zhang, Z.; Wang, J. *Tetrahedron* **2008**, *64*, 6577. (d) Xiao, Q.; Zhang, Y.; Wang, J. *Acc. Chem. Res.* **2012**, *46*, 236.

(2) For selected reviews, see: (a) Doyle, M. P. *Chem. Rev.* **1986**, *86*, 919. (b) Padwa, A.; Weingarten, M. D. *Chem. Rev.* **1996**, *96*, 223. (c) Hodgson, D. M.; Pierard, F. Y. T. M.; Stupple, P. A. *Chem. Soc. Rev.* **2001**, *30*, 50. (d) Rubin, M.; Rubina, M.; Gevorgyan, V. *Chem. Rev.* **2007**, *107*, 3117. (e) Davies, H. M. L.; Manning, J. R. *Nature* **2008**, *451*, 417. (f) Doyle, M. P.; Duffy, R.; Ratnikov, M.; Zhou, L. *Chem. Rev.* **2010**, *110*, 704.

(3) Gothelf, K. V.; Jørgensen, K. A. *Chem. Rev.* **1998**, *98*, 863.

(4) Zhang, Y.; Wang, J. *Chem. Commun.* **2009**, 5350.

(5) (a) Takamura, N.; Mizoguchi, T.; Yamada, S. *Tetrahedron Lett.* **1973**, *14*, 4267. (b) Takamura, N.; Yamada, S. *Chem. Pharm. Bull.* **1976**, *24*, 800. (c) Yasui, E.; Wada, M.; Takamura, N. *Tetrahedron Lett.* **2006**, *47*, 743. (d) Yasui, E.; Wada, M.; Takamura, N. *Tetrahedron* **2009**, *65*, 461.

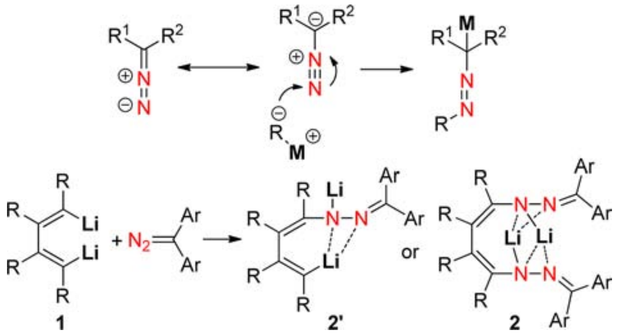
(6) Li, W.; Liu, X.; Hao, X.; Hu, X.; Chu, Y.; Cao, W.; Qin, S.; Hu, C.; Lin, L.; Feng, X. *J. Am. Chem. Soc.* **2011**, *133*, 15268.

(7) (a) Xi, Z.; Zhang, W.-X. *Synlett* **2008**, 2557. (b) Xi, Z. *Acc. Chem. Res.* **2010**, *43*, 1342. See also: (c) Clayden, J. *Organolithiums: Selectivity for Synthesis*; Pergamon: Oxford, 2002. (d) *The Chemistry of Organolithium Compounds*; Rappoport, Z., Marek, I., Eds; Wiley: Chichester, 2004.

(8) (a) Xi, Z.; Song, Q. *J. Org. Chem.* **2000**, *65*, 9157. (b) Song, Q.; Chen, J.; Jin, X.; Xi, Z. *J. Am. Chem. Soc.* **2001**, *123*, 10419. (c) Liu, L.; Zhang, W.-X.; Wang, C.; Wang, C. Y.; Xi, Z. *Angew. Chem., Int. Ed.* **2009**, *48*, 8111. (d) Xi, Z. *Sci. China, Ser. B* **2009**, *39*, 1115. (e) Zhang, S.; Wei, J.; Zhan, M.; Luo, Q.; Wang, C.; Zhang, W.-X.; Xi, Z. *J. Am. Chem. Soc.* **2012**, *134*, 11964.

10.1021/ol401878q

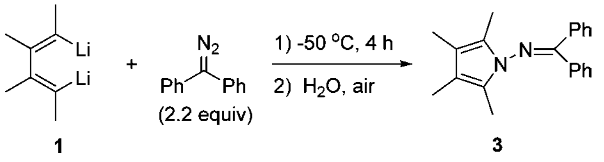
Scheme 1. Diazo Compounds As Electrophiles

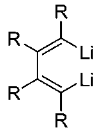
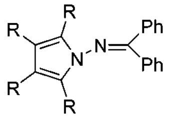
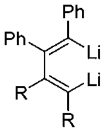
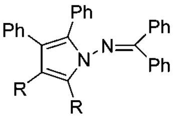
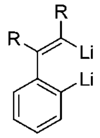
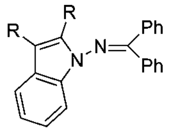


dienes **1** (dilithio reagents for short).[7a,b,8] Because the two Li atoms are bridged by a butadiene moiety and are in close proximity, these dilithio reagents have demonstrated remarkable cooperative effects including cooperative stabilization.[7a,b,8] As illustrated in Scheme 1, we envisioned that the reaction between a dilithio reagent and one or two diazo compounds would form the intermediate **2** or **2′**, which might be stabilized through the intramolecular coordination. Herein we report our preliminary results on the reaction between the dilithio reagents **1** and diazo compounds, in which diazo compounds acted as electrophiles. Multiply substituted 1-imino-pyrrole and indole derivatives were obtained in good to excellent isolated yields.[9,10] Synthetic methods for *N*-imino pyrrole and indole derivatives are very limited.[10] A mechanistic investigation revealed that two diazo compounds reacted with one dilithio reagent affording the intermediate **2**. Furthermore, an unprecedented Zn-complex was obtained via transmetalation of the intermediate **2** with ZnCl$_2$. In this Zn-complex, the *trans*-μ_2-η^1:η^1 coordination mode in the solid state was observed.

1,4-Dilithio-1,3-dienes **1** (dilithio reagents for short) were quantitatively generated from their corresponding 1,4-diiodo-1,3-dienes and *t*-BuLi at −78 °C for 1 h.[7b] When the *in situ* generated dilithio reagent **1a** (R = Et) was treated with 1.0 equiv of diphenyldiazomethane, the multiply substituted 1-imino-pyrrole derivative **3a** was obtained in 41% isolated yield upon quench of the reaction mixture with H$_2$O in air. The unreacted **1a** changed into its corresponding diene after quenching. When 2.2 equiv of diphenyldiazomethane were used, **3a** was obtained in 86% isolated yield. Given in Table 1 are representative results. In addition to those symmetrically substituted dilithio reagents (**1a**–**c**), the unsymmetrically substituted dilithio reagents (**1d**,**e**) and the vinylphenyl dilithio reagents (**1f**,**g**) could all react with diphenyldiazomethane to afford their corresponding 1-imino-pyrrole or indole derivatives. The structure of **3e** was determined by single-crystal X-ray structural analysis (Figure 1).

Table 1. Synthesis of 1-Imino-pyrrole and Indole Derivatives from 1,4-Dilithio-1,3-dienes and Diphenyldiazomethane



dilithio reagent **1**		product **3** (isolated yield)	
	**1a:** R = Et **1b:** R = Pr **1c:** R = Bu		**3a:** R = Et, 86% **3b:** R = Pr, 93% **3c:** R = Bu, 94%
	**1d:** R = Me **1e:** R = Et		**3d:** R = Me, 56% **3e:** R = Et, 71%
	**1f:** R = Me **1g:** R = Et		**3f:** R = Me, 50% **3g:** R = Et, 80%

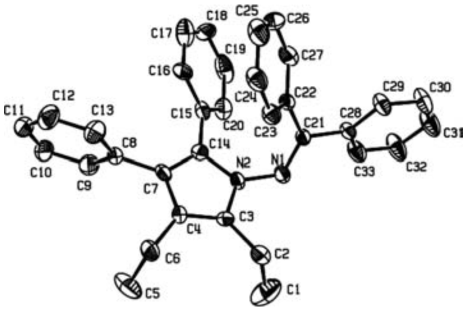


Figure 1. ORTEP drawing of **3e** with 35% thermal ellipsoids. Hydrogen atoms are omitted for clarity. Selected bond lengths [Å]: C(3)−N(2) 1.381(4), C(3)−C(4) 1.359(5), C(4)−C(7) 1.425(5), C(7)−C(14) 1.370(5), C(14)−N(2) 1.397(4), N(1)−N(2) 1.428(4), C(21)−N(1) 1.293(4).

Given in Figure 2 are representative results obtained from the reaction of the dilithio reagent **1a** with other diazo compounds, following the reaction conditions shown in Table 1.

For those cases with lower yields (**3d**, **3f**, **3i**, **3j**), both their corresponding dienes and decomposition of diazo compounds were observed. The lower reactivity of those dilithio reagents and diazo compounds with different

---

(9) For recent reviews, see: (a) Platon, M.; Amardeil, R.; Djakovitch, L.; Hierso, J.-C. *Chem. Soc. Rev.* **2012**, *41*, 3929. (b) Inman, M.; Moody, C. J. *Chem. Sci.* **2013**, *4*, 29. Also see: (c) Bell, I.; Madroñero, R.; Whiting, M. C. *J. Chem. Soc.* **1958**, 3195. (d) Amon, M.; Ligneau, X.; Schwartz, J.-C.; Stark, H. *Bioorg. Med. Chem. Lett.* **2006**, *16*, 1938. (e) Ferorelli, S.; Abate, C.; Colabufo, N. A.; Niso, M.; Inglese, C.; Berardi, F.; Perrone, R. *J. Med. Chem.* **2007**, *50*, 4648.

(10) Christl, M.; Lesch, S.; Deuerlein, S.; Stalke, D. *Helv. Chim. Acta* **2005**, *88*, 1421.

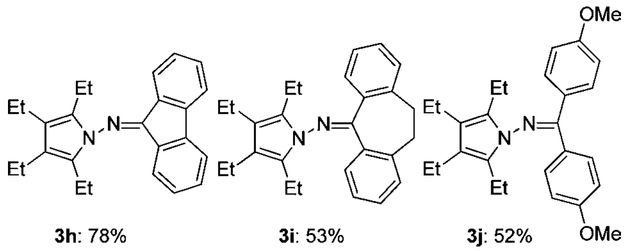
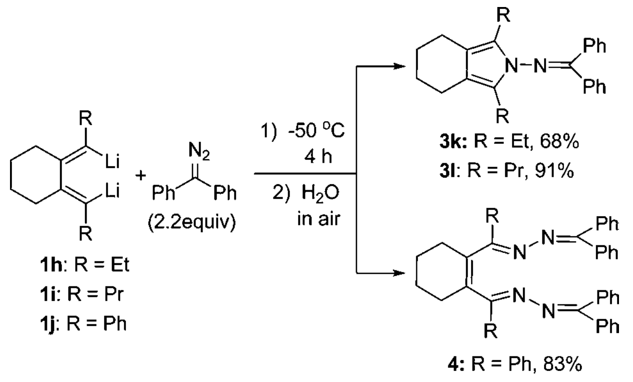


Figure 2. 1-Imino-pyrrole derivatives obtained from the dilithio reagent **1a** and other diazo compounds.

structures is considered the major reason for the lower product yields.

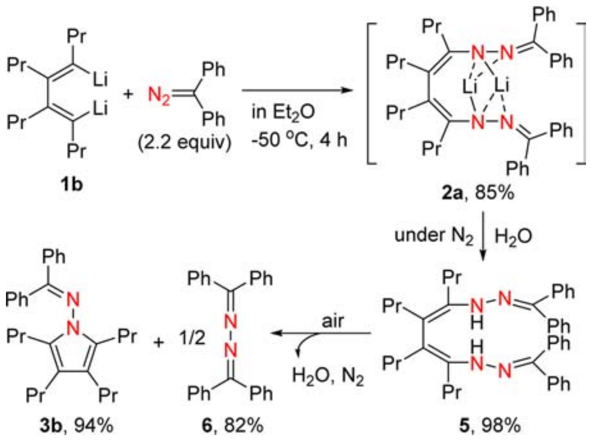
When cyclic dilithio reagents (**1h,i**, Scheme 2) were treated with 2.2 equiv of dipenyldiazomethane, their corresponding *N*-imino tetrahydro *iso*-indole derivatives **3k** and **3l** were obtained. However, in the case of the dilithio reagent **1j** (R = Ph), the unexpected bis(diazo) compound **4** was obtained in 83% isolated yield. Formation of its corresponding tetrahydroisoindole derivative was not observed.

Scheme 2. Reaction of Cyclic Dilithio Reagents with Diphenlydiazomethane

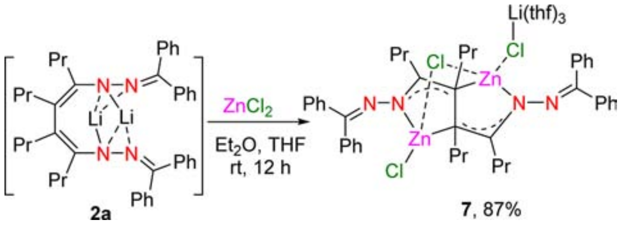


The reaction mechanism between the dilithio reagent and diazo compounds was investigated (Scheme 3). First, we isolated the imtermediate **2a** and obtained its NMR data. The peak at 152.6 ppm in its ^{13}C NMR spectrum shows that an imine carbon exists in its structure. Then, this intermediate was quenched with H_2O under N_2, and the product **5** was formed and structurally characterized by single-crystal X-ray analysis (see Supporting Information for details). When **5** was dissolved and stirred in THF in air, it was oxidized to afford the product **3b** and the diazo compound **6**.[11]

Scheme 3. Reaction Mechanism



Scheme 4. Synthetic Application of **2a**



Furthermore, as a demonstration of the formation and synthetic application of **2**, transmetalation of **2a** with $ZnCl_2$ was performed. An unprecedented organozinc compound **7** was thus obtained in 87% isolated yield (Scheme 4).[12] The structure of **7** was identified by single-crystal X-ray structural analysis (Figure 3).

---

(11) (a) Uno, H.; Okada, S.; Suzuki, H. *Tetrahedron* **1991**, *47*, 6231. (b) Klimenko, I. P.; Medvedev, A. F.; Korolev, V. A.; Kolomnikova, G. D.; Tomilov, Y. V.; Bubnov, Y. N. *J. Organomet. Chem.* **2009**, *694*, 2106. (c) Wang, D. H.; Liu, Q.; Chen, B.; Zhang, L. P.; Tung, C. H.; Wu, L. Z. *Chin. Sci. Bull.* **2010**, *55*, 2855.

(12) For reports on structures of organozinc compounds, see: (a) Uchiyama, M.; Matsumoto, Y.; Nobuto, D.; Furuyama, T.; Yamaguchi, K.; Morokuma, K. *J. Am. Chem. Soc.* **2006**, *128*, 8748. (b) Wooten, A.; Carroll, P. J.; Maestri, A. G.; Walsh, P. J. *J. Am. Chem. Soc.* **2006**, *128*, 4624. (c) Guerrero, A.; Hughes, D. L.; Bochmann, M. *Organometallics* **2006**, *25*, 1525. (d) Mulvey, R. E.; Mongin, F.; Uchiyama, M.; Kondo, Y. *Angew. Chem., Int. Ed.* **2007**, *46*, 3802. (e) Sarazin, Y.; Wright, J. A.; Harding, D. A. J.; Martin, E.; Woodman, T. J.; Hughes, D. L.; Bochmann, M. *J. Organomet. Chem.* **2008**, *693*, 1494. (f) Merkel, S.; Stern, D.; Stalke, D. *Angew. Chem., Int. Ed.* **2009**, *48*, 6350. (g) Clegg, W.; Conway, B.; Garcıa-Alvarez, P.; Kennedy, A. R.; Klett, J.; Mulvey, R. E.; Russo, L. *Dalton Trans.* **2010**, *39*, 62. (h) MacIntosh, I. S.; Sherren, C. N.; Robertson, K. N.; Masuda, J. D.; Pye, C. C.; Clyburne, J. A. C. *Organometallics* **2010**, *29*, 2063. (i) Schmidt, S.; Schulz, S.; Bläser, D.; Boese, R.; Bolte, M. *Organometallics* **2010**, *29*, 6097. (j) Zhou, Y.; Zhang, W.-X.; Xi, Z. *Organometallics* **2012**, *31*, 5546.

(13) (a) Seyferth, D.; Womack, G. B.; Archer, C. M.; Dewan, J. C. *Organometallics* **1989**, *8*, 430. (b) Gunnoe, T. B.; White, P. S.; Templeton, J. L. *Organometallics* **1997**, *16*, 3794. (c) Bailey, P. J.; Liddle, S. T.; Morrison, C. A.; Parsons, S. *Angew. Chem., Int. Ed.* **2001**, *40*, 4463. (d) Li, X.; Baldamus, J.; Nishiura, M.; Tardif, O.; Hou, Z. *Angew. Chem., Int. Ed.* **2006**, *45*, 8184. (e) Lichtenberg, C.; Jochmann, P.; Spaniol, T. P.; Okuda, J. *Angew. Chem., Int. Ed.* **2011**, *50*, 5753. (f) Lichtenberg, C.; Engel, J.; Spaniol, T. P.; Englert, U.; Raabe, G.; Okuda, J. *J. Am. Chem. Soc.* **2012**, *134*, 9805. (g) Ménard, G.; Stephan, D. W. *Angew. Chem., Int. Ed.* **2012**, *51*, 4409. (h) Peterson, J. K.; MacDonald, M. R.; Ziller, J. W.; Evans, W. J. *Organometallics* **2013**, *32*, 2625.

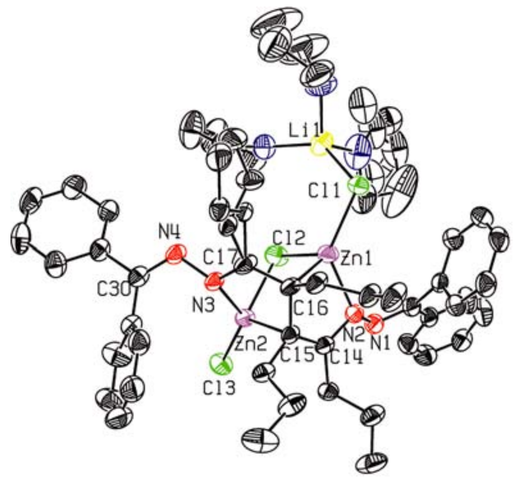


Figure 3. ORTEP drawing of **7** with 30% thermal ellipsoids. Hydrogen atoms are omitted for clarity. Selected bond lengths [Å] for **7**: Zn(1)−Cl(1) 2.2249(7), Zn(1)−Cl(2) 2.4163(7), Zn(1)−N(2) 2.008(2), Zn(1)−C(16) 2.096(3), Zn(2)−Cl(2) 2.3778(8), Zn(2)−Cl(3) 2.1841(7), Zn(2)−N(3) 2.006(2), Zn(2)−C(15) 2.195(2), N(1)−N(2) 1.393(3), N(1)−C(1) 1.294(4), N(2)−C(14) 1.360(3), N(3)−N(4) 1.415(3), N(3)−C(17) 1.321(3), N(4)−C(30) 1.288(4), C(14)−C(15) 1.413(4), C(15)−C(16) 1.535(3), C(16)−C(17) 1.447(4).

The Zn-complex **7** shows a rare azaallyl coordination mode (μ_2-η^1:η^1).[13] The π-electrons within the azaallyl N(3)−C(17)−C(16) and the azaallyl N(2)−C(14)−C(15) are almost perfectly delocalized. The Zn−C bond lengths (2.096−2.195 Å) in **7** are elongated compared to the corresponding values in zinc complexes with η^1 bonded allylic ligands (1.969−2.031 Å).[14] The Zn−N bond lengths (2.006−2.008 Å) in **7** are comparable with the reported Zn−N bond length (2.003 Å) in the NCN′ chelating binding mode.[12i] Thus, the azaallyl ligands of **7** are bonded to the Zn(1) and Zn(2) atoms in a bridging *trans*-μ_2-η^1:η^1 fashion. This is the first example of an azaallyl zinc compound showing such a coordination mode.

In conclusion, an efficient synthesis of 1-imino-pyrrole derivatives has been developed from the reaction between 1,4-dilithio-1,3-dienes and diaryl diazomethanes. It is a rare example demonstrating that diaryldiazomethane acts as an electrophile. The expected effect of cooperative stabilization by 1,4-dilithio-1,3-dienes works well. The azaallyl zinc compound **7** with the bridging *trans*-μ_2-η^1:η^1 coordination mode, generated from the dilithio imtermediate **2a** with $ZnCl_2$, is of further synthetic interest.

Acknowledgment. This paper is dedicated to Professor Teruaki Mukaiyama in celebration of the 40th anniversary of the Mukaiyama aldol reaction. This work was supported by the Natural Science Foundation of China, and the Major State Basic Research Development Program (2011CB808700).

Supporting Information Available. Experimental details; X-ray data for **3e** (CCDC-917412), **4** (CCDC-917411), **5** (CCDC 945229), and **7** (CCDC 945228); scanned NMR spectra of all new products. This material is available free of charge via the Internet at http://pubs.acs.org.

The authors declare no competing financial interest.

---

(14) (a) Yasuda, H.; Ohnuma, Y.; Nakamura, A.; Kai, Y.; Yasuka, N.; Kasai, N. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1101. (b) Ernst, R. D.; Freeman, J. W.; Swepston, P. N.; Wilson, D. R. *J. Organomet. Chem.* **1991**, *402*, 17.