ChemPubSoc Europe

DOI: 10.1002/chem.201500774

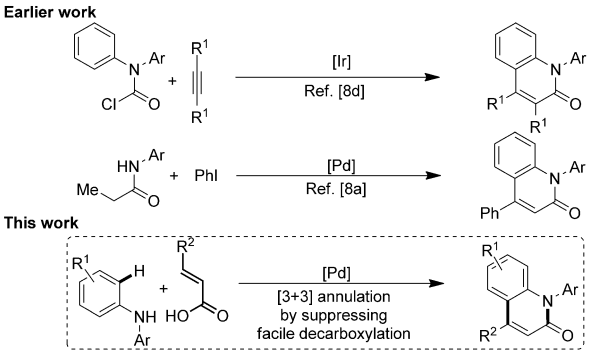
CHEMISTRY
A European Journal
Communication

C–H Activation

Palladium-Catalyzed [3+3] Annulation between Diarylamines and α,β-Unsaturated Acids through C–H Activation: Direct Access to 4-Substituted 2-Quinolinones

Rajesh Kancherla, Togati Naveen, and Debabrata Maiti*[a]

Abstract: A C–H activation strategy has been successfully employed for the high-yielding synthesis of a diverse array of 4-substituted 2-quinolinone species by a palladium-catalyzed dehydrogenative coupling involving diarylamines. This intermolecular annulation approach incorporates readily available α,β-unsaturated carboxylic acids as the coupling partner by suppressing the facile decarboxylation. Based on preliminary mechanistic studies, a reaction sequence is proposed, involving *ortho* palladation, π-coordination, β-migratory insertion, and β-hydride elimination.



Scheme 1. Synthesis of 4-substituted 2-quinolinones.

Quinolinones are an important class of heterocyclic compounds.[1] In particular 4-aryl-2-quinolinones occur naturally[2] and exhibit unique biological properties.[3] They are inhibitors of acyl coenzyme A and cholesterol acyltransferase, and are also potent openers of calcium-activated K^+ channels.[4] The 4-aryl-2-quinolinone derivative tipifarnib is known to exhibit anticancer activity.[5] In addition, various 2-alkoxyquinolines can be derived from 2-quinolinones for their use as ligands in C–H activation reactions.[6] Various methods for the synthesis of 2-quinolinones have been reported[4a,7] and considerable attention has been paid in recent times to the development of 4-substituted 2-quinolinones.[8]

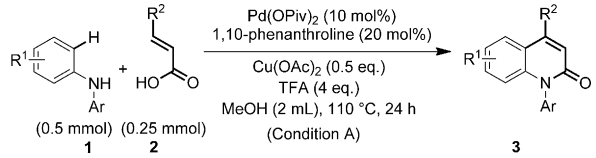
With a view to 4-substituted 2-quinolinone synthesis, Tsuji and co-workers reported the iridium catalyzed reaction of *N*-arylcarbamoyl chlorides with internal alkynes (Scheme 1).[8d] However this intermolecular reaction did not work with terminal alkynes (e.g., 1-decyne and phenylacetylene) and therefore failed to yield 4-alkyl- and 4-aryl-2-quinolinones. Recently, Yu and co-workers successfully constructed 1,4-diaryl-2-quinolinones from propionamides and aryl iodides by a palladium-catalyzed C–H activation method (Scheme 1).[8a] Unfortunately, this novel method could not incorporate aliphatic and heterocyclic substituents at the 4-position of quinolinone. Indeed, direct synthesis of such moieties is yet to be reported. We recently developed a palladium-catalyzed C–H activation pathway for synthesizing heterocycles such as indole, benzofuran and coumarin.[9] Inspired by these studies, we envisaged the synthesis of 4-substituted 2-quinolinones by employing an unexplored variant of Fujiwara–Moritani-type coupling[10] between simple diarylamines and widely available α,β-unsaturated carboxylic acids. This approach (with or without a directing group) remained problematic due to the facile decarboxylation of α,β-unsaturated acid-derived intermediates. Systematic exploration revealed that trifluoroacetic acid (TFA) could suppress decarboxylation under our reaction conditions and thus allowed the formation of 4-substituted 2-quinolinones.[11] The optimized reaction conditions (condition A; Table 1), with diphenylamine (**1a**, 0.5 mmol), cinnamic acid (**2a**, 0.25 mmol), palladium pivalate ($Pd(OPiv)_2$, 10 mol%), 1,10-phenanthroline (20 mol%), and TFA (4 equiv) in methanol (2 mL) using $Cu(OAc)_2$ (0.5 equiv) or air (oxygen) as oxidant produced 1,4-diaryl-2-quinolinone (**3a**) in 98% yield (isolated: 93%).[11]

Systematic variation of substituents at the *para* (**3a**–**g**), *meta* (**3h**–**j**), and *ortho* (**3k**–**m**) positions on the cinnamic acids were studied to reveal the electronic and steric dependence (Table 1). Although all of the substrates reacted successfully, electron-rich cinnamic acids gave better yields (e.g., **3b** vs. **3g**). Various halides at *ortho* or *para* positions were well tolerated (**3d**–**f**, **3l**, and **3m**). Introduction of functional groups such as 3-CF_3 (**3h**, 80%), 4-CO_2Me (**3g**, 71%) and 3-NO_2 (**3i**, 47%) on the aryl ring did not alter the outcome of the reaction. Similarly, hydroxycinnamic acids also gave the desired compounds in preparatively useful yields (**3j** and **3u**). Sterically congested trimethoxycinnamic acid could also be employed under the standard reaction condition (**3x**, 81%). As expected, substituted diarylamines formed quinolinones in excellent yields (**3n**–**r**, **3v**). However, various monoarylamines (ArNHR;

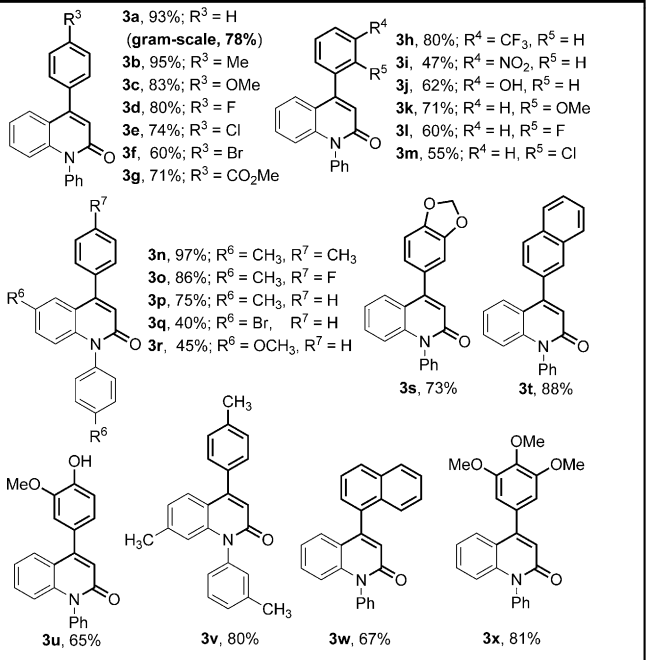
[a] Dr. R. Kancherla, T. Naveen, Prof. D. Maiti
Department of Chemistry, Indian Institute of Technology Bombay
Powai, Mumbai-400076 (India)
E-mail: dmaiti@chem.iitb.ac.in

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/chem.201500774.

Table 1. Scope with symmetrical diphenylamines and aromatic acrylic acids.

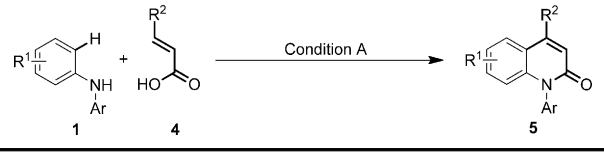


(0.5 mmol) (0.25 mmol)
1 **2** **3**

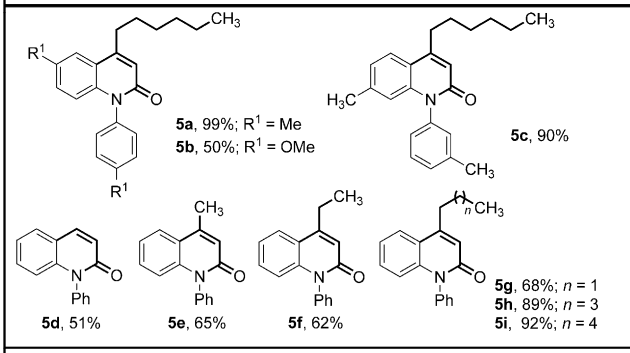


Yields given correspond to isolated products.

Table 2. Scope with aliphatic acrylic acids.

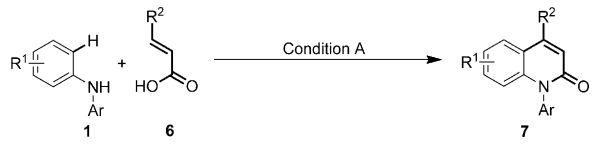


1 **4** **5**

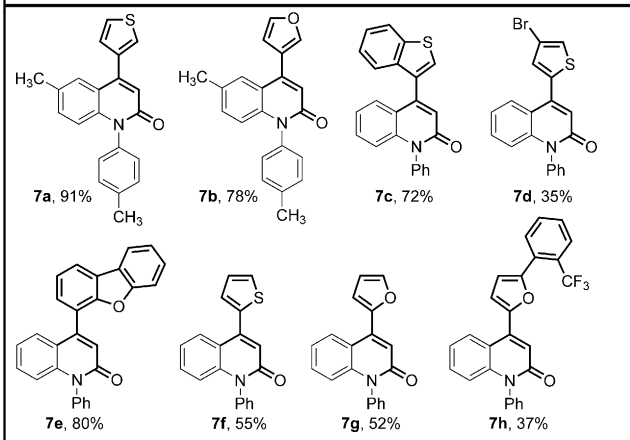


Yields given correspond to isolated products.

Table 3. Scope with heterocyclic acrylic acids.



1 **6** **7**



Yields given correspond to isolated products.

R = H, Me, Et, *i*Pr, Ts and Ac) either formed mixtures of inseparable compounds or gave low yields of the desired quinolinone products.

Aliphatic coupling partners are distinct from their aromatic counterparts due to electronic differences and are often problematic in Pd-catalyzed coupling reactions due to their tendency to undergo β-hydride elimination, which often leads to undesired side products.[12] Interestingly, 4-alkyl-*N*-phenyl-2-quinolinone species (**5a–i**) were successfully synthesized in 51–99% yields by employing a number of aliphatic acrylic acids (Table 2). Notably, the reactivity of the acrylic acids was found to increase with increasing chain length (**5d–i**).

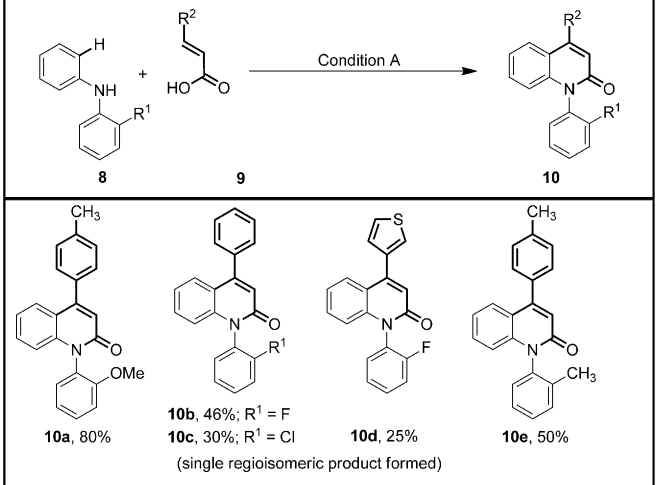
The scope of the method was further tested by employing heterocyclic acrylic acids to produce 4-heteroaryl-*N*-phenyl-2-quinolinones (**7a–h**) in good yields (Table 3). Among the heterocyclic substrates, 3-thienyl acrylic acid gave the maximum yield (**7a**, 91%). Due to incomplete conversion of the starting materials, a significant decrease in yields was observed in case of **7d** [35% and 82% based on recovered starting materials (brsm)] and **7h** (37% and 80% brsm).

Next, we investigated the reactivity of unsymmetrical diarylamines under standard conditions (Tables 4 and 5). Diphenyl amines with 2-OMe (**10a**; 80%), 2-Me (**10e**; 50%), 2-F (**10b** and **10d**; 46% and 25%, respectively), and 2-Cl (**10c**; 30%) substituents underwent successful annulation with different acrylic acids.

Interestingly, with *ortho*-substituted unsymmetrical diarylamines, in spite of the possibility of forming regioisomeric mixtures, only one product was generated exclusively (**10a–e**). This is ascribed to the steric factors, where the palladation on the *o*-substituted ring was disfavored, thereby allowing olefination of the unsubstituted aryl ring. Incomplete conversion of the carboxylic acids was found to be responsible for low yields of the desired products **10b–e** (Table 4).

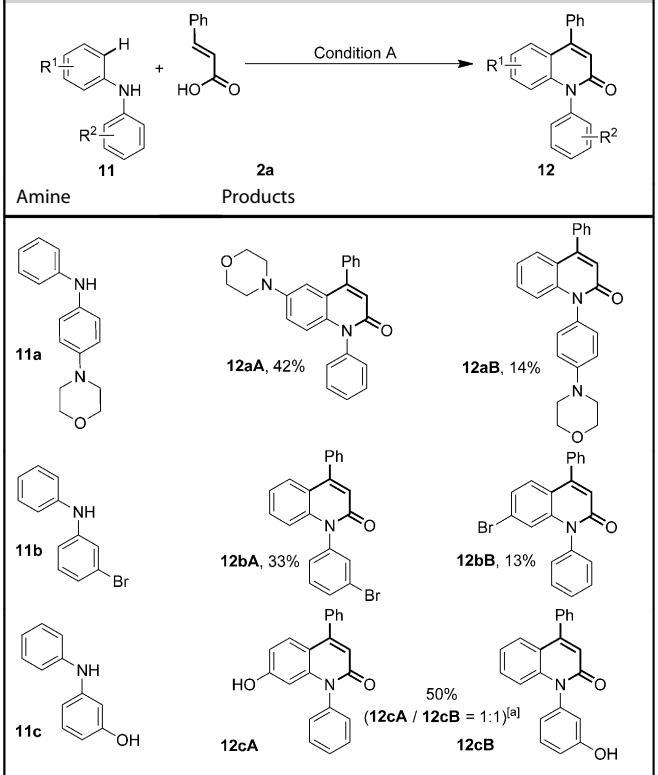
A preference for cyclization of the electron-rich aromatic ring was observed with differentially substituted unsymmetrical diarylamines (Table 5). In case of 4-morpholino-*N*-phenylaniline (**11a**), a 42% isolated yield of the major product **12aA** was obtained through cyclization towards electron rich aryl

Table 4. *o*-Substituted unsymmetrical diphenylamines.



Yields given correspond to isolated products.

Table 5. Scope with unsymmetrical diphenylamines.

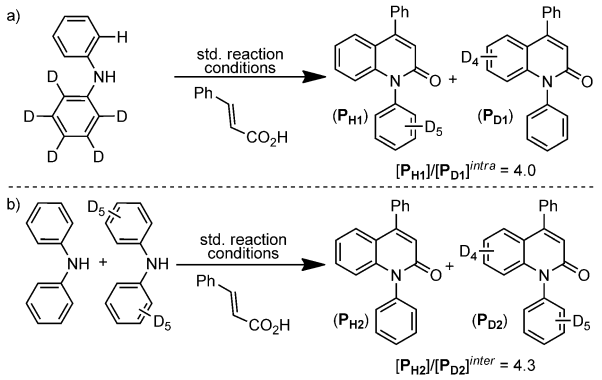


Yields given correspond to isolated products; [a] two isomers were obtained as an inseparable mixture.

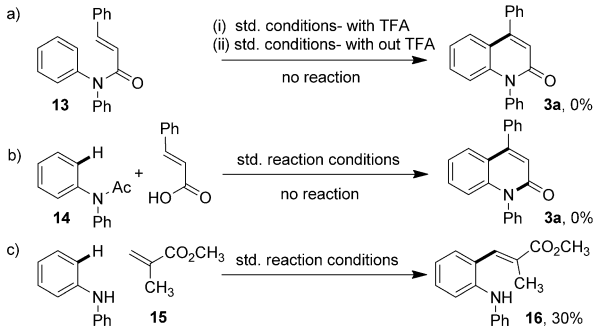
ring. The similar reactivity pattern was also found in case of **11b**, which gave **12bA** as the major product. Using 3-(phenylamino)phenol (**11c**), both the regioisomers **12cA** and **12cB** were obtained in 1:1 ratio.

A number of competition experiments between electronically different acrylic acids and diphenyl amines were carried out in order to understand the reactivity and reaction mechanism.[11] Based on these competition experiments and the results in Table 1, Table 2, Table 3, we found that electron rich acrylic acids as well as electron rich diphenylamines were cyclized preferentially over neutral and electron deficient analog.[11]

Intra- and intermolecular competition experiments with deuterium-labeled diphenylamines were carried out to probe the reaction mechanism. Cyclization at the undeuterated aryl group was observed preferentially with respect to the [D_5]aryl moiety in [D_5]diphenylamine ([$\mathbf{P_{H1}}$]/[$\mathbf{P_{D1}}$] = 4.0; Scheme 2a). Additionally, intermolecular competition between [D_{10}]- and simple (undeuterated) diphenylamine gave a product-distribution value of 4.3 ([$\mathbf{P_{H2}}$]/[$\mathbf{P_{D2}}$]; Scheme 2b). These higher values indicate that C–H bond cleavage is irreversible and can be involved in either the turnover-limiting or product-determining step.[13] Notably, both *N*,*N*-diphenylcinnamide (**13**) and *N*-acyldiphenylamine (**14**) failed completely to produce **3a** under the standard reaction conditions (Scheme 3a and b). Detection of the other plausible intermediate **D** (Scheme 4) was difficult, due to its effective annulation in the presence of TFA to give **E**. In the absence of TFA, *ortho* olefinated intermediate **D** underwent facile decarboxylative coupling to produce a 1,3-diarylindole instead of 2-quinolinone (**3a**). Cinnamic acid (without diarylamine) under the standard reaction condition gave a 10% yield of methylcinnamate. This observation further indi-



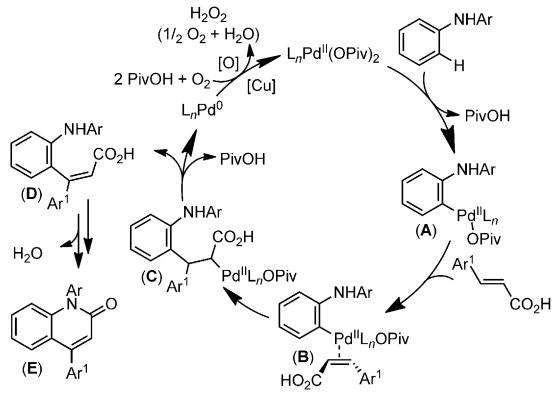
Scheme 2. Intra- and intermolecular deuterium labeling experiments.



Scheme 3. Mechanistic study.

cated that α,β-unsaturated carboxylic acid directly participates in the C–C coupling reaction to give **D**. Structurally similar *ortho*-olefinated intermediate **16** was formed under the standard reaction conditions by reacting diphenylamine with methyl methacrylate (**15**), which further supports **D** as a feasible intermediate in the reaction pathway (Scheme 3c).

Based on these findings, *ortho* palladation of diarylamine (electron-rich ring favors initial *ortho* palladation) was proposed for the generation of intermediate **A** (Scheme 4). Inter-



Scheme 4. Proposed mechanism.

action of **A** with α,β-unsaturated acids would lead to species **B**. Subsequently, β-migratory insertion followed by β-hydride elimination would form *ortho* olefinated intermediate **D**. This would produce **E** by nucleophilic attack of amine in the presence of TFA. The Pd^0 formed could be reoxidized to Pd^{II} by oxygen (air), possibly via a peroxopalladium(II) complex.[14]

In summary, a palladium-catalyzed dehydrogenative coupling between diarylamines and α,β-unsaturated carboxylic acids has been developed for the synthesis of *N*-aryl-2-quinolinones. The use of TFA was crucial for suppressing facile decarboxylation of the α,β-unsaturated acids. The present method proved general and versatile for the synthesis of a variety of 4-substituted 2-quinolinones with aromatic, aliphatic, and heterocyclic substituents at the 4-position. Interestingly, all *ortho*-substituted unsymmetrical diarylamines gave single regioisomeric products. A preliminary mechanistic proposal was presented based on competition experiments, intermediate studies, and deuterium labeling. Detailed mechanistic studies, along with the regioselective synthesis of 3-substituted indoles from the olefinated intermediates, are currently underway in our laboratory.

Acknowledgements

This activity was supported by Science and Engineering Research Board, India (No. SB/S5/GC-05/2013). Financial support received from DST under the Fast Track Scheme (R.K.) and CSIR (T.N.) is gratefully acknowledged. Palladium catalysts were obtained as a gift from Johnson Matthey Chemicals, MIDC Taloja, India.

Keywords: annulation · C–H activation · homogeneous catalysis · N heterocycles · palladium

[1] a) J. P. Michael, *Nat. Prod. Rep.* **1995**, *12*, 465–475; b) J. B. Hanuman, A. Katz, *Nat. Prod. Lett.* **1993**, *3*, 227–231; c) A. K. Gupta, N. Sabarwal, Y. P. Agrawal, S. Prachand, S. Jain, *Eur. J. Med. Chem.* **2010**, *45*, 3472–3479; d) E. A. Larsson, A. Jansson, F. M. Ng, S. W. Then, R. Panicker, B. Liu, K. Sangthongpitag, V. Pendharkar, S. J. Tai, J. Hill, C. Dan, S. Y. Ho, W. W. Cheong, A. Poulsen, S. Blanchard, G. R. Lin, J. Alam, T. H. Keller, P. r. Nordlund, *J. Med. Chem.* **2013**, *56*, 4497–4508; e) S. Jönsson, G. Andersson, T. Fex, T. Fristedt, G. Hedlund, K. Jansson, L. Abramo, I. Fritzson, O. Pekarski, A. Runstrom, H. Sandin, I. Thuvesson, A. Bjork, *J. Med. Chem.* **2004**, *47*, 2075–2088.

[2] a) Y. Kobayashi, T. Harayama, *Org. Lett.* **2009**, *11*, 1603–1606 and references cited therein; b) Y. Kitahara, M. Shimizu, A. Kubo, *Heterocycles* **1990**, *31*, 2085–2090 and references cited therein.

[3] a) J. M. Kraus, C. L. M. J. Verlinde, M. Karimi, G. I. Lepesheva, M. H. Gelb, F. S. Buckner, *J. Med. Chem.* **2009**, *52*, 1639–1647; b) J. M. Kraus, H. B. Tatipaka, S. A. McGuffin, N. K. Chennamaneni, M. Karimi, J. Arif, C. L. M. J. Verlinde, F. S. Buckner, M. H. Gelb, *J. Med. Chem.* **2010**, *53*, 3887–3898; c) B. C. Capell, M. Olive, M. R. Erdos, K. Cao, D. A. Faddah, U. L. Tavarez, K. N. Conneely, X. Qu, H. San, S. K. Ganesh, X. Chen, H. Avallone, F. D. Kolodgie, R. Virmani, E. G. Nabel, F. S. Collins, *Proc. Natl. Acad. Sci. USA* **2008**, *105*, 15902–15907; d) P. R. Angibaud, M. G. Venet, W. Filliers, R. Broeckx, Y. A. Ligny, P. Muller, V. S. Poncelet, D. W. End, *Eur. J. Org. Chem.* **2004**, 479–486; e) P. Cheng, Q. Zhang, Y.-B. Ma, Z.-Y. Jiang, X.-M. Zhang, F.-X. Zhang, J.-J. Chen, *Bioorg. Med. Chem. Lett.* **2008**, *18*, 3787–3789; f) G. Claassen, E. Brin, C. Crogan-Grundy, M. T. Vaillancourt, H. Z. Zhang, S. X. Cai, J. Drewe, B. Tseng, S. Kasibhatla, *Cancer Lett.* **2009**, *274*, 243–249.

[4] a) P. Hewawasam, W. Fan, M. Ding, K. Flint, D. Cook, G. D. Goggins, R. A. Myers, V. K. Gribkoff, C. G. Boissard, S. I. Dworetzky, J. E. Starrett, N. J. Lodge, *J. Med. Chem.* **2003**, *46*, 2819–2822; b) J. Wang, R. P. Discordia, G. A. Crispino, J. Li, J. A. Grosso, R. Polniaszek, V. C. Truc, *Tetrahedron Lett.* **2003**, *44*, 4271–4273.

[5] a) Q. Li, K. W. Woods, W. Wang, N.-H. Lin, A. Claiborne, W.-Z. Gu, J. Cohen, V. S. Stoll, C. Hutchins, D. Frost, S. H. Rosenberg, H. L. Sham, *Bioorg. Med. Chem. Lett.* **2005**, *15*, 2033–2039; b) P. Norman, *Curr. Opin. Invest. Drugs* **2002**, *3*, 313–319; c) M. Venet, D. End, P. Angibaud, *Curr. Top. Med. Chem.* **2003**, *3*, 1095–1102; d) E. van Cutsem, H. van de Velde, P. Karasek, H. Oettle, W. L. Vervenne, A. Szawlowski, P. Schoffski, S. Post, C. Verslype, H. Neumann, H. Safran, Y. Humblet, J. P. Ruixo, Y. Ma, D. von Hoff, *J. Clin. Oncol.* **2004**, *22*, 1430–1438.

[6] a) J. He, S. Li, Y. Deng, H. Fu, B. N. Laforteza, J. E. Spangler, A. Homs, J.-Q. Yu, *Science* **2014**, *343*, 1216–1220; b) M. Wasa, K. S. L. Chan, X.-G. Zhang, J. He, M. Miura, J.-Q. Yu, *J. Am. Chem. Soc.* **2012**, *134*, 18570–18572.

[7] a) T. Shibuya, Y. Shibata, K. Noguchi, K. Tanaka, *Angew. Chem. Int. Ed.* **2011**, *50*, 3963–3967; *Angew. Chem.* **2011**, *123*, 4049–4053; b) M. Wasa, J.-Q. Yu, *J. Am. Chem. Soc.* **2008**, *130*, 14058–14059; c) F. Domínguez-Fernández, J. López-Sanz, E. Pérez-Mayoral, D. Bek, R. M. Martín-Aranda, A. J. López-Peinado, J. Čejka, *ChemCatChem* **2009**, *1*, 241–243; d) M. Marull, O. Lefebvre, M. Schlosser, *Eur. J. Org. Chem.* **2004**, 54–63; e) M. Sridhar Reddy, N. Thirupathi, M. H. Babu, *Eur. J. Org. Chem.* **2012**, 5803–5809; f) C.-C. Huang, N.-C. Chang, *Org. Lett.* **2008**, *10*, 673–676; g) W.-T. Gao, W.-D. Hou, M.-R. Zheng, L.-J. Tang, *Synth. Commun.* **2010**, *40*, 732–738; h) K. M. Boy, J. M. Guernon, S.-Y. Sit, K. Xie, P. Hewawasam, C. G. Boissard, S. I. Dworetzky, J. Natale, V. K. Gribkoff, N. Lodge, J. E. Starrett Jr, *Bioorg. Med. Chem. Lett.* **2004**, *14*, 5089–5093; i) P. Hewawasam, W. Fan, D. A. Cook, K. S. Newberry, C. G. Boissard, V. K. Gribkoff, J. Starrett, N. J. Lodge, *Bioorg. Med. Chem. Lett.* **2004**, *14*, 4479–4482; j) P. Hewawasam, W. Fan, J. Knipe, S. L. Moon, C. G. Boissard, V. K. Gribkoff, J. E. Starrett Jr, *Bioorg. Med. Chem. Lett.* **2002**, *12*, 1779–1783; k) W. W. K. R. Mederski, M. Osswald, D. Dorsch, M. Christadler, C.-J. Schmitges, C. Wilm, *Bioorg. Med. Chem. Lett.* **1997**, *7*, 1883–1886; l) D. V. Kadnikov, R. C. Larock, *J. Org. Chem.* **2004**, *69*, 6772–6780; m) J. Ferguson, F. Zeng, N. Alwis, H. Alper, *Org. Lett.* **2013**, *15*, 1998–2001; n) P. J. Manley, M. T. Bilodeau, *Org. Lett.* **2004**, *6*, 2433–2435; o) C. Jia, D. Piao, T. Kitamura, Y. Fujiwara, *J. Org. Chem.* **2000**, *65*, 7516–7522; p) K. Inamoto, T.

Saito, K. Hiroya, T. Doi, *J. Org. Chem.* **2010**, *75*, 3900 – 3903; q) G. Battistuzzi, R. Bernini, S. Cacchi, I. De Salve, G. Fabrizi, *Adv. Synth. Catal.* **2007**, *349*, 297 – 302; r) N. A. Cortese, C. B. Ziegler, B. J. Hrnjez, R. F. Heck, *J. Org. Chem.* **1978**, *43*, 2952 – 2958.

[8] a) Y. Deng, W. Gong, J. He, J.-Q. Yu, *Angew. Chem. Int. Ed.* **2014**, *53*, 6692 – 6695; b) R. Zeng, G. Dong, *J. Am. Chem. Soc.* **2015**, *137*, 1408 – 1411; c) K. Nakai, T. Kurahashi, S. Matsubara, *Org. Lett.* **2013**, *15*, 856 – 859; d) T. Iwai, T. Fujihara, J. Terao, Y. Tsuji, *J. Am. Chem. Soc.* **2010**, *132*, 9602 – 9603; e) Y. Dong, B. Liu, P. Chen, Q. Liu, M. Wang, *Angew. Chem. Int. Ed.* **2014**, *53*, 3442 – 3446; f) W. Qian, H. Wang, J. Allen, *Angew. Chem. Int. Ed.* **2013**, *52*, 10992 – 10996; *Angew. Chem.* **2013**, *125*, 11198 – 11202; g) R. Manikandan, M. Jeganmohan, *Org. Lett.* **2014**, *16*, 3568 – 3571; h) J. Wu, S. Xiang, J. Zeng, M. Leow, X.-W. Liu, *Org. Lett.* **2015**, *17*, 222 – 225.

[9] a) U. Sharma, R. Kancherla, T. Naveen, S. Agasti, D. Maiti, *Angew. Chem. Int. Ed.* **2014**, *53*, 11895 – 11899; b) U. Sharma, T. Naveen, A. Maji, S. Manna, D. Maiti, *Angew. Chem. Int. Ed.* **2013**, *52*, 12669 – 12673; *Angew. Chem.* **2013**, *125*, 12901 – 12905; c) S. Agasti, U. Sharma, T. Naveen, D. Maiti, *Chem. Commun.* **2015**, *51*, 5375 – 5378.

[10] a) I. Moritani, Y. Fujiwara, *Tetrahedron Lett.* **1967**, *8*, 1119 – 1122; b) L. Zhou, W. Lu, *Chem. Eur. J.* **2014**, *20*, 634 – 642; c) Y. Fujiwara, I. Moritani, S. Danno, R. Asano, S. Teranishi, *J. Am. Chem. Soc.* **1969**, *91*, 7166 – 7169; d) Y. Fujiwara, I. Moritani, M. Matsuda, S. Teranishi, *Tetrahedron Lett.* **1968**, *9*, 3863 – 3865; e) Y. Fujiwara, I. Moritani, M. Matsuda, S. Teranishi, *Tetrahedron Lett.* **1968**, *9*, 633 – 636; f) G. G. Pawar, G. Singh, V. K. Tiwari, M. Kapur, *Adv. Synth. Catal.* **2013**, *355*, 2185 – 2190; g) T. Nishikata, B. H. Lipshutz, *Org. Lett.* **2010**, *12*, 1972 – 1975; h) X. Chen, K. M. Engle, D.-H. Wang, J.-Q. Yu, *Angew. Chem. Int. Ed.* **2009**, *48*, 5094 – 5115; *Angew. Chem.* **2009**, *121*, 5196 – 5217; i) J. Wencel-Delord, T. Droge, F. Liu, F. Glorius, *Chem. Soc. Rev.* **2011**, *40*, 4740 – 4761; j) G. Cai, Y. Fu, Y. Li, X. Wan, Z. Shi, *J. Am. Chem. Soc.* **2007**, *129*, 7666 – 7673; k) M. Miura, T. Tsuda, T. Satoh, S. Pivsa-Art, M. Nomura, *J. Org. Chem.* **1998**, *63*, 5211 – 5215.

[11] See the Supporting Information for a detailed description.

[12] a) A. C. Bissember, A. Levina, G. C. Fu, *J. Am. Chem. Soc.* **2012**, *134*, 14232 – 14237; b) K. Menzel, G. C. Fu, *J. Am. Chem. Soc.* **2003**, *125*, 3718 – 3719; c) L. Qin, H. Hirao, J. Zhou, *Chem. Commun.* **2013**, *49*, 10236 – 10238; d) L. Qin, X. Ren, Y. Lu, Y. Li, J. Zhou, *Angew. Chem. Int. Ed.* **2012**, *51*, 5915 – 5919; *Angew. Chem.* **2012**, *124*, 6017 – 6021; e) C. S. Sevov, J. Zhou, J. F. Hartwig, *J. Am. Chem. Soc.* **2014**, *136*, 3200 – 3207; f) Y. Zou, L. Qin, X. Ren, Y. Lu, Y. Li, J. Zhou, *Chem. Eur. J.* **2013**, *19*, 3504 – 3511; g) A. Deb, S. Bag, R. Kancherla, D. Maiti, *J. Am. Chem. Soc.* **2014**, *136*, 13602 – 13605.

[13] E. M. Simmons, J. F. Hartwig, *Angew. Chem. Int. Ed.* **2012**, *51*, 3066 – 3072; *Angew. Chem.* **2012**, *124*, 3120 – 3126.

[14] For the oxidation of Pd^0 to Pd^{II} by O_2, see: a) D. Wang, Y. Izawa, S. S. Stahl, *J. Am. Chem. Soc.* **2014**, *136*, 9914 – 9917; b) M. M. Konnick, N. Decharin, B. V. Popp, S. S. Stahl, *Chem. Sci.* **2011**, *2*, 326 – 330; c) Y. Izawa, D. Pun, S. S. Stahl, *Science* **2011**, *333*, 209 – 213; d) A. N. Campbell, P. B. White, I. A. Guzei, S. S. Stahl, *J. Am. Chem. Soc.* **2010**, *132*, 15116 – 15119; e) B. V. Popp, S. S. Stahl, *Chem. Eur. J.* **2009**, *15*, 2915 – 2933; f) S. S. Stahl, J. L. Thorman, R. C. Nelson, M. A. Kozee, *J. Am. Chem. Soc.* **2001**, *123*, 7188 – 7189.

Received: February 25, 2015
Published online on ■■ ■■, 0000

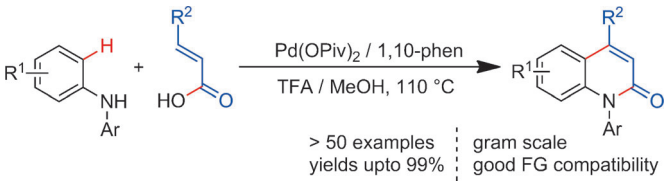
COMMUNICATION

C–H Activation

*R. Kancherla, T. Naveen, D. Maiti**

■■ – ■■

Palladium-Catalyzed [3+3] Annulation between Diarylamines and α,β-Unsaturated Acids through C–H Activation: Direct Access to 4-Substituted 2-Quinolinones



4-substituted 2-quinolinone species are been synthesized in high yields by a palladium-catalyzed dehydrogenative coupling involving diarylamines. This intermolecular annulation approach incorporates readily available α,β-unsaturated carboxylic acids as the coupling partner by suppressing decarboxylation.