ChemPubSoc Europe

DOI: 10.1002/chem.201602792

CHEMISTRY
A European Journal
Communication

Synthetic Methods

Enantioselective and Regiodivergent Functionalization of *N*-Allylcarbamates by Mechanistically Divergent Multicatalysis

Edward Richmond,[a] Ismat Ullah Khan,[a, b] and Joseph Moran*[a]

Abstract: A pair of mechanistically divergent multicatalytic reaction sequences has been developed consisting of nickel-catalyzed isomerization of *N*-allylcarbamates and subsequent phosphoric-acid-catalyzed enantioselective functionalization of the resulting intermediates. By appropriate selection of reaction partners, in situ generated imines and ene-carbamates are mechanistically partitioned to yield opposing functionalized products. Formal α-functionalization to give protected α-arylamines is achieved upon enantioselective Friedel–Crafts reaction with arene nucleophiles, whereas formal β-functionalization is achieved upon reaction with diarylimine electrophiles in an enantioselective Povarov-[4+2] cycloaddition.

The complex catalytic reaction networks of biosynthesis have long provided inspiration for chemists looking for efficient approaches to increasing molecular complexity. On one hand, nature is capable of achieving mechanistically distinct divergent catalytic reactions from a single biosynthetic intermediate, a strategy increasingly copied by chemists interested in diversity-oriented synthesis.[1] On the other hand, nature uses mutually compatible enzymatic catalysts to mediate multiple catalytic reactions in sequence, the inspiration for the emerging area of multicatalysis.[2,3,4] Developing abiotic catalytic chemistry that simultaneously embodies both of these aspects poses a formidable challenge. Here, we report an example of mechanistically divergent multicatalysis, in which a starting material is converted by a primary catalyst into an equilibrating mixture of two molecules possessing mechanistically distinct reactivity modes. The divergent reactivity of the intermediates is then unleashed by a secondary catalyst to yield substantial molecular diversity beginning from a common starting material and by a common set of catalysts (Figure 1). Specifically, we describe a nickel-catalyzed isomerization of *N*-allylcarbamates to an equilibrating mixture of ene-carbamates and imines, compounds that subsequently undergo Brønsted acid catalyzed nucleophilic and electrophilic reactivity, respectively.[5,6]

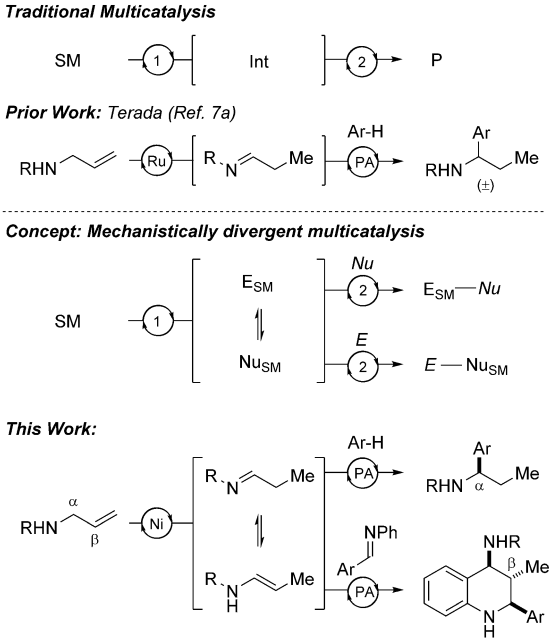


Figure 1. Traditional multicatalysis in contrast to mechanistically divergent multicatalysis and the design concept of a divergent nickel/chiral phosphoric-acid-catalyzed functionalization of *N*-allylcarbamates.

In 2008, Terada and co-workers reported a multicatalytic sequence involving ruthenium-catalyzed isomerization of *N*-allylcarbamates to imines followed by a racemic phosphoric-acid-catalyzed Friedel–Crafts reaction.[7] However, this Friedel–Crafts reaction of imines was demonstrated enantioselectively by the same research group one year prior.[8] This inconsistency highlights the non-trivial nature of developing multicatalytic sequences capable of delivering enantio-enriched products. Our interest in developing a regiodivergent enantioselective multicatalytic sequence arose from prior work on catalyst discovery by screening and deconvoluting complex mixtures of catalyst components.[9] We reasoned that robust catalytic systems discovered in such a manner would have a high likelihood of being compatible with subsequent catalytic reaction steps. In our prior investigations, it was noted that (*Z*)-to-(*E*)-olefin isomerization could be catalyzed by an in situ formed nickel/triphos complex in the presence of zinc.[10] With this information in hand, we thought that this nickel/triphos complex might also be an effective catalyst for the positional isomerization of

[a] Dr. E. Richmond, I. U. Khan, Dr. J. Moran
Institut de Science et d'Ingénierie Supramoleculaires (ISIS)
Centre International de Recherche aux Frontières de la Chimie (icFRC)
Université de Strasbourg, CNRS, 8 allée Gaspard Monge
67000, Strasbourg (France)
E-mail: moran@unistra.fr

[b] I. U. Khan
Department of Chemistry, Quaid i Azam University
Islamabad 45320 (Pakistan)

Supporting information and the ORCID number(s) for the author(s) of this article are available under http://dx.doi.org/10.1002/chem.201602792.

N-allylcarbamates,[11] and show compatibility with chiral Brønsted acid catalysts.

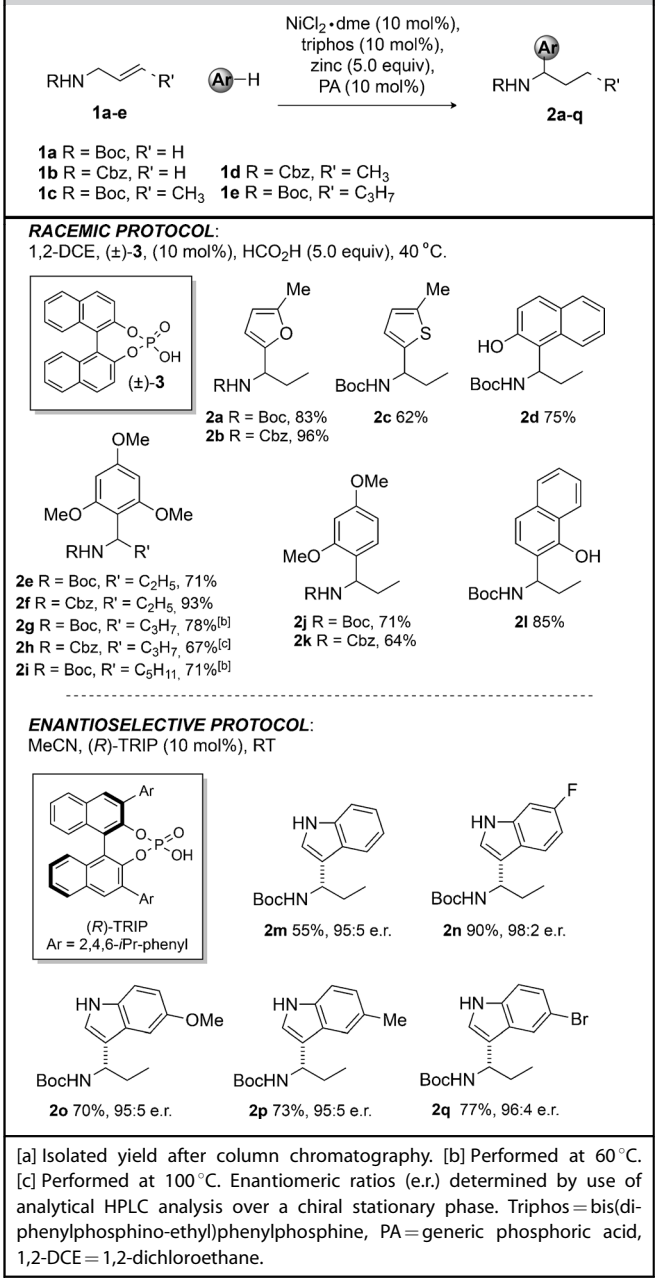
In our initial studies, treatment of *N*-allylcarbamates with a slight excess of arene, 10 mol% $NiCl_2$·dme, 10 mol% triphos, 10 mol% of the commercially available BINOL-derived phosphoric acid ((±)-**3**) with 5 equiv of zinc, and HCO_2H gave access to a range of α-aryl carbamates in good to excellent isolated yields (Table 1, racemic protocol). The developed catalytic conditions proved applicable to arylation of both *tert*-butoxycarbonyl- and carboxybenzyl-protected (Boc and Cbz, respectively) *N*-allylcarbamates with a range of electron-rich arene nucleophiles in good to excellent yields. 2-Methylfuran and 2-methylthiophene proved compatible nucleophiles (**2a**–**c**), providing the desired α-heteroaryl carbamates in excellent yields. 1,3,5-Trimethoxy- and 1,3-dimethoxybenzene proved to be excellent nucleophiles in this catalytic system, yielding the expected α-aryl carbamates **2e**–**k**.

Internal unsaturated carbamates could also be employed as starting materials with arylated products **2g**–**i**, isolated in 67–78% yield. In a survey of other aromatic nucleophiles, 1- and 2- naphthol were both well tolerated by the reaction (**2d** and **2l**, respectively). Intriguingly, it was observed that allylcarbamate isomerization occurred in the absence of formic acid when MeCN was used as solvent under an argon atmosphere.[12] Enantioselective reactivity could thus be achieved with indole nucleophiles by employing a sequential multicatalysis protocol without the necessity to isolate reaction intermediates.[13] The chiral phosphoric acid *(R)*-TRIP [*(R)*-3,3′-bis(2,4,6-triisopropylphenyl)-1,1′-binaphthyl-2,2′-diyl hydrogen phosphate], in combination with *N*-Boc allylcarbamates **1a** and **1c**, allowed the desired α-indolyl carbamates **2m**–**r** to be obtained in good yields and uniformly excellent enantioselectivities (Table 1, enantioselective protocol).

With a reliable procedure for the multicatalytic enantioselective α-functionalization of *N*-allylcarbamates established, we next sought to apply the same catalytic reaction conditions to a formal β-functionalization of *N*-allylcarbamates simply by variation of the reaction partner. Considering that Masson, Zhu, and co-workers have recently demonstrated a phosphoric-acid-catalyzed enantioselective Povarov reaction[14] between enecarbamates and imines,[15] we elected to probe the development of a multicatalytic version of this reaction using *N*-allylcarbamates as starting materials. Initial experiments employing the aforementioned reaction conditions resulted in poor yields of the expected tetrahydroquinoline product. It was found that improved yields could be obtained by reducing the formic acid equivalents and by pre-isomerization of the *N*-allylcarbamate for 1 h at 40 °C. According to the newly optimized 'sequential multicatalysis' reaction procedure, and employing racemic (±)-**3**, a range of racemic tetrahydroquinolines were prepared in good yields and good diastereoselectivities (see the Supporting Information for details of racemic scope).[16]

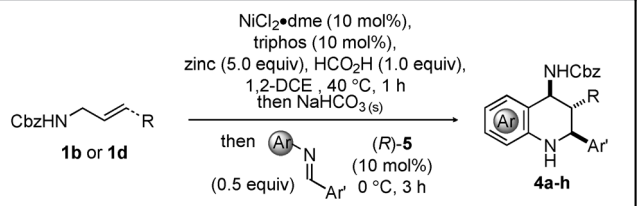
Optimization of the sequential catalysis procedure for the enantioselective preparation of tetrahydroquinolines then followed. Phosphoric acid (*R*)-**5**, similar to the optimal catalyst structure of Zhu and Masson, delivered promising initial results in combination with *N*-Cbz allylcarbamates, albeit with reduced enantiomeric excess (*ee*). This decrease was established to be caused by a competing racemic background reaction catalyzed by residual HCO_2H. Gratifyingly, simply by adding solid $NaHCO_3$ after completion of the isomerization step, a series of enantioenriched tetrahydroquinolines (**4a**–**h**) could be prepared in good yield, diastereomeric (d.r.) and enantiomeric ratios (e.r.) (Table 2). To demonstrate that no erosion of enantiocontrol occured as a consequence of the sequential catalytic protocol, tetrahydroquinoline **4f** was prepared from an isolated sample of the requisite ene-carbamate using catalyst (*R*)-**5**. Indeed, the discrete Povarov reaction and the sequential procedure furnished tetrahydroquinoline **4f** with almost identical e.r. values (92:8 vs 90:10, respectively) and comparable yields (85% over one step vs 76% over two steps, respectively).

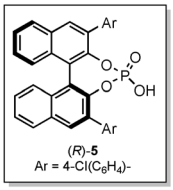
Table 1. Generality of the multicatalytic isomerization/arylation.[a]

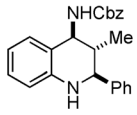


[a] Isolated yield after column chromatography. [b] Performed at 60 °C. [c] Performed at 100 °C. Enantiomeric ratios (e.r.) determined by use of analytical HPLC analysis over a chiral stationary phase. Triphos = bis(diphenylphosphino-ethyl)phenylphosphine, PA = generic phosphoric acid, 1,2-DCE = 1,2-dichloroethane.

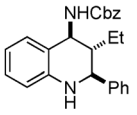
Table 2. Scope of sequential multicatalytic isomerization/enantioselective Povarov reaction.[a]



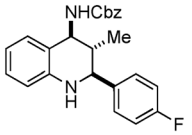




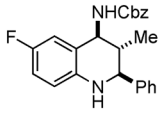
4a 78%, >10:1 d.r., 91:9 e.r.



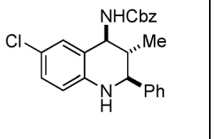
4b 67%,[b] 6:1 d.r., 73:27 e.r.



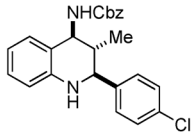
4c 77%, 5:1 d.r., 89:11 e.r.



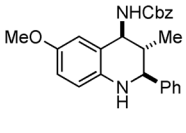
4d 56%, 4:1 d.r., 87:13 e.r.



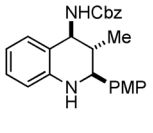
4e 63%, >15:1 d.r., 94:6 e.r.



4f 76%, 7:1 d.r., 90:10 e.r.



4g 68%, 5:1 d.r., 87:13 e.r.

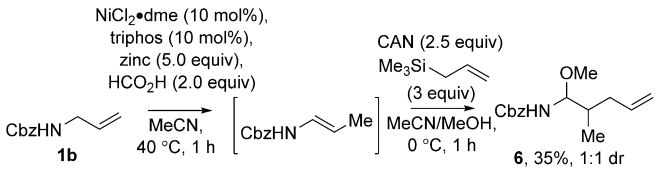


4h 50%, >10:1 d.r., 91:9 e.r.

[a] Isolated yield after column chromatography. [b] Isomerization step performed at 90 °C. d.r. values determined by ^{1}H NMR analysis of the crude reaction mixtures and e.r. determined by analytical HPLC analysis over a chiral stationary phase.

With multicatalytic conditions for the selective functionalization of *N*-allylcarbamates through both the 'iminium-' and 'enamine-' reactivity modes in hand, access to the singly occupied molecular orbital (SOMO) activation mode was next investigated.[17] After pre-isomerization according to the standard procedure reported here, treatment with ceric ammonium nitrate (CAN), allyltrimethylsilane, and MeOH gave allylated hemi-aminal **6** as a 1:1 mixture of diastereoisomers in an unoptimized 35% yield (Scheme 1).[18] This simple demonstration further emphasizes the potential to access a vista of differently functionalized products in future mechanistically divergent multicatalytic scenarios.

In summary, a multicatalysis system for the isomerization and divergent functionalization of *N*-allylcarbamates has been developed and applied in two distinct reaction manifolds: 1) α-functionalization through a Friedel–Crafts reaction and 2) formal β- functionalization through a [4+2]-Povarov cycloaddition. Divergence of the nascent ene-carbamate intermediate prior to a second catalytic event, as part of a mechanistically divergent multicatalysis scenario, allows this opposing reactivity to be realized. In addition, such a scenario has been demonstrated to be fully compatible with enantioselective catalysis. The two reaction systems described here are rare examples of the productive combination of nickel and organocatalysis.[19,20] The system involving the cycloaddition represents the first telescoped exploitation of the inherent nucleophilicity of ene-carbamates after a catalytic isomerization event. Further studies will seek to apply the concept of mechanistically divergent multicatalysis in related transformations and to achieve progressively longer sequences.



Scheme 1. Relay isomerization/allylation through a SOMO activation mode.

Acknowledgements

This work was supported in part by grants from LabEx CSC and the Marie Curie Actions FP7-PEOPLE Program (CIG-2012-326112). E.R. and I.U.K thank the Leverhulme Trust and the HEC-Pakistan/French Embassy for fellowships, respectively.

Keywords: Brønsted acids · carbamates · imines · isomerization · multicatalysis · nickel

[1] For selected examples, see: a) N. Kumagai, G. Muncipinto, S. L. Schreiber, *Angew. Chem. Int. Ed.* **2006**, *45*, 3635 – 3638; *Angew. Chem.* **2006**, *118*, 3717 – 3720; b) L. A. Marcaurelle, *J. Am. Chem. Soc.* **2010**, *132*, 16962 – 16976; c) G. Valot, J. Garcia, V. Duplan, C. Serba, S. Barluenga, N. Winssinger, *Angew. Chem. Int. Ed.* **2012**, *51*, 5391 – 5394; *Angew. Chem.* **2012**, *124*, 5487 – 5490; d) B. R. Balthaser, M. C. Maloney, A. B. Beeler, J. A. Porco Jr., J. K. Snyder, *Nat. Chem.* **2011**, *3*, 969 – 973; e) H. S. G. Beckmann, F. Nie, C. E. Hagerman, H. Johansson, Y. S. Tan, D. Wilcke, D. R. Spring, *Nat. Chem.* **2013**, *5*, 861 – 867; f) B. M. Ibbeson, L. Laraia, E. Alza, C. J. O'Connor, Y. S. Tan, H. M. L. Davies, G. McKenzie, A. R. Venkitaraman, D. R. Spring, *Nat. Commun.* **2014**, *5*, 3155.

[2] For recent reviews focusing on synergistic catalysis, see: a) L. M. Ambrosini, T. H. Lambert, *ChemCatChem* **2010**, *2*, 1373 – 1380; b) S. P. Simonovich, J. F. Van Humbeck, D. W. C. MacMillan, *Chem. Sci.* **2012**, *3*, 58 – 61; c) A. E. Allen, D. W. C MacMillan, *Chem. Sci.* **2012**, *3*, 633 – 658; d) Y. Deng, S. Kumar, H. Wang, *Chem. Commun.* **2014**, *50*, 4272 – 4284; e) M. N. Hopkinson, B. Sahoo, J.-L. Li, F. Glorius, *Chem. Eur. J.* **2014**, *20*, 3874 – 3886. For selected examples, see: f) I. Ibrahem, A. Córdova, *Angew. Chem. Int. Ed.* **2006**, *45*, 1952 – 1956; *Angew. Chem.* **2006**, *118*, 1986 – 1990; g) D. Raup, B. Cardinal-David, D. Holte, K. A. Scheidt, *Nat. Chem.* **2010**, *2*, 766; h) D. A. Nicewicz, D. W. C. MacMillan, *Science* **2008**, *322*, 77 – 80; i) D. A. Nagib, M. E. Scott, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2009**, *131*, 10875 – 10877; j) B. M. Trost, X. Luan, *J. Am. Chem. Soc.* **2011**, *133*, 1706 – 1709; k) S. Krautwald, D. Sarlah, M. A. Schafroth, E. M. Carreira, *Science* **2013**, *340*, 1065 – 1068.

[3] For reviews focusing on relay or sequential catalysis, see: a) J.-C. Wasilke, S. J. Obrey, R. T. Baker, G. C. Bazan, *Chem. Rev.* **2005**, *105*, 1001 – 1020; b) J. M. Lee, Y. Na, H. Han, S. Chang, *Chem. Soc. Rev.* **2004**, *33*, 302 – 312; c) Z.-P. Yang, W. Zhang, S.-L. You, *J. Org. Chem.* **2014**, *79*, 7785 – 7798; d) C. M. R. Volla, I. Atodiresei, M. Rueping, *Chem. Rev.* **2014**, *114*, 2390 – 2431. For selected examples, see: e) Y. Huang, A. M. Walji, C. H. Larsen, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2005**, *127*, 15051 – 15053; f) Q. Cai, Z.-A. Zhao, S.-L. You, *Angew. Chem. Int. Ed.* **2009**, *48*, 7428 – 7431; *Angew. Chem.* **2009**, *121*, 7564 – 7567; g) S. P. Lathrop, T. Rovis, *J. Am. Chem. Soc.* **2009**, *131*, 13628; h) T. A. Cernak, T. H. Lambert, *J. Am. Chem. Soc.* **2009**, *131*, 3124 – 3125.

[4] For reviews focusing on the merger of transition metal and organocatalysis, see: a) Z. Shao, H. Zhang, *Chem. Soc. Rev.* **2009**, *38*, 2745 – 2755; b) C. Zhong, X. Shi, *Eur. J. Org. Chem.* **2010**, 2999 – 3025; c) Z. Du, Z.

Shao, *Chem. Soc. Rev.* **2013**, *42*, 1337 – 1378; d) M. Rueping, R. M. Koenigs, I. Atodiresei, *Chem. Eur. J.* **2010**, *16*, 9350 – 9365; e) A. S. K. Hashmi, C. Hubbert, *Angew. Chem. Int. Ed.* **2010**, *49*, 1010 – 1012; *Angew. Chem.* **2010**, *122*, 1026 – 1028; f) C. C. J. Loh, D. Enders, *Chem. Eur. J.* **2012**, *18*, 10212 – 10225; g) L. Stegbauer, F. Sladojevich, D. J. Dixon, *Chem. Sci.* **2012**, *3*, 942 – 958; h) R. C. Wende, P. R. Schreiner, *Green Chem.* **2012**, *14*, 1821 – 1849.

[5] For reviews, see: a) S.-L. You, Q. Cai, M. Zeng, *Chem. Soc. Rev.* **2009**, *38*, 2190 – 2201; b) G. Bernadat, G. Masson, *Synlett* **2014**, *25*, 2842 – 2867.

[6] a) R. Matsubara, S. Kobayashi, *Acc. Chem. Res.* **2008**, *41*, 292 – 301; b) M. Terada, K. Soga, N. Momiyama, *Angew. Chem. Int. Ed.* **2008**, *47*, 4122; *Angew. Chem.* **2008**, *120*, 4190; c) L. Zu, H. Xie, H. Li, J. Wang, X. Yu, W. Wang, *Chem. Eur. J.* **2008**, *14*, 6333; d) M. Terada, K. Machioka, K. Sorimachi, *Angew. Chem. Int. Ed.* **2009**, *48*, 2553; *Angew. Chem.* **2009**, *121*, 2591; e) T. Honjo, R. J. Phipps, V. Rauniyar, F. D. Toste, *Angew. Chem. Int. Ed.* **2012**, *51*, 9684 – 9688; *Angew. Chem.* **2012**, *124*, 9822 – 9826; f) L. He, G. Laurent, P. Retailleau, B. Folleas, J.-L. Brayer, G. Masson, *Angew. Chem. Int. Ed.* **2013**, *52*, 11088 – 11091; *Angew. Chem.* **2013**, *125*, 11294 – 11297; g) A. Alix, C. Lalli, P. Retailleau, G. Masson, *J. Am. Chem. Soc.* **2012**, *134*, 10389 – 10392; h) L. He, M. Bekkaye, P. Retailleau, G. Masson, *Org. Lett.* **2012**, *14*, 3158 – 3161; i) A. Dumoulin, C. Lalli, P. Retailleau, G. Masson, *Chem. Commun.* **2015**, *51*, 5383 – 5386.

[7] a) K. Sorimachi, M. Terada, *J. Am. Chem. Soc.* **2008**, *130*, 14452 – 14453. See also: b) Y. Toda, M. Terada, *Synlett* **2013**, *24*, 752 – 756; c) Y.-C. Shi, S.-G. Wang, Q. Yin, S.-L. You, *Org. Chem. Front.* **2014**, *1*, 39.

[8] M. Terada, K. Sorimachi, *J. Am. Chem. Soc.* **2007**, *129*, 292 – 293.

[9] E. Wolf, E. Richmond, J. Moran, *Chem. Sci.* **2015**, *6*, 2501 – 2505.

[10] E. Richmond, J. Moran, *J. Org. Chem.* **2015**, *80*, 6922 – 6929.

[11] For nickel-catalyzed allylamine/carbamate isomerization, see: a) L. Wang, C. Liu, R. Bai, Y. Pan, A. Lei, *Chem. Commun.* **2013**, *49*, 7923 – 7925; b) S. Krompiec, M. Pigulla, M. Krompiec, S. Baj, J. Mrowiec-Bialon, J. Kasperczyk, *Tetrahedron Lett.* **2004**, *45*, 5257 – 5261. For other nickel-catalyzed olefin isomerizations, see: c) C. Malanga, A. Urso, L. Lardicci, *Tetrahedron Lett.* **1995**, *36*, 1133 – 1136; d) C. F. Lochow, R. G. Miller, *J. Org. Chem.* **1976**, *41*, 3020 – 3022; e) A. Wille, S. Tomm, H. Frauenrath, *Synthesis* **1998**, 305 – 308. For allylamine/carbamate isomerization catalyzed by other transition metals, see: f) S. Krompiec, M. Krompiec, R. Penczek, H. Ignasiak, *Coord. Chem. Rev.* **2008**, *252*, 1819 – 1841; g) S. Escoubet, S. Gastaldi, M. Bertrand, *Eur. J. Org. Chem.* **2005**, 3855 – 3873; h) S. Krompiec, M. Pigulla, W. Szczepankiewicz, T. Bieg, N. Kuznik, K. Leszczynska-Sedja, M. Kubicki, T. Borowiak, *Tetrahedron Lett.* **2001**, *42*, 7095 – 7098; i) V. A. Ershova, A. V. Golovin, V. M. Pogerbnyak, *J. Organomet. Chem.* **2002**, *658*, 147 – 152; j) B. Neugnot, J.-C. Cintrat, B. Rousseau, *Tetrahedron* **2004**, *60*, 3575 – 3579; k) S. A. Sergeyev, M. Hesse, *Helv. Chim. Acta* **2003**, *86*, 750 – 755; l) S. Inoue, H. Takaya, K. Tani, S. Otsuka, T. Sato, R. Noyori, *J. Am. Chem. Soc.* **1990**, *112*, 4897 – 4905.

[12] Initial deuterium-labelling studies had suggested a nickel-hydride species as the active catalyst in these transformations (see the Supporting Information for further details).

[13] A one-pot reaction is also capable of delivering the desired products, however, yields and enantioselectivities were found to be highly irreproducible.

[14] a) V. V. Kouznetsov, *Tetrahedron* **2009**, *65*, 2721 – 2750; b) M. Fochi, L. Caruana, L. Bernadi, *Synthesis* **2013**, *46*, 135 – 157.

[15] a) H. Liu, G. Dagousset, G. Masson, P. Retailleau, J. Zhu, *J. Am. Chem. Soc.* **2009**, *131*, 4598 – 4599; b) G. Dagousset, J. Zhu, G. Masson, *J. Am. Chem. Soc.* **2011**, *133*, 14804 – 14813.

[16] In our initial studies it was noted that the initial nickel-catalyzed isomerization of *N*-Boc and *N*-Cbz allylamines yielded a 1:1 *E*/*Z* mixture of enecarbamates. Although inconsequential for the α-arylation system described here, this mixture of geometric isomers has the potential to give a 1:1 mixture of tetrahydroquinoline diastereomers. However, due to the significantly faster rate of reaction between the (*E*)-configured ene-carbamates and the imines used in this study, high levels of diastereomeric preference could be obtained simply by using a two-fold excess of allylcarbamate starting material, thereby yielding the *anti*-tetrahydroquinoline as the major product. The significantly faster reaction rate of the (*E*)-configured ene-carbamates is in agreement with observations by Zhu and Masson (see ref. [15]).

[17] a) K. Narasaka, T. Okauchi, K. Tanaka, M. Murakami, *Chem. Lett.* **1992**, *21*, 2099 – 2102; b) T. D. Beeson, A. Mastracchio, J.-B. Hong, K. Ashton, D. W. C. MacMillan, *Science* **2007**, *316*, 582 – 585; c) H. Kim, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2008**, *130*, 398 – 399; d) A. Mastracchio, A. A. Warkentin, A. M. Walji, D. W. C. MacMillan, *Proc. Natl. Acad. Sci. USA* **2010**, *107*, 20648 – 20651.

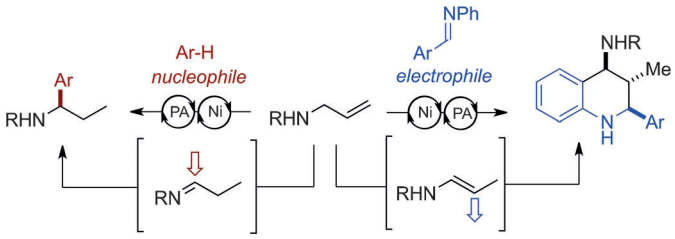
[18] M. Bekkaye, G. Masson, *Org. Lett.* **2014**, *16*, 1510 – 1513.

[19] To the best of our knowledge, the sole example of multicatalysis arising from the combination of nickel and organocatalysis: M. Terada, Y. Toda, *J. Am. Chem. Soc.* **2009**, *131*, 6354 – 6355.

[20] While the scope of transformations enabled by tandem nickel and organocatalysis is limited, nickel catalysts have found widespread application in conjunction with other transition metal catalysts, and have recently been applied in the realm of photoredox catalysis. For lead references, see: a) J. C. Tellis, D. N. Primer, G. A. Molander, *Science* **2014**, *345*, 433 – 436; b) Z. Zuo, D. T. Ahneman, L. Chu, J. A. Terrett, A. G. Doyle, D. W. C. MacMillan, *Science* **2014**, *345*, 437 – 440.

Received: June 13, 2016
Published online on ■■ ■■, 0000

COMMUNICATION



Simple divergence: A pair of mechanistically divergent multicatalytic reaction sequences has been developed consisting of nickel-catalyzed isomerization of *N*-allylcarbamates and subsequent phosphoric-acid-catalyzed enantioselective functionalization of the resulting intermediates. Formal α-functionalization to give protected α-arylamines is achieved upon enantioselective Friedel–Crafts reaction with arene nucleophiles, whereas formal β-functionalization is achieved upon reaction with diarylimine electrophiles in an enantioselective Povarov-[4+2] cycloaddition.

Synthetic Methods

*E. Richmond, I. U. Khan, J. Moran**

■■ – ■■

Enantioselective and Regiodivergent Functionalization of *N*-Allylcarbamates by Mechanistically Divergent Multicatalysis