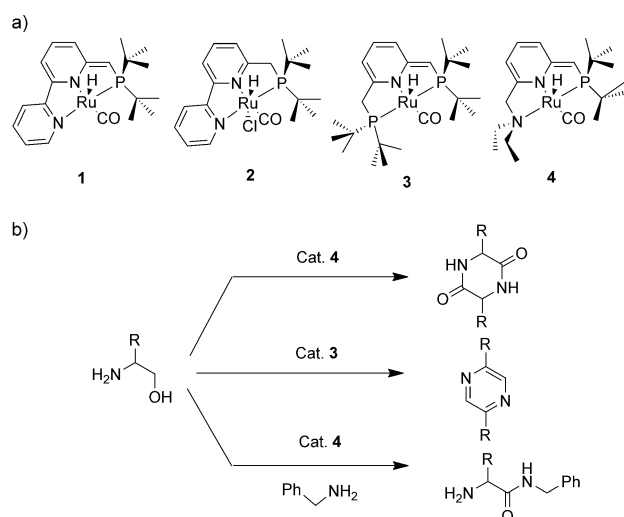


Direct Synthesis of Pyrroles by Dehydrogenative Coupling of β -Aminoalcohols with Secondary Alcohols Catalyzed by Ruthenium Pincer Complexes**

Dipankar Srimani, Yehoshua Ben-David, and David Milstein*

The search for new atom-economical and green synthetic methods for the synthesis of functionalized pyrrole derivatives has attracted much attention owing to their potential medicinal value.^[1] Pyrroles are important owing to their antitumor,^[2a,b] anti-inflammatory,^[2c] antibacterial,^[2d] antioxidant,^[2e] and antifungal properties.^[2f,g] Furthermore, they have applications in conducting polymers,^[3a-c] molecular optics,^[3d,e] electronics,^[3f] and as gas sensors for organic compounds.^[3 g] Although the classical methods for the synthesis of pyrroles, for example, Hantzsch,^[4] Knorr,^[5] and Paal–Knorr^[6] reactions are effective, they suffer from several drawbacks, such as availability of the starting materials, multisteps synthetic operations, functional group compatibility, regioselectivity, and harsh reaction conditions. To overcome these limitations, new strategies, such as multicomponent coupling^[7] and metal-catalyzed^[8b-e,j,m,n] reactions, have recently been developed. Recently, interesting dehydrogenative coupling of 1,4-diols and amines to form pyrroles was developed,^[8x] and very recently an attractive synthesis of aryl-substituted pyrroles catalyzed by an in situ generated catalyst from $[\text{Ru}_3(\text{CO})_{12}]$ (1 mol %) and xantphos (3 mol %), using arylketones, 1,2-diols, amines, and K_2CO_3 was reported.^[8w]

There is an urgent need to develop sustainable, one-step, atom-economical efficient methodologies for the preparation of valuable synthetic building blocks. In this regard, our group has demonstrated several environmentally benign reactions with concomitant liberation of H_2 , catalyzed by pincer complexes of ruthenium based on pyridine^[9] and acridine^[10] backbones. These reactions include the synthesis of esters by dehydrogenative coupling of alcohols,^[9b,g] coupling of alcohols with amines to generate imines^[11] and amides^[9d,e] with liberation of hydrogen, amidation of esters,^[9e] and acylation of alcohols using esters.^[9f,12] Recently we synthesized peptides and pyrazines from β -amino alcohols by the extrusion of molecular hydrogen.^[13] A β -amino alcohol can also undergo dehydrogenative coupling with benzylamine to form an amide



Scheme 1. a) PNN- and PNP-type ruthenium pincer complexes. b) Peptide and pyrazine formation from β -amino alcohols catalyzed by Ru^{II} pincer complexes.

(Scheme 1 b). Here we present an efficient, atom-economical, one-step synthesis of pyrroles based on dehydrogenative coupling of β -aminoalcohols with secondary alcohols, catalyzed by well-defined pincer ruthenium catalysts. The reaction is quite general, and not limited to aryl pyrroles.

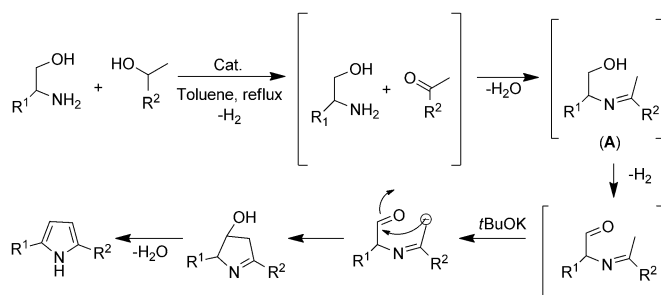
The Knorr pyrrole synthesis consists of the condensation of an α -amino ketone or α -amino ketoester with a ketone or ketoester. As we have previously described the acceptorless dehydrogenation of alcohols by ruthenium pincer complexes,^[9a] we envisioned, that α -amino aldehydes and ketones can be formed in situ from the β -amino alcohols and secondary alcohols by our Ru pincer complex, and the resulting products can be further coupled in the presence of base to form substituted pyrroles. Indeed, we demonstrate here the reaction of β -amino alcohols with secondary alcohols (equivalent amounts) catalyzed by a Ru pincer complex, in the presence of base, thereby leading to formation of pyrroles through selective and consecutive C–C and C–N bond formations (Scheme 2). Very recently, such an attractive reaction efficiently catalyzed by an iridium complex (0.5–0.03 mol %) using β -amino alcohols (1 equiv), secondary alcohols (2 equiv), and base (1.1 equiv) was reported.^[14]

Initially, the reaction of 2-amino-1-butanol with 1-phenylethanol was chosen as a model system for dehydrogenative cross-coupling to form a 2,5-disubstituted pyrrole. Disappointingly, conducting this reaction in the presence of catalyst

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Scheme 2. Plausible mechanism of pyrrole formation through dehydrogenation and selective C–C and C–N bond formation.

1 (0.5 mol %) and K_2CO_3 (1 equiv relative to the substrate) in dioxane heated to reflux resulted in only traces (6 %) of the desired coupling product, in addition to 48 % of acetophenone, which was obtained by the dehydrogenation of 1-phenylethanol (Table 1, entry 1). However, using a stronger

Table 1: Optimization of reaction conditions for pyrrole synthesis.^[a]

Entry	Base	Amount of base [equiv]	Solvent	Yield [%] ^[b]
1	K_2CO_3	1	dioxane	6 ^[c]
2	KOH	1	dioxane	72
3	KOtBu	1	dioxane	78
4	KOtBu	0.07	dioxane	28
5	KOtBu	0.5	dioxane	82
6	KOtBu	0.5	THF	77
7	KOtBu	0.5	benzene	71
8	KOtBu	0.5	toluene	88
9	KOtBu	0.5	toluene	80 ^[d]
10	KOtBu	0.5	toluene	82 ^[e]

[a] Reaction conditions: 2-amino-1-butanol (2 mmol), 1-phenylethanol (2 mmol) and catalyst (0.5 mol %) were heated at reflux under argon. [b] Yields of the products were determined by gas chromatographic (GC) analysis of the crude reaction mixture by using *m*-xylene as an internal standard. [c] Complex **1** was used. [d] Complex **3** was used. [e] Complex **4** was used.

base to improve the C–C coupling step resulted in the desired pyrrole in good yield. Actually, the dearomatized complex **1** can be formed in situ by deprotonation of the air-stable complex **2** under the basic reaction conditions.^[15]

Thus, heating 2-amino-1-butanol and 1-phenylethanol to reflux in the presence of complex **2** (0.5 mol %) and KOH (1 equiv) in dioxane for 24 h resulted in 72 % of 2-ethyl-5-phenylpyrrole (Table 1, entry 2) together with 19 % acetophenone. A slightly higher yield (78 %) was obtained when using the stronger base KOtBu in dioxane (Table 1, entry 3). When using a catalytic amount of KOtBu (0.07 equiv), the yield of the desired pyrrole was only 28 % (Table 1, entry 4), 40 % 1-phenyl ethanol remained unreacted, and 24 % acetophenone was formed by dehydrogenation of 1-phenylethanol. However, 0.5 equivalents of KOtBu are sufficient and result in an even slightly better yield (82 %) than one equivalent of base (Table 1, entry 5). The solvent effect on the reaction was

relatively minor. Thus, the yield of the desired pyrrole in toluene (88 %) was slightly higher than in dioxane (82 %), THF (77 %), or benzene (71 %), the difference likely resulting from the difference in reflux temperatures (Table 1, entries 6–8). The reaction in the presence of catalysts **3** or **4** also led to good yields (80 % and 82 %, respectively) of the desired pyrrole (Table 1, entry 9, 10).

With the optimized reaction conditions in hand, we set out to test the reactivity of other β -amino alcohols with 1-phenylethanol. A toluene solution containing 2-aminopropan-1-ol (2 mmol), 1-phenylethanol (2 mmol), KOtBu (1 mmol), and catalyst **2** (0.01 mmol) was heated to reflux for 24 h and then cooled to room temperature. Then the reaction mixture was quenched with water and extracted three times with diethylether. After purification of the crude mixture by column chromatography 71 % yield of 2-methyl-5-phenylpyrrole was obtained (Table 2 entry 2). To explore the synthetic utility of this reaction, various β -amino alcohols were studied. A toluene solution containing 2-amino-3-methylpentan-1-ol (2 mmol), 1-phenylethanol, and catalyst **2** (0.01 mmol) was heated to reflux for 24 h, resulting in isolation of 2-(sec-butyl)-5-phenylpyrrole in good yield (67 %) after purification (Table 2 entry 3). Under the same conditions, coupling of the aminoalcohols 2-amino-3-methylbutan-1-ol, 2-amino-3-phenylpropan-1-ol, 2-amino-4-methylpentan-1-ol, and 2-amino-2-phenylethanol with 1-phenyl ethanol resulted in isolation of the corresponding desired pyrroles 2-isopropyl-5-phenylpyrrole (83 %), 2-benzyl-5-phenylpyrrole (85 %), 2-isobutyl-5-phenylpyrrole (78 %), and 2,5-diphenylpyrrole (62 %) in good yields (Table 2, entries 4–7).

Next, the scope with regard to the secondary alcohol was studied. In case of 2-octanol, formation of two regioisomers is possible. Deprotonations at the less hindered side gave 2-benzyl-5-hexylpyrrole as the major product in 82 % yield, (a very small amount of the other pyrrole isomer was also observed by 1H NMR spectroscopy). Although selective primary C-alkylation was observed here, C-alkylation can also take place at a secondary aliphatic carbon atom, thereby resulting in the conversion of cyclic secondary alcohols to bicyclic pyrroles. Thus, coupling of cycloheptanol, cyclohexanol, and cyclopentanol with 1-phenyl ethanol resulted in the desired bicyclic pyrrole in moderate yields (Table 2, entries 9–11). Finally the coupling between 2-amino-1-butanol and 1-phenylethanol was repeated on a 10 mmol scale without affecting the yield, thus indicating that the reaction can be scaled up without difficulty.

To gain mechanistic insight, a toluene solution containing equimolar amounts of 1-phenylethanol and 2-amino-1-butanol was heated to reflux for 1 h in the presence of catalyst **1** (0.5 mol %), in the absence of *t*BuOK, resulting in formation of acetophenone (95 %) and unreacted 2-amino-1-butanol, as analyzed by GC–MS. In addition, 2-[(1-phenylethylidene)amino]butan-1-ol (Scheme 2, **A**, $R^1 = Et$, $R^2 = Ph$) was prepared by the condensation of acetophenone and 2-aminobutanol^[12] and heated to reflux in toluene in the presence of **2** (0.5 mol %) and *t*BuOK resulting in the product 2-ethyl-5-phenylpyrrole, whereas using only *t*BuOK failed to produce the same under reflux in toluene. Thus, we suggest

Table 2: Pyrrole synthesis using various amino alcohols and secondary alcohols catalyzed by the Ru pincer complex **2**.^[a]

$\text{R}^1\text{-CH(OH)-CH}_2\text{NH}_2 + \text{R}^2\text{-CH(OH)-CH}_3 \xrightarrow[\text{-2 H}_2, \text{-2 H}_2\text{O}]{\text{Cat. 2, Toluene, reflux, 24 h, KOtBu}}$				
Entry	Alcohol	Aminoalcohol	Product	Yield [%] ^[b]
1				75
2				71
3				67
4				83
5				85
6				78
7				62
8				82
9				50
10				59
11				55

[a] Reaction conditions: β -aminoalcohols (2 mmol), secondary alcohols (2 mmol), KOtBu (1 mmol), catalyst (0.5 mol%) were heated in 2 mL toluene at reflux. [b] Yields of the isolated products.

that O–H activation of the secondary alcohol by complex **1** (in situ generated by deprotonation of **2**), resulting in aromatization of the pincer complex, occurs first. Then H₂ liberation leads to formation of the corresponding ketone. A sequence involving nucleophilic attack by the amine group of the β -amino alcohol molecule on the ketone to produce an imine intermediate, subsequent dehydrogenation of the alcohol part, and condensation under basic conditions eventually lead to the desired pyrrole product.

In summary, a general method for pyrrole synthesis was achieved by selective and successive C–N and C–C bond formations catalyzed by 0.5 mol % of the dearomatized PNN ruthenium complex **1**, which can be formed in situ by using the air-stable complex **2** and a base. We believe that this environmentally friendly, atom-economical, and efficient dehydrogenative condensation protocol is attractive for the preparation of a diverse range of pyrroles, using readily available starting materials under mild conditions.

Experimental Section

Complex **2** (0.01 mmol), amino alcohol (2 mmol), secondary alcohol (2 mmol), KOtBu (1 mmol), and toluene (2 mL) were added to a Schlenk flask in an atmosphere of nitrogen in a Vacuum Atmospheres glovebox. The flask was equipped with a condenser, and the solution was refluxed with stirring in an open system under argon at 135 °C (oil bath temperature). The reaction products were analyzed by GC–MS. After cooling to room temperature, the reaction mixture was quenched with water and extracted three times with diethylether. Pure pyrroles were obtained either by Kugelrohr distillation or by column chromatography. Characterization data is available in the Supporting Information.

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- Recent references: a) V. Estévez, M. Villacampa, J. C. Menéndez, *Chem. Soc. Rev.* **2010**, 39, 4402; b) F. R. de Sa Alves, E. J. Barreiro, C. A. M. Fraga, *Mini-Rev. Med. Chem.* **2009**, 9, 782; c) H. Fan, J. Peng, M. T. Hamann, J.-F. Hu, *Chem. Rev.* **2008**, 108, 264; d) A. Hall, S. Atkinson, S. H. Brown, I. P. Chessell, A. Chowdhury, G. M. P. Giblin, P. Goldsmith, M. P. Healy, K. S. Jandu, M. R. Johnson, A. D. Michel, A. Naylor, J. A. Sweeting, *Bioorg. Med. Chem. Lett.* **2007**, 17, 1200; e) F. Bellina, R. Rossi, *Tetrahedron* **2006**, 62, 7213; f) F. Micheli, R. Di Fabio, R. Benedetti, A. M. Capelli, P. Cavallini, P. Cavanni, S. Davalli, D. Donati, A. Feriani, S. Gehanne, M. Hamdan, M. Maffei, F. M. Sabbatini, M. E. Tranquillini, M. V. A. Vizio, *Farmaco* **2004**, 59, 175.
- a) N. Amishiro, S. Nagamura, E. Kobayashi, A. Okamoto, K. Gomi, H. Saito, *Chem. Pharm. Bull.* **1999**, 47, 1393; b) N. Amishiro, S. Nagamura, E. Kobayashi, A. Okamoto, K. Gomi, M. Okabe, H. Saito, *Bioorg. Med. Chem.* **2000**, 8, 1637; c) V. J. Demopoulos, E. Rekka, *J. Pharm. Sci.* **1995**, 84, 79; d) R. W. Bürl, D. McMin, J. A. Kaizerman, W. Hu, Y. Ge, Q. Pack, V. Jiang, M. Gross, M. Garcia, R. Tanaka, H. E. Moser, *Bioorg. Med. Chem. Lett.* **2004**, 14, 1253; e) D. Wang, X. Hu, G. Zhao, *Int. J. Food Sci. Technol.* **2008**, 43, 1880; f) M. Del Poeta, W. A. Schell, C. C. Dykstra, S. Jones, R. R. Tidwell, A. Czarny, M. Bajic, A. Kumar, D. Boykin, J. R. Perfect, *Antimicrob. Agents Chemother.* **1998**, 42, 2495; g) M. Wang, H. Xu, T. Liu, Q. Feng, S. Yu, S. Wang, Z. Li, *Eur. J. Med. Chem.* **2011**, 46, 1463.
- a) P. Plüger, M. Krounbi, G. B. Street, G. Weiser, *J. Chem. Phys.* **1983**, 78, 3212; b) I. F. Gimenez, O. L. Alves, *J. Braz. Chem. Soc.* **1999**, 10, 167; c) J. R. Reynolds, P. A. Poropatic, R. L. Toyooka, *Macromolecules* **1987**, 20, 958; d) R. E. Nizurski-Mann, M. P. Cava, *Heterocycles* **1992**, 34, 2003; e) S. S. P. Chou, Y.-H. Yeh, *Tetrahedron Lett.* **2001**, 42, 1309; f) C. D'Silva, D. A. Walker, *J. Org. Chem.* **1998**, 63, 6715; g) B. P. J. de Lacy Costello, P. Evans,

- N. Guernion, N. M. Ratcliffe, P. S. Sivanand, G. C. Teare, *Synth. Met.* **2000**, *114*, 181.
- [4] a) A. W. Trautwein, R. D. Süßmuth, G. Jung, *Bioorg. Med. Chem. Lett.* **1998**, *8*, 2381; b) L. Calvo, A. González-Ortega, M. C. Sañudo, *Synthesis* **2002**, 2450; c) V. S. Matiychuk, R. L. Martyak, N. D. Obushak, Y. V. Ostapiuk, N. I. Pidlypnyi, *Chem. Heterocycl. Compd.* **2004**, *40*, 1218.
- [5] a) A. Alberola, A. G. M. L. Ortega, C. Sadaba, C. Sanudo, *Tetrahedron* **1999**, *55*, 6555; b) I. Elghamry, *Synth. Commun.* **2002**, *32*, 897; c) J. M. Manley, M. J. Kalman, B. G. Conway, C. C. Ball, J. L. Havens, R. J. Vaidyanathan, *J. Org. Chem.* **2003**, *68*, 6447; d) R. K. Bellingham, J. S. Carey, N. Hussain, D. O. Morgan, P. Oxley, L. C. Powling, *Org. Process Res. Dev.* **2004**, *8*, 279; e) C. M. Shiner, T. D. Lash, *Tetrahedron* **2005**, *61*, 11628.
- [6] a) R. A. Jones, G. P. Been, *The Chemistry of Pyrroles*, Academic Press, New York, **1977**, chap. 3; b) P. K. Chiu, K. H. Lui, P. N. Maini, M. P. Sammes, *J. Chem. Soc. Chem. Commun.* **1987**, 109; c) P. K. Chiu, M. P. Sannes, *Tetrahedron* **1990**, *46*, 3439; d) B. K. Banik, S. Samajdar, I. Banik, *J. Org. Chem.* **2004**, *69*, 213; e) J. Chen, H. Wu, Z. Zheng, C. Jin, X. Zhang, W. Su, *Tetrahedron Lett.* **2006**, *47*, 5383; f) G. Minetto, L. F. Raveglia, A. Segà, M. Taddei, *Eur. J. Org. Chem.* **2005**, 5277.
- [7] a) H. Shiraishi, T. Nishitani, S. Sakaguchi, Y. Ishii, *J. Org. Chem.* **1998**, *63*, 6234; b) Y. Nishibayashi, M. Yoshikawa, Y. Inada, M. D. Milton, M. Hidai, S. Uemura, *Angew. Chem.* **2003**, *115*, 2785; *Angew. Chem. Int. Ed.* **2003**, *42*, 2681; c) R. Dhawan, B. A. Arndtsen, *J. Am. Chem. Soc.* **2004**, *126*, 468; d) D. Tejedor, D. González-Cruz, F. García-Tellado, J. J. Marrero-Tellado, M. L. Rodríguez, *J. Am. Chem. Soc.* **2004**, *126*, 8390; e) Y. Yamamoto, H. Hayashi, T. Saigoku, H. Nishiyama, *J. Am. Chem. Soc.* **2005**, *127*, 10804; f) O. V. Larionov, A. Meijere, *Angew. Chem.* **2005**, *117*, 5809; *Angew. Chem. Int. Ed.* **2005**, *44*, 5664; g) D. J. St. Cyr, N. Martin, B. A. Arndtsen, *Org. Lett.* **2007**, *9*, 449; h) M. Shimizu, A. Takahashi, S. Kawai, *Org. Lett.* **2006**, *8*, 3585; i) I. Bergner, T. Opatz, *J. Org. Chem.* **2007**, *72*, 7083; j) C. V. Galliford, K. A. Scheidt, *J. Org. Chem.* **2007**, *72*, 1811; k) B. Khalili, P. Jajarmi, B. M. M. Eftekhari-SisHashemi, *J. Org. Chem.* **2008**, *73*, 2090; l) X. Chen, L. Hou, X. Li, *Synlett* **2009**, 828; m) E. Merkul, C. Boersch, W. Frank, T. J. J. Müller, *Org. Lett.* **2009**, *11*, 2269; n) Y. Lu, X. Fu, H. Chen, X. Du, X. Jia, Y. Liu, *Adv. Synth. Catal.* **2009**, *351*, 129.
- [8] a) C. A. Merlic, A. Baur, C. C. Aldrich, *J. Am. Chem. Soc.* **2000**, *122*, 7398; b) A. V. Kel'in, A. W. Sromek, V. Gevorgyan, *J. Am. Chem. Soc.* **2001**, *123*, 2074; c) R. U. Braun, K. Zeitler, T. J. J. Müller, *Org. Lett.* **2001**, *3*, 3297; d) H. Takaya, S. Kojima, S.-I. Murahashi, *Org. Lett.* **2001**, *3*, 421; e) Y. Wang, S. Zhu, *Org. Lett.* **2003**, *5*, 745; f) I. Nakamura, Y. Yamamoto, *Chem. Rev.* **2004**, *104*, 2127; g) B. Ramanathan, A. J. Keith, D. Armstrong, A. L. Odom, *Org. Lett.* **2004**, *6*, 2957; h) A. I. Siriwardana, K. K. A. D. S. Kathirarachchi, I. Nakamura, I. D. Gridnev, Y. Yamamoto, *J. Am. Chem. Soc.* **2004**, *126*, 13898; i) S. Kamijo, C. Kanazawa, Y. Yamamoto, *J. Am. Chem. Soc.* **2005**, *127*, 9260; j) D. J. Gorin, N. R. Davis, F. D. Toste, *J. Am. Chem. Soc.* **2005**, *127*, 11260; k) R. P. Wurz, A. B. Charette, *Org. Lett.* **2005**, *7*, 2313; l) R. Martín, M. R. Rivero, S. L. Buchwald, *Angew. Chem.* **2006**, *118*, 7237; *Angew. Chem. Int. Ed.* **2006**, *45*, 7079; m) J. F. Hartwig, *Synlett* **2006**, 1283; n) L. Lu, G. Chen, S. Ma, *Org. Lett.* **2006**, *8*, 835; o) J. T. Binder, S. F. Kirsch, *Org. Lett.* **2006**, *8*, 2151; p) K. Hiroya, S. Matsumoto, M. Ashikawa, K. Ogiwara, T. Sakamoto, *Org. Lett.* **2006**, *8*, 5349; q) D. J. S. Cyr, B. A. Arndtsen, *J. Am. Chem. Soc.* **2007**, *129*, 12366; r) F. M. Istrate, F. Gagosz, *Org. Lett.* **2007**, *9*, 3181; s) X.-Z. Shu, X.-Y. Liu, H.-Q. Xiao, K.-G. Ji, L.-N. Guo, Y.-M. Liang, *Adv. Synth. Catal.* **2008**, *350*, 243; t) A. Aponick, C.-Y. Li, J. Malinge, E. F. Marques, *Org. Lett.* **2009**, *11*, 4624; u) S. Maiti, S. Biswas, U. Jana, *J. Org. Chem.* **2010**, *75*, 1674; v) W. Liu, H. Jiang, L. Huang, *Org. Lett.* **2010**, *12*, 312; w) M. Zhang, H. Neumann, M. Beller, *Angew. Chem.* **2013**, *125*, 625; *Angew. Chem. Int. Ed.* **2013**, *52*, 597; x) N. D. Schley, G. E. Dobereiner, R. H. Crabtree, *Organometallics* **2011**, *30*, 4174.
- [9] a) J. Zhang, M. Gandelman, L. J. W. Shimon, D. Milstein, *Organometallics* **2004**, *23*, 4026; b) J. Zhang, G. Leitius, Y. Ben-David, D. Milstein, *J. Am. Chem. Soc.* **2005**, *127*, 10840; c) J. Zhang, G. Leitius, Y. Ben-David, D. Milstein, *Angew. Chem.* **2006**, *118*, 1131; *Angew. Chem. Int. Ed.* **2006**, *45*, 1113; d) C. Gunanathan, Y. Ben-David, D. Milstein, *Science* **2007**, *317*, 790; e) D. Milstein, *Top. Catal.* **2010**, *53*, 915; f) B. Gnanaprakasam, Y. Ben-David, D. Milstein, *Adv. Synth. Catal.* **2010**, *352*, 3169; g) B. Gnanaprakasam, D. Milstein, *J. Am. Chem. Soc.* **2011**, *133*, 1682; h) C. Gunanathan, D. Milstein, *Acc. Chem. Res.* **2011**, *44*, 588; i) D. Srimani, M. Feller, Y. Ben-David, D. Milstein, *Chem. Commun.* **2012**, 48, 11853.
- [10] a) C. Gunanathan, L. J. W. Shimon, D. Milstein, *J. Am. Chem. Soc.* **2009**, *131*, 3146; b) C. Gunanathan, D. Milstein, *Angew. Chem.* **2008**, *120*, 8789; *Angew. Chem. Int. Ed.* **2008**, *47*, 8661; c) C. Gunanathan, B. Gnanaprakasam, M. A. Iron, L. J. W. Shimon, D. Milstein, *J. Am. Chem. Soc.* **2010**, *132*, 14763.
- [11] B. Gnanaprakasam, J. Zhang, D. Milstein, *Angew. Chem.* **2010**, *122*, 1510; *Angew. Chem. Int. Ed.* **2010**, *49*, 1468.
- [12] D. Srimani, E. Balaraman, B. Ganaprakasam, Y. Ben-David, D. Milstein, *Adv. Synth. Catal.* **2012**, *354*, 2403.
- [13] B. Gnanaprakasam, E. Balaraman, Y. Ben-David, D. Milstein, *Angew. Chem.* **2011**, *123*, 12448; *Angew. Chem. Int. Ed.* **2011**, *50*, 12240.
- [14] S. Michlik, R. Kempe, *Nat. Chem.* **2013**, *5*, 140.
- [15] a) E. Balaraman, B. Ganaprakasam, L. J. W. Shimon, D. Milstein, *J. Am. Chem. Soc.* **2010**, *132*, 16756; b) E. Balaraman, C. Gunanathan, J. Zhang, L. J. W. Shimon, D. Milstein, *Nat. Chem.* **2011**, *3*, 609.