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Tertiary Amines as Synthetic Equivalents of Vinyl Cations: Zinc Bromide Promoted Coupling of Propargylamines with α-Isocyanoacetamides to Give 2,4,5-Trisubstituted Oxazoles Initiated by an Internal Redox Process

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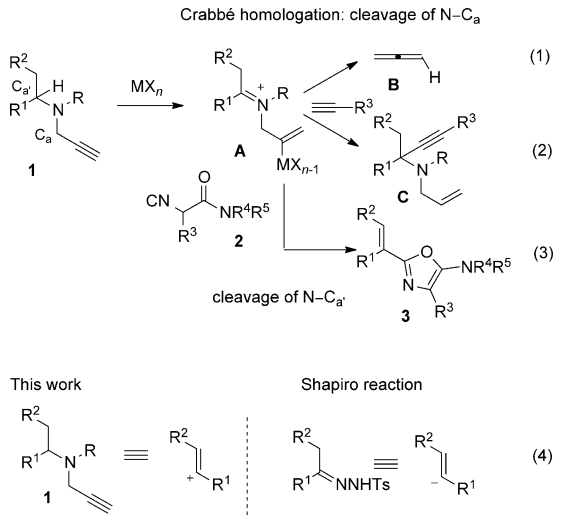
The Crabbé homologation allows the synthesis of allenes from in situ generated propargylamines through a 1,5-hydride shift/1,2-elimination sequence (Equation (1), Scheme 1).[1] Initially developed for the synthesis of monosubstituted allenes, reaction conditions have now been established allowing access to di- and trisubstituted allenes.[2–3] A recent important discovery came from the research group of Nakamura who reported the first examples of intermolecular nucleophilic trapping of incipient iminium intermediate **A** for the synthesis of N-tethered 1,6-enynes **C** (Equation (2), Scheme 1).[4] Although there is recent interest in the domino 1,5-hydride shift/cyclization of zwitterionic intermediates,[5] examples of using an external nucleophile to trap the cationic intermediate resulting from intramolecular hydride shift are rare.[4,6–7] We report herein that isonitriles can interrupt the Crabbé homologation leading to 2-vinyl oxazoles **3** by an unprecedented domino 1,5-hydride shift/intermolecular trapping/cyclization/elimination sequence (Equation (3), Scheme 1). In this transformation, propargylamine **1** acts formally as a synthetic equivalent of a vinyl cation.[8] We note that a vinyl anion can be easily generated from tosylhydrazone in the presence of a strong base and is widely used in organic synthesis (the Shapiro reaction; Equation (4), Scheme 1).[9] However, to the best of our knowledge, the use of tertiary aliphatic amines as vinyl cation synthetic equivalents has not yet been reported.[10]



Scheme 1. Tertiary propargylamine as a synthetic equivalent of a vinyl cation: synthesis of 2-vinyl oxazoles.

We began our studies by investigating the reaction between *N*,*N*-diisopropylprop-2-yn-1-amine (**1a**) and α-isocyanoacetamide **2a**[11] in the presence of different metal salts. It was found that neither CuI nor $Zn(OTf)_2$ was able to promote the reaction. However, in the presence of a catalytic amount of $ZnBr_2$, the reaction produced a small amount of unexpected 2-vinyl oxazole **3a** (Table 1).[12] Intrigued by the mechanism of this unprecedented reaction and the importance of oxazoles in natural product and medicinal chemistry,[13] the reaction conditions were optimized by varying the amount of $ZnBr_2$, the solvent, the temperature, and the additives. Using the optimized reaction conditions—**1a** (1.0 equiv, 0.1 M), **2a** (2.0 equiv), $ZnBr_2$ (1.5 equiv), toluene, reflux—oxazole **3a** was isolated in 74% yield (Table 1). The use of a stoichiometric amount of $ZnBr_2$ was necessary for the success of this transformation, the requirement originating from product inhibition, oxazoles being known to coordinate strongly to Zn^{2+}.[14]

Using **2a** as the isocyanide component, the scope of the tertiary amine was first examined (Table 1). In the case of *N*-(pentan-3-yl)-*N*-(prop-2-yn-1-yl)pentan-3-amine (**1b**), a mixture of two stereoisomers was obtained in 74% yield in favor of the *Z* isomer. With *N*-(*sec*-butyl)-*N*-(prop-2-yn-1-yl)butan-2-amine (**1c**), less-substituted terminal olefin **3c** was formed together with a small amount of internal alkene **3c′** (**3c**/**3c′**, 10:1). Therefore, the regioselectivity of olefin formation follows the Hofmann rule. Dicycloalkylpropargylamines **1d**–**1g** participated in this reaction without problems to afford the corresponding products, namely, cyclopent-1-en-1-yl, cyclohex-1-en-1-yl, cyclohept-1-en-1-yl, and cyclooct-1-en-1-yl oxazoles (**3d**–**g**), respectively, in good yields. Notably, the reaction also worked with *N*-methyl-propargylamines **1h**–**1j**. In accordance with the notion that a tertiary C–H bond is a better hydride donor than a primary C–H

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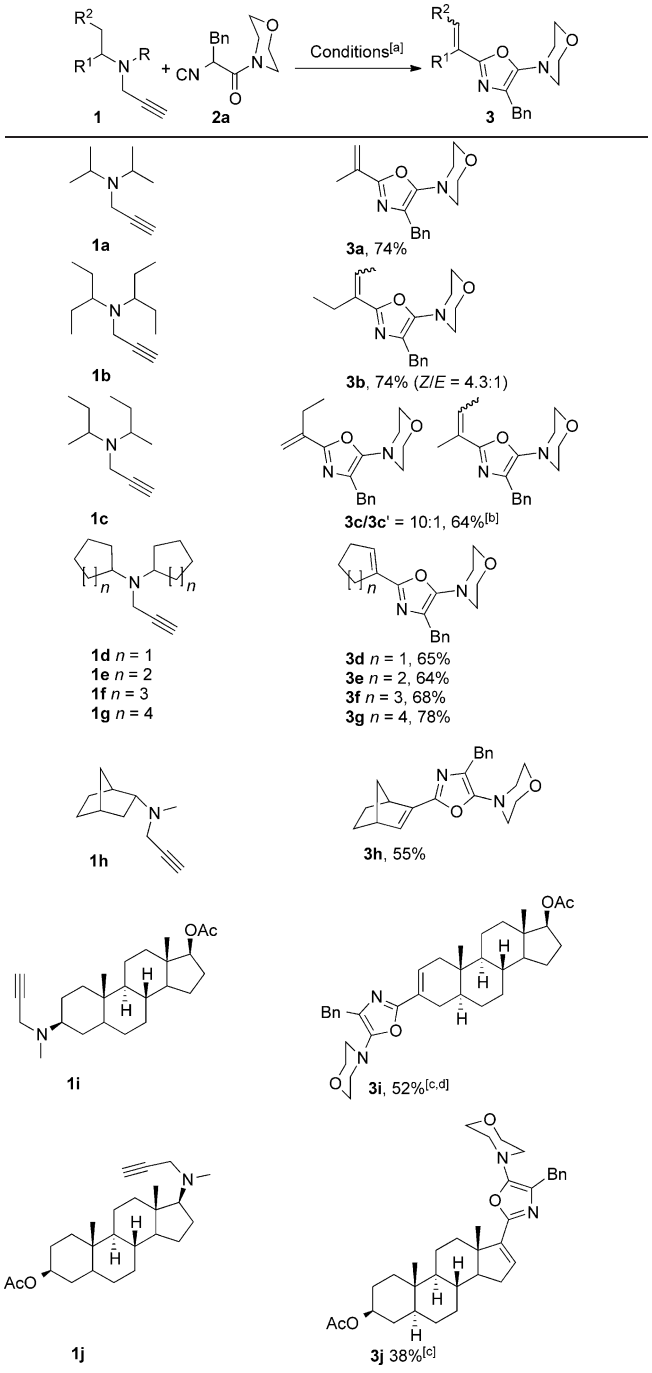
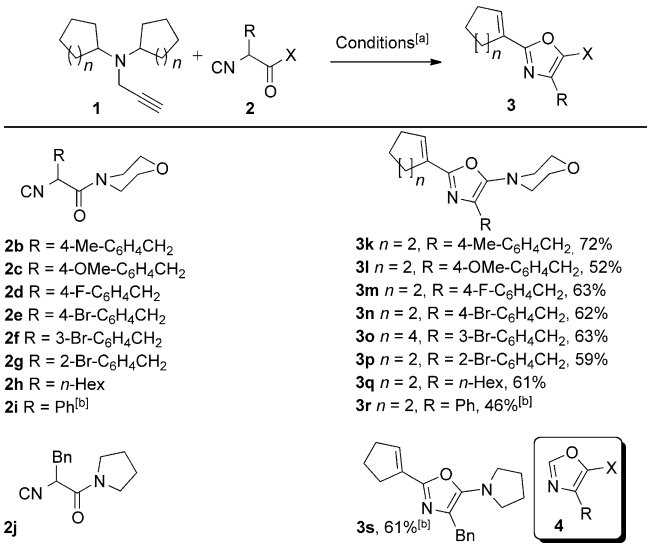
Table 1. Scope of the propargylamine component.



[a] **1** (0.10 mmol, 0.1 M), **2a** (0.20 mmol), $ZnBr_2$ (0.15 mmol), toluene 100 °C. [b] Reactions were carried out with 3.0 equiv of the isocyanoacetamide **2a** and 1.5 equiv of $ZnBr_2$. [c] Reactions were carried out with 5.0 equiv of the isocyanoacetamide **2a** and 5.0 equiv of $ZnBr_2$. [d] Together with an inseparable 3,4-unsaturated isomer (5:1).

bond, the α-hydrogen atom of the more substituted N-alkyl group was transferred preferentially, thus providing more functionalized alkenes **3h**–**3j** exclusively. Notably, oxazoles **3i** and **3j**, which incorporate a steroid skeleton and are known to be potent $P450_{17\alpha}$ inhibitors, were prepared with ease.[15]

Table 2. Scope of the α-isocyanoacetamide component.



[a] **1** (0.10 mmol, 0.1 M), **2** (0.20 mmol), $ZnBr_2$ (0.15 mmol), toluene, 100 °C. [b] Reactions were carried out with 3.0 equiv of the isocyanoacetamide, either **2i** or **2j**, and 1.5 equiv of $ZnBr_2$.

The scope of α-isocyanoacetamides **2** was next examined (Table 2). Benzyl, alkyl, and aryl substituents with different electronic properties at the α position of α-isocyanoacetamides **2** were well tolerated, thus affording oxazoles **3k**–**3r** in good yields. However, a large excess (3.0 equiv) of **2i** and **2j** was required owing to their facile ring-chain isomerization leading to C-2 unsubstituted 5-aminooxazole **4**. The reaction was also attempted with methyl α-(4-nitrophenyl)-α-isocyanoacetate,[16] but no desired product was isolated.

It is known that the structure of the secondary amine influences the efficiency of the Crabbé homologation,[17] although it was previously impossible to quantitatively evaluate the hydride-donor capability of the two N-alkyl groups. Because only one of the two N–C_{alkyl} groups in the propargylamine component was cleaved in our reaction, it provided a unique opportunity for us to quantify the hydride-transfer capability of the N-alkyl groups by an internal competition experiment. Two propargylamines bearing two different α-tertiary alkyl groups (**1k** and **1l**) were therefore prepared. Whereas the reaction of **1k** with **2a** under the standard reaction conditions afforded cyclohex-1-en-1-yl oxazole **3e** and isopropenyl oxazole **3a** in a 6:1 ratio, the reaction of **1l** with **2a** afforded 2-(cyclopent-1-en-1-yl)oxazole **3d** and 2-(cyclohex-1-en-1-yl) oxazole **3e** in 60% and 14% yields (**3d**/**3e**, 4.3:1), respectively (Scheme 2). Therefore, the hydride-donor ability of α-tertiary alkyl groups was determined to be as follows: cyclopentyl > cyclohexyl > isopropyl.

To gain mechanistic insights on this transformation, deuterated substrates [D_1]-**5**, [D_2]-**5**, **6**, and **7** were prepared. Reaction of [D_1]-**5** with **2a** followed by acylation produced *N*-allyl-*N*-cyclohexyl acetamide **8a** and **8a′** with 24% deuterium incorporation ($K_H/K_D = 3:1$) at the terminal carbon of olefin **8a'** (Equation (1), Scheme 3). No doubly deuterated allylamine was detected by mass spectrometry, thus indicat-

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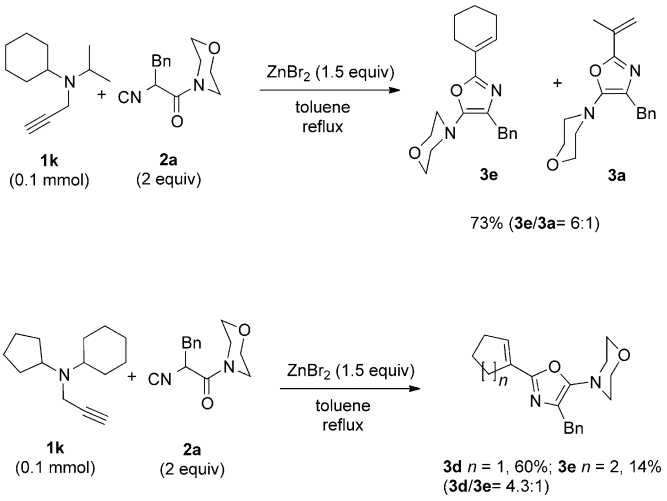
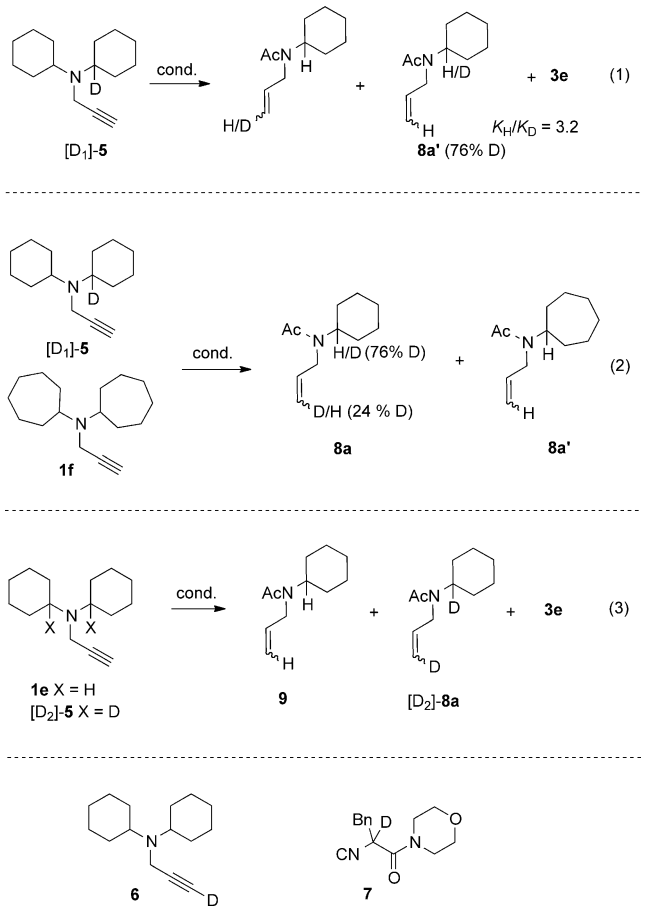


Scheme 2. Competitive hydride-transfer reactions.

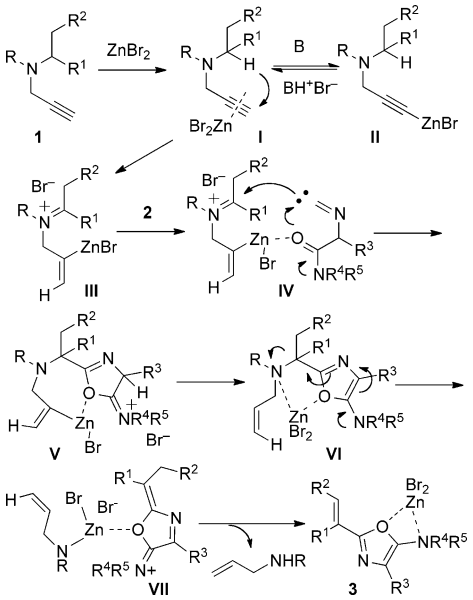


Scheme 3. Deuterium labeling experiments. Conditions: i) **2a** (2.0 equiv), $ZnBr_2$ (1.5 equiv), toluene, reflux; ii) Ac_2O, Et_3N, CH_2Cl_2.

ing that the redox process occurred exclusively in an intramolecular fashion. Further evidence in line with this conclusion was obtained by a crossover experiment involving mixing equimolar amounts of $[D_1]$-**5** and **1f** with **2a** (Equation (2), Scheme 3). An intermolecular competition experiment involving **1e** and $[D_2]$-**5** with **2a** provided a KIE of 2:1 (Equation (3), Scheme 3). This result indicated that the 1,5-hydride shift was the rate-limiting step of the domino process. Finally, deuterium was lost to a great extent (95%) when compound **6** was submitted to the above reaction conditions and no deuterium transfer from α-D-α-isocyanoacetamide **7** to propargylamine **1e** was observed (reaction conditions: i) **1e** (1.0 equiv), $ZnBr_2$ (1.5 equiv), toluene, reflux; ii) Ac_2O, Et_3N, CH_2Cl_2).

Two additional control experiments were performed as follows. Firstly, reaction of authentic 5-aminooxazole **4a** (R = Bn, X = morpholinyl) with **1e** under standard reaction conditions did not produce **3e**. Secondly, heating a toluene solution of **2a** in the presence of $ZnBr_2$ (1.0 equiv) followed by addition of a solution of **1e** and $ZnBr_2$ (0.5 equiv) also failed to produce vinyl oxazole **3a**. These results indicated that neither oxazole **4a** nor the corresponding oxazol-2-yl zinc bromide was involved in the formation of 2-vinyl oxazole.

Based on the results of these control experiments, a possible reaction pathway leading to vinyl oxazoles **3** from propargylamines **1** and α-isocyano acetamides **2** was proposed as shown in Scheme 4. Formation of alkyne–$ZnBr_2$ π complex **I**



Scheme 4. Possible reaction pathway leading to **3**.

could lead to zinc acetylide **II**, thus accounting for the loss of deuterium in **6**, as observed in the control experiment. Alternatively, the formation of **I** could trigger the 1,5-hydride shift, thus leading to iminium ion **III**. Coordination of vinyl zinc bromide to isocyanoacetamide to give **IV** would facilitate the nucleophilic addition of isocyanide to the iminium ion, thus leading to a nitrilium intermediate that could cyclize to **V**.[18] It is apparent that this step outpaced the elimination of imine, which leads to allene and is the normal Crabbé reaction pathway. We assumed that the formation of

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complex **IV** was important for the success of the reaction. In fact, control experiments indicated that reaction of **2a** with cyclohexanone and allylcyclohexylamine under our optimized reaction conditions failed to produce vinyl oxazole **3e**. Aromatization of **V** could then afford zinc bromide chelated oxazole **VI**. The coordination of the tertiary allylamine to zinc bromide could also make it a potentially good leaving group. Assisted by the lone pair of the 5-dialkylamino group, 1,6-elimination of allylamine could occur to provide **VII** that, upon proton transfer and isomerization, would be converted into 5-amino-2-vinyloxazole **3**, most probably coordinated to $ZnBr_2$.

In summary, we developed a novel synthesis of 2-vinyl-5-aminooxazoles by a $ZnBr_2$-promoted reaction between tertiary propargylamines and α-isocyanoacetamides. The reaction went through an unprecedented 1,5-hydride shift/intermolecular nucleophilic addition/cyclization/elimination sequence. The propargylamine formally serves as a synthetic equivalent of a vinyl cation. The present domino process represents a rare example of an interrupted Crabbé reaction wherein the in situ generated iminium salt is trapped by an external nucleophile.

Experimental Section

General procedure: A suspension of propargylamine **1a** (0.1 mmol, 0.1 M), isocyanoacetamide **2a** (0.2 mmol, 2.0 equiv), and zinc bromide (0.15 mmol, 1.5 equiv) in toluene (1 mL) was heated to reflux under Ar. After being stirred for 6 h, the reaction mixture was cooled to room temperature and was quenched by addition of aqueous K_2CO_3. The aqueous phase was extracted with CH_2Cl_2. The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The crude material was purified by flash chromatography (silica gel; petroleum ether/AcOEt, 93:7) to give desired oxazole **3a** (21.0 mg, 74% yield). ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 7.35$–7.24 (m, 4H), 7.23–7.16 (m, 1H), 5.80–5.75 (m, 1H), 5.27 (quintet, $J = 1.4$ Hz, 1H), 3.87 (s, 2H), 3.74–3.69 (m, 4H), 3.05–2.97 (m, 4H), 2.12 (dd, $J = 1.4$, 1.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 156.9$, 151.6, 139.6, 131.9, 128.5, 128.3, 126.1, 125.3, 116.3, 66.8, 50.8, 32.0, 18.7; IR (ATR-IR: $\tilde{\nu} = 2959$, 2916, 2853, 1652, 1621, 1453, 1116, 917 cm^{-1}; HRMS (ESI): m/z calcd for $C_{17}H_{21}N_2O_2^+$: 285.1598 [M+H$^+$]; found: 285.1595.

Acknowledgements

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Keywords: Crabbé homologation · domino processes · isonitriles · oxazoles · redox processes

[1] a) P. Crabbé, H. Fillion, D. André, J.-L. Luche, *J. Chem. Soc. Chem. Commun.* **1979**, 859–860; b) H. Fillion, D. André, J.-L. Luche, *Tetrahedron Lett.* **1980**, *21*, 929–930; c) S. Searles, Y. Li, B. Nassim, M.-T. R. Lopes, P. T. Tran, P. Crabbé, *J. Chem. Soc. Perkin Trans. 1* **1984**, 747–751.

[2] For recent examples, see: a) J. Kuang, S. Ma, *J. Am. Chem. Soc.* **2010**, *132*, 1786–1787; b) S. Kitagaki, M. Komizu, C. Mukai, *Synlett* **2011**, 1129–1132; c) J. Kuang, H. Luo, S. Ma, *Adv. Synth. Catal.* **2012**, *354*, 933–944; d) M. Periasamy, N. Sanjeevakumar, M. Dalai, R. Gurubrahamam, P. O. Reddy, *Org. Lett.* **2012**, *14*, 2932–2935; e) J. Ye, S. Li, B. Chen, W. Fan, J. Kuang, J. Liu, Y. Liu, B. Miao, B. Wan, Y. Wang, X. Xie, Q. Yu, W. Yuan, S. Ma, *Org. Lett.* **2012**, *14*, 1346–1349; f) J. Ye, W. Fan, S. Ma, *Chem. Eur. J.* **2013**, *19*, 716–720; for a review, see: g) S. Yu, S. Ma, *Chem. Commun.* **2011**, *47*, 5384–5418.

[3] For variations of the Crabbé homologation, see: a) H. Nakamura, T. Kamakura, M. Ishikura, J.-F. Biellmann, *J. Am. Chem. Soc.* **2004**, *126*, 5958–5959; b) V. K.-Y. Lo, M.-K. Wong, C.-M. Che, *Org. Lett.* **2008**, *10*, 517–519; c) V. K.-Y. Lo, C.-Y. Zhou, M.-K. Wong, C.-M. Che, *Chem. Commun.* **2010**, *46*, 213–215; d) B. Bolte, Y. Odabachian, F. Gagosz, *J. Am. Chem. Soc.* **2010**, *132*, 7294–7296.

[4] T. Sugiishi, H. Nakamura, *J. Am. Chem. Soc.* **2012**, *134*, 2504–2507.

[5] For selected recent examples, see: a) S. J. Pastine, K. M. McQuaid, D. Sames, *J. Am. Chem. Soc.* **2005**, *127*, 12180–12181; b) C. Zhang, C. K. De, R. Mak, D. Seidel, *J. Am. Chem. Soc.* **2008**, *130*, 416–417; c) L. Zheng, F. Yang, Q. Dang, X. Bai, *Org. Lett.* **2008**, *10*, 889–892; d) P. A. Vadola, D. Sames, *J. Am. Chem. Soc.* **2009**, *131*, 16525–16528; e) Y. K. Kang, S. M. Kim, D. Y. Kim, *J. Am. Chem. Soc.* **2010**, *132*, 11847–11849; f) I. D. Jurberg, Y. Odabachian, F. Gagosz, *J. Am. Chem. Soc.* **2010**, *132*, 3543–3552; g) K. Mori, T. Kawasaki, S. Sueoka, T. Akiyama, *Org. Lett.* **2010**, *12*, 1732–1735; h) G. Zhou, J. Zhang, *Chem. Commun.* **2010**, *46*, 6593–6595; i) M. Alajarin, M. Marin-Luna, A. Vidal, *Adv. Synth. Catal.* **2011**, *353*, 557–562; j) B. Bolte, F. Gagosz, *J. Am. Chem. Soc.* **2011**, *133*, 7696–7699; k) K. Mori, S. Sueoka, T. Akiyama, *J. Am. Chem. Soc.* **2011**, *133*, 2424–2426; l) J. Barluenga, R. Sigüeiro, R. Vicente, A. Ballesteros, M. Tomás, M. A. Rodríguez, *Angew. Chem.* **2012**, *124*, 10523–10527; *Angew. Chem. Int. Ed.* **2012**, *51*, 10377–10381; m) D.-F. Chen, Z.-Y. Han, Y.-P. He, J. Yu, L.-Z. Gong, *Angew. Chem.* **2012**, *124*, 12473–12476; *Angew. Chem. Int. Ed.* **2012**, *51*, 12307–12310; n) L. Chen, L. Zhang, J. Lv, J.-P. Cheng, S. Luo, *Chem. Eur. J.* **2012**, *18*, 8891–8895; o) X. Gao, V. Gaddam, E. Altenhofer, R. R. Tata, Z. Cai, N. Yongpruksa, A. K. Garimallaprabhakaran, M. Harmata, *Angew. Chem.* **2012**, *124*, 7122–7125; *Angew. Chem. Int. Ed.* **2012**, *51*, 7016–7019; p) Z.-W. Jiao, S.-Y. Zhang, C. He, Y.-Q. Tu, S.-H. Wang, F.-M. Zhang, Y.-Q. Zhang, H. Li, *Angew. Chem.* **2012**, *124*, 8941–8945; *Angew. Chem. Int. Ed.* **2012**, *51*, 8811–8815; q) K. Mori, T. Kawasaki, T. Akiyama, *Org. Lett.* **2012**, *14*, 1436–1439; r) P. A. Vadola, I. Carrera, D. Sames, *J. Org. Chem.* **2012**, *77*, 6689–6702; s) X.-F. Xia, X.-R. Song, N. Wang, H.-L. Wei, X.-Y. Liu, Y.-M. Liang, *RSC Adv.* **2012**, *2*, 560–565; t) C. Ma, Z.-J. Jia, J.-X. Liu, Q.-Q. Zhou, L. Dong, Y.-C. Chen, *Angew. Chem.* **2013**, *125*, 982–985; *Angew. Chem. Int. Ed.* **2013**, *52*, 948–951.

[6] For an example of intermolecular nucleophilic trapping of in situ generated 1,3-dipoles, see: D. Das, A. X. Sun, D. Seidel, *Angew. Chem.* **2013**, *125*, 3853–3857; *Angew. Chem. Int. Ed.* **2013**, *52*, 3765–3769.

[7] For a sequence involving a 1,5-hydride shift, cyclization, and ring opening by an external nucleophile, see: I. D. Jurberg, B. Peng, E. Wöstefeld, M. Wasserloos, N. Maulide, *Angew. Chem.* **2012**, *124*, 1986–1989; *Angew. Chem. Int. Ed.* **2012**, *51*, 1950–1953.

[8] For the development of propargylamine as a donor of acetylide, see: T. Sugiishi, A. Kimura, H. Nakamura, *J. Am. Chem. Soc.* **2010**, *132*, 5332–5333.

[9] R. H. Shapiro, *Org. React.* **1976**, *23*, 405.

[10] For the development of intramolecular vinyl transfer of *N*-benzyl-*N*′-alkenyl urea in the presence of a strong base, see: J. Lefranc, A. M. Fournier, G. Mingat, S. Herbert, T. Marcelli, J. Clayden, *J. Am. Chem. Soc.* **2012**, *134*, 7286–7289.

[11] a) J. Zhu, *Eur. J. Org. Chem.* **2003**, 1133–1144; b) A. Dömling, *Chem. Rev.* **2006**, *106*, 17–89; c) L. El Kaim, L. Grimaud, *Tetrahedron* **2009**, *65*, 2153–2171; d) A. V. Gulevich, A. G. Zhdanko, R. V. Orru, V. G. Nenajdenko, *Chem. Rev.* **2010**, *110*, 5235–5331.

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[12] For recent examples of oxazole synthesis, see: a) S. X. Wang, M. X. Wang, D. X. Wang, J. Zhu, *Org. Lett.* **2007**, *9*, 3615–3618; b) N. Elders, E. Ruijter, F. J. J. de Kanter, R. V. A. Orru, *Chem. Eur. J.* **2008**, *14*, 4961–4973; c) T. Yue, M.-X. Wang, D.-X. Wang, G. Masson, J. Zhu, *J. Org. Chem.* **2009**, *74*, 8396–8399; d) J. Zhang, P.-Y. Coqueron, J.-P. Vors, M. A. Ciufolini, *Org. Lett.* **2010**, *12*, 3942–3945; e) J. Wu, W. Chen, M. Hu, H. Zou, Y. Yu, *Org. Lett.* **2010**, *12*, 616–619; f) R. Mossetti, T. Pirali, G. C. Tron, J. Zhu, *Org. Lett.* **2010**, *12*, 820–823; g) J. P. Weyrauch, A. S. K. Hashmi, A. Schuster, T. Hengst, S. Schetter, A. Littmann, M. Rudolph, M. Hamzic, J. Visus, F. Rominger, W. Frey, J. W. Bats, *Chem. Eur. J.* **2010**, *16*, 956–963; h) I. Cano, E. Alvarez, M. C. Nicasio, P. J. Pérez, *J. Am. Chem. Soc.* **2011**, *133*, 191–193; i) P. W. Davies, A. Cremonesi, L. Dumitrescu, *Angew. Chem.* **2011**, *123*, 9093–9097; *Angew. Chem. Int. Ed.* **2011**, *50*, 8931–8935; j) Y. Li, X. Xu, J. Tan, C. Xia, D. Zhang, Q. Liu, *J. Am. Chem. Soc.* **2011**, *133*, 1775–1777; k) C. Lalli, M. J. Bouma, D. Bonne, G. Masson, J. Zhu, *Chem. Eur. J.* **2011**, *17*, 880–889; l) T. Lechel, M. Gerhard, D. Trawny, B. Brusilowskij, L. Schefzig, R. Zimmer, D. Lentz, C. A. Schalley, H.-U. Reissig, *Chem. Eur. J.* **2011**, *17*, 7480–7491; m) S. V. Kumar, B. Saraiah, N. C. Misra, H. Ila, *J. Org. Chem.* **2012**, *77*, 10752–10763; n) C. L. Zhong, B. Y. Tang, P. Yin, Y. Chen, L. He, *J. Org. Chem.* **2012**, *77*, 4271–4277; o) L. El Kaïm, L. Grimaud, P. Patil, *Synlett* **2012**, 1361–1363; p) Y. Luo, K. Ji, Y. Li, L. Zhang, *J. Am. Chem. Soc.* **2012**, *134*, 17412–17415; q) X. Xu, P. Y. Zavalij, W. Hu, M. P. Doyle, *Chem. Commun.* **2012**, *48*, 11522–11524; r) A. Y. Shaw, Z. Xu, C. Hulme, *Tetrahedron Lett.* **2012**, *53*, 1998–2000; s) Z. Xu, C. Zhang, N. Jiao, *Angew. Chem.* **2012**, *124*, 11529–11532; *Angew. Chem. Int. Ed.* **2012**, *51*, 11367–11370; t) X. Li, L. Huang, H. Chen, W. Wu, H. Huang, H. Jiang, *Chem. Sci.* **2012**, *3*, 3463–3467.

[13] a) P. Wipf, *Chem. Rev.* **1995**, *95*, 2115–2134; b) V. S. C. Yeh, *Tetrahedron* **2004**, *60*, 11995–12042; c) Z. Jin, *Nat. Prod. Rep.* **2011**, *28*, 1143–1191; d) J. Zhang, P.-Y. Coqueron, M. A. Ciufolini, *Heterocycles* **2011**, *82*, 949–980.

[14] a) R. C. Jones, M. W. Chojnacka, J. W. Quail, M. G. Gardiner, A. Decken, B. F. Yates, R. A. Gossage, *Dalton Trans.* **2011**, *40*, 1594–1600; b) M.-T. Chen, C.-T. Chen, *Dalton Trans.* **2011**, *40*, 12886–12894.

[15] N. Zhu, Y. Ling, X. Lei, V. Handratta, A. M. H. Brodie, *Steroids* **2003**, *68*, 603–611.

[16] D. Bonne, M. Dekhane, J. Zhu, *Angew. Chem.* **2007**, *119*, 2537–2540; *Angew. Chem. Int. Ed.* **2007**, *46*, 2485–2488.

[17] a) H. Nakamura, M. Ishikura, T. Sugiishi, T. Kamakura, J.-F. Biellmann, *Org. Biomol. Chem.* **2008**, *6*, 1471–1477; b) J. Kuang, S. Ma, *J. Org. Chem.* 2009, 74, 1763–1765.

[18] a) P. Janvier, X. Sun, H. Bienaymé, J. Zhu, *J. Am. Chem. Soc.* **2002**, *124*, 2560–2567; b) R. Gámez-Montaño, E. González-Zamora, P. Potier, J. Zhu, *Tetrahedron* **2002**, *58*, 6351–6358; c) A. Fayol, J. Zhu, *Org. Lett.* **2004**, *6*, 115–118; d) A. Fayol, J. Zhu, *Org. Lett.* **2005**, *7*, 239–242; e) S. Wang, M.-X. Wang, D.-X. Wang, J. Zhu, *Eur. J. Org. Chem.* **2007**, 4076–4080.

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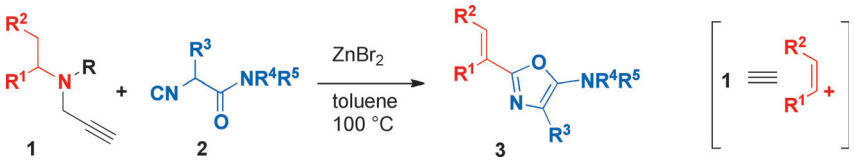
Coupling Reactions



Crabée interrupted: Propargylamines **1** react with α-isocyanoacetamides **2** in the presence of zinc bromide to afford vinyl oxazoles **3**. The transformation, wherein the propargylamine acts as a vinyl cation synthetic equivalent, involves a domino sequence incorporating a 1,5-hydride shift, intermolecular trapping/cyclization, and a 1,6-elimination (see scheme).

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