A New Access to 4*H*-Quinolizines from 2-Vinylpyridine and Alkynes Promoted by Rhodium-N-Heterocyclic Carbene Catalysts

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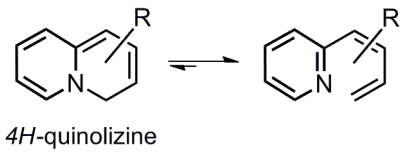
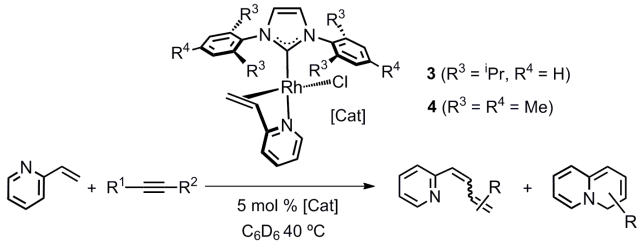
N-bridgehead heterocycles are prevalent in many natural and synthetic biologically active alkaloids.[1] The development of efficient synthetic methodologies for the preparation of these intricate structures has been the focus of intense research,[2] among which transition metal catalysts have played a preeminent role.[3] However, derivatives based on the quinolizine skeleton have received little attention, probably due to their instability, and are mainly limited to quinolizidine,[4] quinolizinium salts[5] or quinolizinone[6] compounds. Indeed, 4*H*-quinolizines are very scarce,[7] particularly the 4-unsubstituted counterparts,[8] and are usually involved in a tautomeric equilibrium with the corresponding butadienylpyridine derivatives (Scheme 1).[9] Interestingly, we have now observed that the process can be shifted towards the quinolizine tautomer depending on the presence and position of certain substituents on the dienyl fragment. However, a straightforward and general method for the preparation of butadienylpyridines is still an important challenge for which organometallic catalysts emerge as a crucial node, as they can potentially achieve this task from 2-vinylpyridine and alkynes through sequential C-H activation and C-C coupling reactions.[10] Particularly, we have been interested in the design of rhodium catalysts based on N-heterocyclic carbenes (NHCs)[11] for new C-C and C-X bond forming reactions.[12] Now, we have discovered that rhodium catalysts bearing NHC ligands give access to the elusive 4*H*-quinolizines with total atom economy under mild conditions.



Scheme 1. Tautomerization of 4*H*-quinolizines.

Our research group has recently reported that isolable mononuclear Rh-NHC species can be obtained by N-donor ligand promoted bridge cleavage reaction of the corresponding dimer.[12c] Similarly, we have now observed that the treatment of $[Rh(\mu\text{-Cl})(NHC)(\eta^2\text{-coe})]_2$ (NHC = IPr (**1**), IMes (**2**); coe = cyclooctene; IPr = 1,3-bis-(2,6-diisopropylphenyl)imidazol-2-carbene; IMes = 1,3-bis-(2,4,6-trimethylphenyl)imidazol-2-carbene) with 2-vinylpyridine afforded $RhCl(NHC)(\kappa\text{-N},\eta^2\text{-}CH_2{=}CHC_5H_4N)$ (NHC = IPr (**3**), IMes (**4**)) in good yields (see Supporting Information for synthetic details and NMR data). The chelating coordination of vinylpyridine is corroborated by an upfield shift for the olefinic protons (3.39-2.13 ppm) and the occurrence of $J_{C\text{-}Rh}$ coupling for the carbon atoms of the alkenyl fragment (16-12 Hz) in the ^1H and $^{13}C\{^1H\}$ NMR spectra, respectively.

It has been previously described that rhodium-phosphane catalysts promote efficiently the C-C coupling between alkenylpyridines and olefins,[13] though the coupling with alkynes has not been reported up to date. Now, we have discovered that the introduction of an NHC ligand in complexes **3** and **4** allow for the straightforward preparation of butadienylpyridines from 2-vinylpyridine and alkynes (Scheme 2). Indeed, it is noticeable the ability of **3**-**4** to involve terminal alkynes in these type of transformation without the observation of competitive dimerization or polymerization processes.



Scheme 2. C-C coupling reactions mediated by Rh-NHC catalysts.

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Catalytic reactions were carried out in an NMR tube in C_6D_6 using a 1:1 pyridine:alkyne ratio. Preliminary tests with phenylacetylene under the optimized conditions, 40 ºC at 5 mol % catalyst loading, showed that **4** was slightly more active than **3** (see table S1 in supporting information). Initially, it was observed the formation of (1*Z*,3*E*)-2-(4-phenylbuta-1,3-dien-1-yl)pyridine (Figure 1), however, unexpectedly it was accompanied with a new set of resonances that were unequivocally ascribed to 3-phenyl-4*H*-quinolizine (see below). The formation of this product may arise from a 6π electrocyclization involving the two conjugated double bonds and one C=N of the pyridine moiety within an

undetected (1*Z*,3*gem)*-butadienylpyridine species. Similar transformation has been previously observed for conjugated imines[14] or oximes[15] but dearomatization of a pyridine moiety is considerably more challenging.[16] The similar initial rate for the formation of both organic products points out to a lack of regioisomeric preference in the C-C coupling process, but the (1*Z*,3*E*)-butadienylpyridine product smoothly isomerizes to produce the (1*E*,3*E*) derivative. A conversion of 97% was reached after 4 h with a $TOF_{1/2}$ value of 35 h^{-1} calculated at 50 % conversion of vinylpyridine. It is noticeable that the formation of 4-phenyl-4*H*-quinolizine was not detected. Both butadienylpyridine isomers were isolated by column chromatography methods but, unfortunately, the quinolizine derivative could not be recovered despite several attempts under different conditions.[14c]

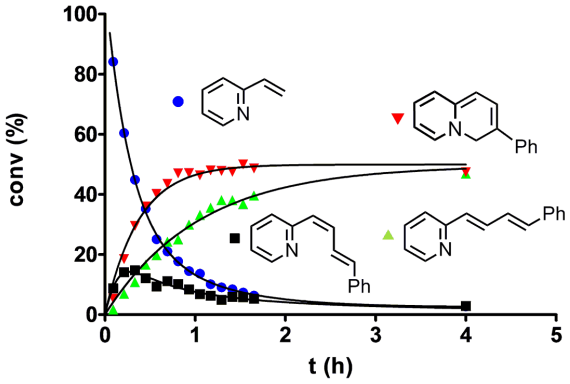


Figure 1. Monitoring of the reaction between 2-vinylpyridine and phenylacetylene catalyzed by **4** in C_6D_6 at 40 ºC.C-C coupling reactions mediated by Rh-NHC catalysts.

The nature of the new organic product as 3-phenyl-4*H*-quinolizine was confirmed by multinuclear NMR experiments. A striking feature of the ^{1}H NMR spectrum is an unusual set of resonances at higher field (6.6-4.9 ppm) compared to that corresponding to aromatic protons, which is fully consistent with the presence of non-aromatic bicyclic system. The 4*H*-quinolizine structure was further confirmed by HSQC and HMBC ^{1}H-^{13}C experiments. Remarkably, the methylene fragment at 4-positon of the quinolizine skeleton was observed as a singlet at 4.38 ppm. Moreover, long range HSQC ^{1}H-^{15}N correlation confirms the presence of a N-bridgehead heterocycle (Figure 2) with a $\delta(^{15}N)$ of 117.5 ppm, which falls within the typical range for a trisubstituted amine. In sharp contrast, the (1*E*,3*E*)-butadienylpyridine compound was observed at 309.8 ppm.

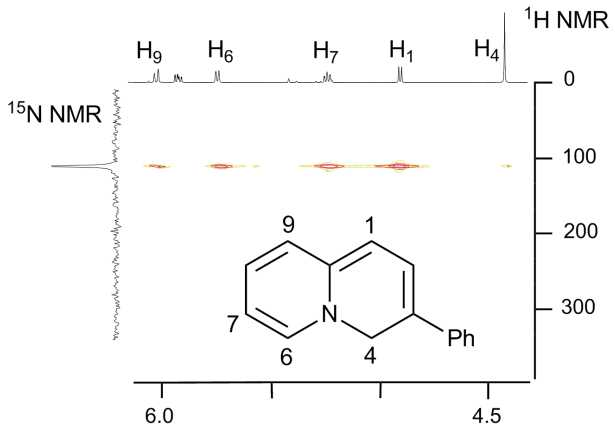
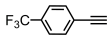
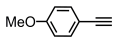
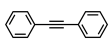


Figure 2. ^{1}H-^{15}N NMR correlation spectrum for a 4*H*-quinolizine.

Catalyst **4** is a versatile precursor for coupling reactions between 2-vinylpyridine and diverse terminal and internal alkynes (Table 1). Aromatic terminal alkynes reacted faster than aliphatic ones and with higher selectivity to 4*H*-quinolizine (entries 1-3 *vs* 4-6). Isomerization of the internal double bond from *Z* to *E* occurred also faster for aromatic than aliphatic substituted dienyl derivatives. The presence of an electron-withdrawing substituent on the phenyl ring increased the rate whereas selectivity to the N-bridgehead heterocycle decreased for both, electron-donating or -withdrawing groups (entries 1-3).

Table 1. Coupling reaction between 2-vinylpyridine and alkynes[a]

Entry	substrate	t(h)	4*H*-*q*[b]	*Z*-*E*[c]	*E*-*E*[c]	*Z*-*g*[d]	*E*-*g*[d]	vipy[e]	$TOF_{1/2}(h^{-1})$
1		4	48	3	46	-	-	3	35
2		1	43	2	48	-	-	7	51
3		6	36	16	31	8	-	8	29
4		5	7	37	-	45	10	1	26
5		9	9	39	-	38	11	3	23
6		20	7	74	2	14	-	2	4
7		14	16	47	-	-	-	37	3
8		14	51	36	12	-	-	1	15
9		12	23	69	6[f]	-	-	2	3
10		3	45[g]	25[h]	23[h]	-	-	6	18

[a]0.5 mL of C_6D_6 with 5 mol % of catalyst at 40 ºC; [subs] = 1M. [b]4*H*-quinolizine; ratio of ^{1}H NMR integration. [c]2-(buta-1,3-dien-1-yl)pyridine. [d]gem. [e]unreacted 2-vinylpyridine. [f]*E*-*Z* isomer. [g]4-methyl. [h]4-phenyl.

The presence of bulky substituents in aliphatic alkynes reduced the activity (entries 6-7). It is noticeable that the key (1*Z*,3*gem*)-butadienylpyridine isomers were detected for aliphatic alkynes, and consequently, the conversion to 3-R-4*H*-quinolizine is lower, which suggests that the tautomerization is disfavored in these cases.[17] Monitoring of the reaction showed that the initially formed *Z*-*gem*-butadienylpyridine isomerizes to *E*-*gem* derivatives and tautomerizes to the 4*H*-quinolizine compounds (Figure 3). It is worthy of note that for aliphatic alkynes the isomerization of 1*Z*,3*E* to 1*E*,3*E* butadienylpyridines was not detected under catalytic conditions.[18] Internal alkynes reacted

smoothly (entries 8-10). The configuration of the conjugated double bonds of the butadienyl products was confirmed by ^{1}H-NOE NMR experiments (see Supporting Information). In the case of 3-hexyne, the formation of the 1*Z*,3*E* derivative was initially observed with subsequent isomerization to 1*E*,3*E* and 4*H*-quinolizine compounds. However, diphenylacetylene behaved somewhat different. The initial rate for the 4*H*-quinolizine formation was higher but the N-heterocycle experimented a reopening to afford the (1*Z*,3*E*)-2-(3,4-diphenylbuta-1,3-dien-1-yl)pyridine derivative with both phenyl groups disposed mutually *trans* (Figure 4). Dissymmetric 1-phenyl-1-propyne gave exclusively 4-methyl-3-phenyl-4*H*-quinolizine and 2-(3-methyl-4-phenylbuta-1,3-dien-1-yl)pyridine.

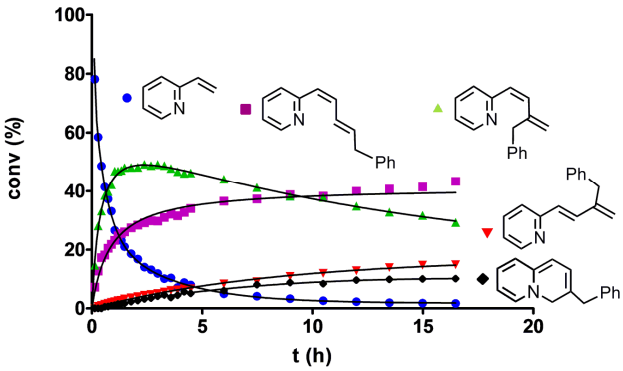


Figure 3. Monitoring of the reaction between 2-vinylpyridine and 3-phenyl-1-propyne catalyzed by **4** in C_6D_6 at 40 ºC.

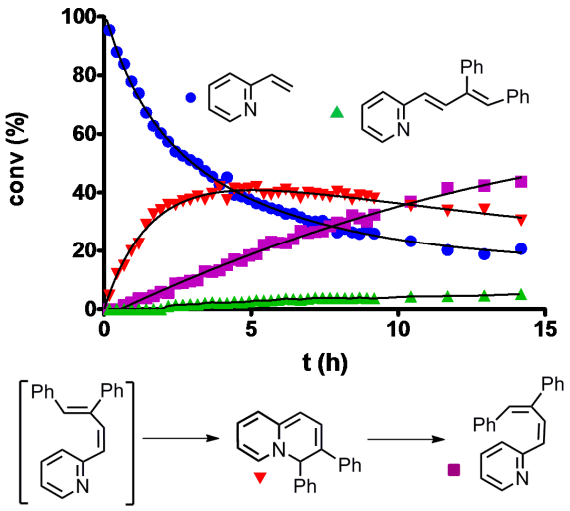


Figure 4. Monitoring of the reaction between 2-vinylpyridine and diphenylacetylene catalyzed by **4** in C_6D_6 at 40 ºC. DFT calculated ΔG (Kcal.mol^{-1}) for the tautomerization butadienylpyridine↔4*H*-quinolizine.

Scheme 3 shows a plausible mechanism for the formation of the 3-R-4*H*-quinolizine compounds. Initially, the activation of a terminal C-H bond of the 2-vinylpyiridine to generate rhodium-alkenyl-hydride species is proposed.[19] The subsequent coordination of the alkyne, migratory insertion and reductive elimination should generate both (1*Z*,3*E*)- or (1*Z*,3*gem*)-butadienyl-pyridine products depending on the regioselectivity. In both cases, the Z configuration of the internal double bond is kinetically favored if a concerted insertion mechanism is assumed. Then, formation of 4*H*-quinolizine skeletons can be rationalized via a metal-mediated or thermal electrocyclization. To shed light on this point, a solution of pure *Z-gem* isomer, (*Z*)-2-(3-benzylbuta-1,3-dien-1-yl)pyridine, in C_6D_6 was heated at 60 ºC. Monitoring of the reaction by NMR evidenced the smoothly formation of the 4*H*-quinolizine isomer, thus, pointing to a thermal activated cyclization process. In fact, an equilibrium mixture of 75/25, butadienylpyridine/heterocycle, was reached after 3 h, which was corroborated by the exchange peaks observed in the ^{1}H-NOE NMR spectrum at 80 ºC. It is noticeable that the formation of the *E-gem* regioisomer was not observed indicating that metal catalyst accounts for the *Z* to E isomerization of the internal double bond. A *cisoidal* configuration of the conjugated double bonds is essential for the electrocyclic reaction to take place, thus isomerization of the internal double bond a handicap to be overcome. A similar equilibrium mixture was observed after heating the (1*Z*,3*E*)-butadienylpyridine obtained from 3-hexyne, but in this case the equilibrium is further shifted to the quinolizine compound in 60/40 molar ratio.

Insert Scheme 3

Scheme 3. Plausible mechanism for the formation of 4*H*-quinolizine derivatives mediated by **4**.

Theoretical calculations (DFT/m06-2x/Kcal·mol^{-1}) for the thermodynamics of the tautomerization process were performed. In full agreement with experimental results, it was found that 3-phenyl-4*H*-quinolizine is 1.83 Kcal·mol^{-1} more stable than *Z-gem*-butadienylpyridine whereas the formation of 4-phenyl-4*H*-quinolizine from the (1*E*-3*Z*)-butadienylpyridine isomer is disfavored by 2.04 Kcal·mol^{-1} (Figure 5). On the other hand, the calculated energies for diphenylacetylene were also in agrement with the experimental results. Although the 4*H*-quinolizine is 3.24 Kcal·mol^{-1} more stable than the (1*Z*,3*Z*)-butadienylpyridine isomer, not detected in the catalytic reaction, tautomerization to the (1*Z*,3*E*) counterpart is also slightly favored (-0.68 Kcal·mol^{-1}), thus explaining the smoothly tautometization observed experimentally (Figure 4).

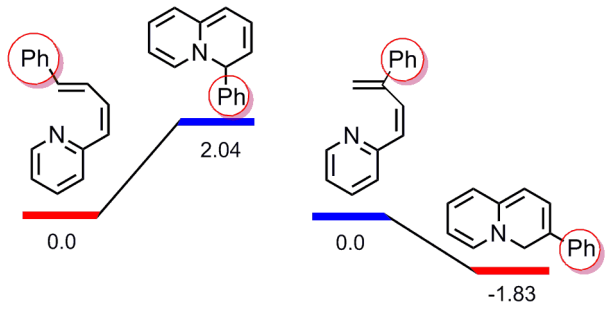


Figure 5. Thermodynamic DFT-calculated free energies (ΔG, Kcal·mol^{-1}) for the tautomerization butadienylpyridine↔quinolizine.

In conclusion, we have described the outstanding catalytic performance in C-C coupling reactions of new Rh-NHC catalyst leading to the formation of 4*H*-quinolizine derivatives under mild conditions with total atom economy. We have shown that the thermal 6π electrocyclization process leading to the formation of

N-bridgehead heterocycles is favored for internal- versus terminal-substituted butadienylpiridine derivatives. The design of improved catalysts for selective Z-*gem*-butadienylpyridine formation and reduced Z to E isomerization of the internal double bond is ongoing in our laboratories.

Experimental Section

Synthesis of catalysts. **3:** A yellow solution of **1** (300 mg, 0.235 mmol) in 10 mL of toluene was treated with 2-vinylpyridine (50 µL, 0.470 mmol) and was stirred at room temperature for 1 h. After filtration through Celite the solvent evaporated to dryness. Addition of hexane caused precipitation of a yellow solid, which was washed with hexane (3 x 4 mL) and dried in vacuo. Yield: 250 mg (84%). Anal. Calcd. for $C_{34}H_{43}N_3ClRh$: C, 64.61; H, 6.86; N, 6.65. Found: C, 64.92; H, 6.89; N, 6.62. **4:** The complex was prepared as described for **3** starting from **2** (300 mg, 0.271 mmol) and 2-vinylpyridine (58 µL, 0.542 mmol). Yield: 260 mg (87%). Anal. Calcd for $C_{29}H_{35}N_3ClRh$: C, 61.38; H, 5.70; N, 7.67. Found: C, 61.05; H, 5.80; N, 7.26.

Standard procedure for the catalytic C-C coupling between 2-vinylpyridine and alkynes. A NMR tube containing a solution of 0.025 mmol of catalyst in 0.5 mL of C_6D_6 was treated with 0.5 mmol of 2-vinylpyridine and 0.5 mmol of the alkyne and heated at 40ºC. The reaction course was monitored by NMR and the conversion determined by integration of the corresponding resonances in the ^{1}H NMR spectra of 2-vinylpyridine and the products.

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Keywords: quinolizine · N-heterocyclic carbene · C-C coupling · C-H activation · Electrocyclization

[1] a) J. P. Michael, *Nat. Prod. Rep.* **2008**, *25*, 139; b) H. -F. Ji, L. Shen, *Molecules* **2011**, *16*, 6732; c) R. A. Saporito, M. A. Donelly, T. F. Spande, H. M. Garraffo, *Chemoecology* **2012**, *22*, 159.

[2] a) S. F. Martin, *Pure Appl. Chem.* **2009**, *81*, 195; b) *Modern Heterocyclic Chemistry*, Vol. 4 (Eds: J. Alvarez-Builla, J. J. Vaquero, J. Barluenga), WILEY-VCH, Weinheim, **2011**; c) H. T. Pham, I. Chataigner, J.-L. Renaud, *Curr Org. Chem.* **2012**, *16*, 1754.

[3] a) J. A. Varela, C. Saa, *Chem. Rev.* **2003**, *103*, 3787; b) I. Nakamura, Y. Yamamoto, *Chem. Rev.* **2004**, *104*, 2127; c) D. M. D'Souza, T. J. J. Müller, *Chem. Soc. Rev.* **2007**, *36*, 1095; d) S. Perreault, T. Rovis, *Chem. Soc. Rev.* **2009**, *38*, 3149.

[4] a) W. E. Doëring, R. A. N. Weil, *J. Am. Chem. Soc.* **1947**, *69*, 2461; b) K. A. Tehrani, M. D'hooghe, N. De Kimpe *Tetrahedron* **2003**, *59*, 3099; c) C. Tsukano, A. Oimura, I. Enkhtaivan, Y. Takemoto, *Org. Lett.* **2012**, *14*, 1902; d) L. Liu, L. Zhang, *Angew. Chem. Int. Ed.* **2012**, *51*, 7301.

[5] a) B. S. Thyagarajan, *Adv. Heterocycl. Chem.* **1965**, *5*, 291; b) C. Sotiriou-Leventis, A. -M. M. Rawashdeh, W. S. Oh, N. Leventis, *Org. Lett.* **2002**, *4*, 4113; c) A. Nuñez, B. Abarca, A. M. Cuadro, J. Alvarez-Builla, J. J. Vaquero, *J. Org. Chem.* **2009**, *74*, 4166; d) M. Tian, H. Ihmels, S. Ye, *Org. Biomol. Chem.* **2012**, *10*, 3010.

[6] a) V. Boekelheide, C. -T. Liu, *J. Am. Chem. Soc.* **1952**, *74*, 4920; b) A. Schwartz, Z. Pál, L. Szabo, K. Simon, I. Hermecz, Z. Mészáros, *J. Heterocycl. Chem.* **1987**, *24*, 645; c) M. Hagimori, S. Matsui, N. Mizuyama, K. Yokota, J. Nagaoka, Y. Tominaga, *Eur. J. Org. Chem.* **2009**, 5847; d) S. Mochida, N. Umeda, K. Hirano, T. Satoh, M. Miura, *Chem. Lett.* **2011**, *39*, 744.

[7] a) O. Diels, K. Alder, *Liebigs Ann. Chem.* **1932**, *498*, 16; b) R. M. Acheson, G. A. Taylor, *J. Chem. Soc.* **1960**, 1691; c) W. K. Gibson, D. Leaver, *J. Chem. Soc.* **1966**, 324; d) T. N. Grant, C. L. Benson, F. G. West, *Org. Lett.* **2008**, *10*, 3985.

[8] R. M. Acheson, S. J. Hodgson, R. G. M. Wright, *J. Chem. Soc., Perkin Trans. 1* **1976**, 1911.

[9] a) V. Boekelheide, W. G. Gall, *J. Am. Chem. Soc.* **1954**, *76*, 1832; T. Miyadera, E. Ohki, I. Iwai, *Chem. Pharm. Bull.* **1964**, *12*, 1344; c) T. Miyadera, Y. Kishida, *Tet. Lett.* **1969**, *25*, 397; d) G. G. Abbot, D. Leaver, K. C. Mathur, *J. Chem. Res.* **1978**, 224

[10] a) F. Kakiuchi, S. Murai, *Acc. Chem. Res.* **2002**, *35*, 826; b) V. Ritleng, C. Sirling, M. Pfeffer, *Chem. Rev.* **2002**, *102*, 1731; c) Y. J. Park, J. -W. Park, C. -H. Jun, *Acc. Chem. Res.* **2008**, *41*, 222; d) D. A. Colby, R. G. Bergman, J. A. Ellman, *Chem. Rev.* **2010**, *110*, 624; e) T. W. Lyons, M. S. Sanford, *Chem. Rev.* **2010**, *110*, 1147; f) P. B. Arockiam, C. Bruneau, P. H. Dixneuf, *Chem. Rev.* **2012**, *112*, 5879.

[11] a) W. Hermann, *Angew. Chem. Int. Ed.* **2002**, *41*, 1290; b) S. Würtz, F. Glorius, *Acc. Chem. Res.* **2008**, *41*, 1523; c) J. M. Praetorius, C. M. Crudden, *Dalton Trans.* **2008**, 4079; d) S. Díez-González, N. Marion, S. P. Nolan, *Chem. Rev.* **2009**, *109*, 3612.

[12] a) M. V. Jiménez, J. J. Pérez-Torrente, V. I. Bartolomé, V. Gierz, F. J. Lahoz, L. A. Oro, *Organometallics* **2008**, *27*, 224; b) A. Di Giuseppe, R. Castarlenas, J. J. Pérez-Torrente, F. J. Lahoz, V. Polo, L. A. Oro, *Angew. Chem. Int. Ed.* **2011**, *50*, 3938; c) L. Palacios, X. Miao, A. Di Giuseppe, S. Pascal, C. Cunchillos, R. Castarlenas, J. J. Pérez-Torrente, F. J. Lahoz, P. H. Dixneuf, L. A. Oro, *Organometallics* **2011**, *30*, 5208; d) A. Di Giuseppe, R. Castarlenas, J. J. Pérez-Torrente, M. Crucianelli, V. Polo, R. Sancho, F. J. Lahoz, L. A. Oro, *J. Am. Chem. Soc.* **2012**, *134*, 8171; e) G. Lázaro, M. Iglesias, F. J. Fernández-Alvarez, P. J. Sanz-Miguel, J. J. Pérez-Torrente, L. A. Oro, *ChemCatChem*, *In press* DOI:10.1002/cctc.201200309.

[13] a) N. Fujii, F. Kakiuchi, N. Chatani, S. Murai, *Chem. Lett.* **1996**, *25*, 939; b) Y. -G. Lin, J. -B. Kang, Y. H. Kim, *Chem. Commun.* **1996**, 585; c) N. Fujii, F. Kakiuchi, A. Yamada, N. Chatani, S. Murai, *Chem. Lett.* **1997**, *26*, 425; d) Y. -G. Lin, J.-B. Kang, K. Lee, Y. H. Kim, *Heteroatom Chem.* **2002**, *13*, 346; e) P. Buskens, D. Giunta, W. Leitner, *Inorg. Chim. Acta* **2004**, *357*, 1969.

[14] a) I. Hasan, F. W. Fowler, *J. Am. Chem. Soc.* **1978**, *100*, 6696; b) C. Cao, Y. Li, Y. shi, A. L. Odom, *Chem. Commun.* **2004**, 2002; c) D. A. Colby, R. G. Bergman, J. A. Ellman, *J. Am. Chem. Soc.* **2008**, *130*, 3645; d) T. Kobayashi, K. Takeushi, J. Miwa, H. Tsuchikawa, S. Katsumura, *Chem. Commun.* **2009**, 3363; e) H. Wei, Y. Wang, B. Yue, P. -F. Xu, *Adv. Synth. Catal.* **2010**, *352*, 2450; f) K. Tanaka, K. Fukase, S. Katsumura *Synlett* **2011**, 2115; g) S. Duttwyler, C. Lu, A. L. Rheingold, R. G. Bergman, J. A. Ellman, *J. Am. Chem. Soc.* **2012**, *134*, 4064.

[15] a) M. L. Meketa, S. M. Weinreb, Y. Nakao, N. Fusetani, *J. Org. Chem.* **2007**, *72*, 4892; b) K. Parthasarathy, M. Jeganmohan, C. -H. Cheng, *Org. Lett.* **2008**, *10*, 325; c) K. Kohno, S. Azuma, T. Choshi, J. Nobuhiro, S. Hibino, *Tet. Lett.* **2009**, *50*, 590; d) R. M. Martin, R. G. Bergman, J. A. Ellman, *J. Org. Chem.* **2012**, *77*, 2501.

[16] a) H. Wang, Y. Wang, C. Peng, J. Zhang, Q. Zhu, *J. Am. Chem. Soc.* **2010**, *132*, 13217; b) S. P. Roche, J. A. Porco Jr., *Angew. Chem. Int. Ed.* **2011**, *50*, 4068.

[17] Although other metal catalysts promote the formation of *Z-Z* butadienylpyridines, the presence of quinolizine tautomers has not been detected: a) Y. Nakao, K. S. Kanyiva, T. Hiyama, *J. Am. Chem. Soc.* **2008**, *130*, 2448; b) Y. Kuninobu, Y. Fujii, T. Matsuki, Y. Nishina, K. Takai, *Org. Lett.* **2009**, *11*, 2711.

[18] A pure sample of 2-((1*Z*,3*E*)-5-phenylpenta-1,3-dien-1-yl)pyridine in the presence of 5 mol% of **4** gave 33 mol% of the (*E*,*E*) isomer after 16 h at 80 ºC.

[19] a) G. Jia, D. W. Meek, G. C. Galluci, *Organometallics* **1990**, *9*, 2549; b) R. Castro-Rodrigo, M. A. Esteruelas, S. Fuertes, A. M. López, S. Mozo, E. Oñate, *Organometallics* **2009**, *28*, 5941.