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Nickel-Catalyzed Highly Selective Hydrovinylation of α-Ketals of Vinylarenes

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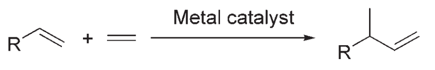
Abstract: A nickel-catalyzed hydrovinylation of α-ketal derivatives of vinylarenes has been developed, providing a new method for preparing functional olefins with a quarternary carbon center in high yields and selectivities.

Keywords: C−C bond formation; functionalized olefins; hydrovinylation; nickel

Carbon-carbon bond formation is the essence of organic synthesis and provides the foundation for generating complicated organic compounds from simpler ones. The transition metal-catalyzed hydrovinylation reaction (Scheme 1), the addition of a vinyl group and a hydrogen atom across a double bond, is an atom-economical carbon-carbon bond formation reaction.[1] Owing to the abundant availability of starting materials the hydrovinylation reacion has received increasing attention in the fine chemical and pharmaceutical industries. In the past decades, several transition metal catalysts have been developed for hydrovinylation of unfunctionalized olefins such as vinylarenes, α-alkylvinylarenes, strained olefins and 1,3-dienes.[2] However, the examples of successful hydrovinylation of functionalized olefins, which would provide synthetically useful multifunctional compounds, are limited. In 1965, Alderson and co-workers[3] reported a hydrovinylation of methyl acrylate catalyzed by rhodium or ruthenium at high temperature and obtained a mixture of hydrovinylation product and the dimer of methyl acrylate. In the ruthenium hydride complex-catalyzed hydrovinylation of α,β-unsaturated ketones and esters Yi et al.[4] gained the hydrovinylation products with a double bond migration. Palladium[5] and nickel[6] catalysts with different ligands were also tested in the hydrovinylation of various functionalized olefins, however, low conversions or poor selectivities were generally obtained. As part of an effort to search for efficient catalysts for the hydrovinylation of functionalized olefins, herein we report a highly selective nickel-catalyzed hydrovinylation of α-ketal derivatives of vinylarenes.

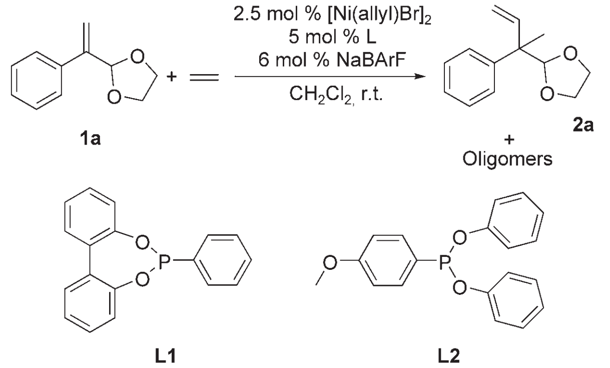


Scheme 1.

The hydrovinylation of 2-(1-phenylvinyl)-1,3-dioxolane (**1a**) was performed in CH_2Cl_2 at room temperature using a nickel catalyst generated *in situ* from 2.5 mol% $[Ni(allyl)Br]_2$, 5 mol% ligand, and 6 mol% NaBArF.[7] Firstly, the effect of phosphorus ligands was examined. With the ligand PPh_3, a 90% conversion with 75% yield of hydrovinylation product (selectivity) and oligomers[8] were obtained (Table 1, entry 1). Very high selectivity (98%) was achieved by using the electron-rich trialkylphosphine ligand $P(n\text{-}Bu)_3$, but the conversion of reaction was low (40%) (entry 2). The negligible conversion in the reaction with the ligand PCy_3 indicated that a sterically hindered phosphine ligand is unfavourable for the hydrovinylation of **1a** (entry 3). Systematic modification of the ligand PPh_3 revealed that the phosphonite **L2** was the best choice of ligand, affording the hydrovinylation product in full conversion and 97% selectivity (entry 8). Use of two equivalents of ligand **L2** or one equivalent of a bidentate phosphine ligand such as dppe[9] impeded the reaction, which showed that the active catalyst provides only one coordinating site for the ligand in the nickel-catalyzed hydrovinylation reaction.[1] The presence of the additive NaBArF is necessary for the current reaction. No conversion was observed in the hydrovinylation of **1a** without NaBArF.

Various α-ketal derivatives of vinylarenes were examined to extend the substrate scope of the reaction.

Table 1. Ni-catalyzed hydrovinylation with different ligands.[a]

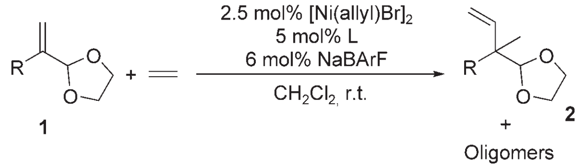


Entry	Ligand	Time [h][b]	Conv. [%][b]	Select. [%][b]
1	PPh_3	4	90	75
2	$P(nBu)_3$	4	40	98
3	PCy_3	4	<5	-
4	$PPh_2(OPh)$	2	96	94
5	$PPh(OPh)_2$	2	99	93
6	$P(OPh)_3$	2	100	78
7	**L1**	2	91	97
8	**L2**	2	100	97

[a] *Reaction conditions:* [Ni] (0.04 mmol), ligand (0.04 mmol), NaBArF (0.048 mmol), **1a** (0.8 mmol), ethylene (1 atm), CH_2Cl_2 (5 mL).

[b] Determined by GC with HP-5 column.

Table 2. Ni-catalyzed hydrovinylation of α-ketal derivatives of vinylarenes.[a]



Entry	Substrate	Products	Yield [%][b]	Select. [%][c]
1	R = Ph **1a**	**2a**	94	97
2	R = 4-MeC_6H_4 **1b**	**2b**	92	96
3	R = 4-$MeOC_6H_4$ **1c**	**2c**	83	95
4	R = 4-ClC_6H_4 **1d**	**2d**	89	92
5	R = 4-BrC_6H_4 **1e**	**2e**	82	82
6	R = 4-FC_6H_4 **1f**	**2f**	91[d]	76
7	R = 4-PhC_6H_4 **1g**	**2g**	88	93
8	R = 3-$MeOC_6H_4$ **1h**	**2h**	87	88
9	R = 3-ClC_6H_4 **1i**	**2i**	88[d]	83
10	R = 3-BrC_6H_4 **1j**	**2j**	91	96
11	R = 3,4-diMeC_6H_3 **1k**	**2k**	83	95
12	R = 2-naphthyl **1l**	**2l**	87	97

[a] The reaction conditions were the same as those in Table 1, entry 8. All reactions were completed within 3 h unless otherwise noted. For details of operation and analysis, see Supporting Information.

[b] Isolated yield.

[c] Determined by GC (HP-5 column).

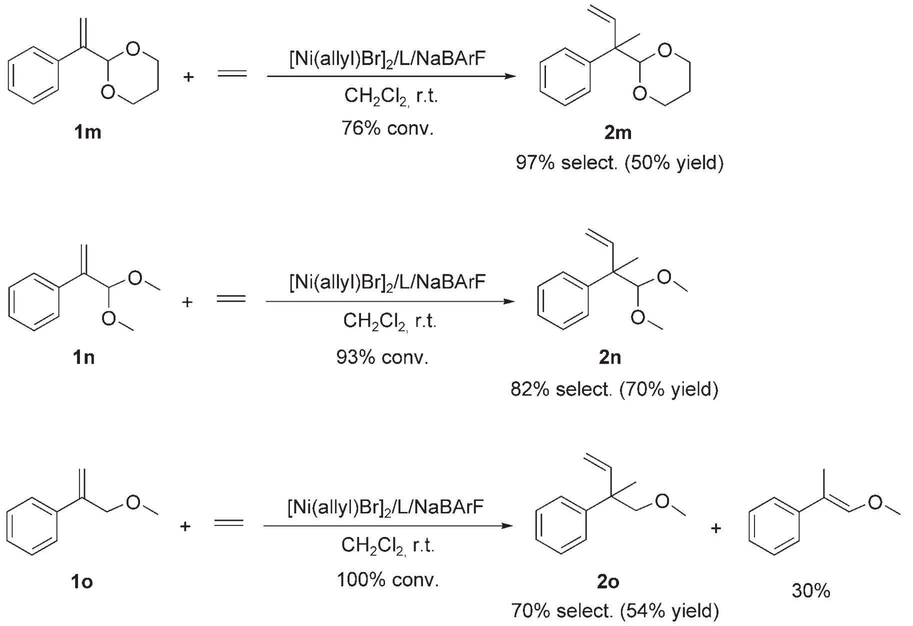
[d] Contains oligomers.

All 2-(1-arylvinyl)-1,3-dioxolane substrates with substituents at the *para*- or *meta*-position of phenyl ring gave satisfactory results under the standard conditions (Table 2, entries 1–12). The presence of an electron-withdrawing group in the substrate slightly reduced the selectivity of the hydrovinylation reaction, with the 2-[1-(4-fluorophenyl)vinyl]-1,3-dioxolane (**1f**) being the least selective substrate (entry 6). When the phenyl ring of substrate contained two strong electron-withdrawing groups at the 3,5-positions, no conversion of substrate was observed. Replacement of the phenyl group of **1a** with 2-phenylethyl led to formation of the double bond-migration compound as a major product (date not shown). The olefins with a 1,3-propanediol ketal **1m** and a dimethanol ketal **1n** were less active compared to the substrate **1a**. The methyl allyl ether **1o** was also examined in this reaction, and 30% of the double bond-migration product was obtained along with the desired hydrovinylation product **2o** (Scheme 2). However, vinylarenes with other functional groups such as α-formylstyrene, α-acetamidostyrene and α-pyrrolidinylmethylstyrene were inert to this reaction under identical conditions.

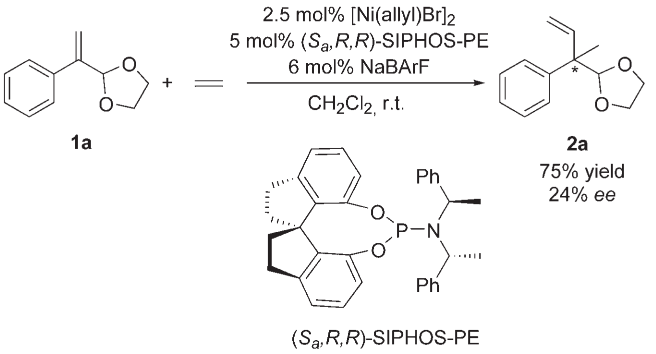
The asymmetric version of this reaction was tested by using a spirophosphoramidite ligand (S_a,R,R)-SIPHOS-PE, which was highly enantioselective in the asymmetric hydrovinylation of α-alkylstyrene.[2g] In the asymmetric hydrovinylation of substrate **1a** catalyzed by $[Ni(allyl)Br]_2/(S_a,R,R)$-SIPHOS-PE/NaBArF, the product **2a** was isolated in a yield of 75%, but with only 24% *ee* (Scheme 3). The α-ketals of styrenes are sterically similar to α-isopropylstyrene, which affords high enantioselectivity (99% *ee*) in the hydrovinylation reaction under similar conditions. The low enantioselectivity of the α-ketal of styrene is possibly due to the weak coordination of the oxygen atom of the substrate to the metal of catalyst.

The double bond and ketal group existing in the hydrovinylation products provide a good opportunity for further functional group transformations. As an example, compound **2a** was converted easily to the homoallylic alcohol **3** by deprotection[10] and reduction.[11] The alcohol **3** was oxidized successively with ozone and hydrogen peroxide to α-methyltropic acid (**4**), a key intermediate for the synthesis of antispasmodics (Scheme 4).[12]

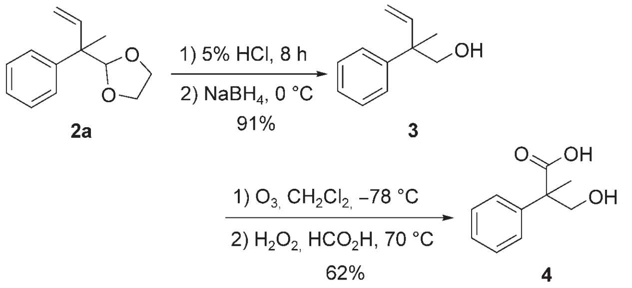
In summary, an efficient nickel-catalyzed hydrovinylation of α-ketal derivatives of vinylarenes was developed. This reaction provides a practically useful and atom-economic method for the construction of multifunctional compounds with a quaternary carbon center. Further studies including the hydrovinylation of other functionalized olefins are in progress.



Scheme 2.



Scheme 3.



Scheme 4.

Experimental Section

General Procedure for Catalytic Hydrovinylation of α-Ketal Derivatives of Vinylarenes

Under a nitrogen atmosphere, $[Ni(allyl)Br]_2$ (20 μmol), the phosphorus ligand (40 μmol) and fresh distilled CH_2Cl_2 (3.0 mL) were added into a Schlenk tube equipped with a stirring bar. The mixture was stirred at room temperature for 1 min and transferred to another Schlenk tube containing NaBArF (48 μmol) and CH_2Cl_2 (2.0 mL). After stirring for 5 min. The inert atmosphere in the Schlenk tube was replaced by ethylene three times and the α-ketal derivative of the vinylarene was introduced. The reaction mixture was stirred at room temperature for an appropriate time (monitored by GC). After the reaction had gone to completion, the selectivity for the product was determined by GC (HP-5 column). The reaction mixture was concentrated under reduced pressure, and the residue was chromatographed on silica gel column to give the pure product. The analytical data of the products are listed in the Supporting Information.

Acknowledgements

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References

[1] For reviews, see: a) P. W. Jolly, G. Wilke, in: *Applied Homogeneous Catalysis with Organometallic Compounds*, Vol. 2, (Eds.: B. Cornils, W. A. Herrmann), Wiley-VCH, New York, **1996**, pp 1024–1048; b) L. J. Goossen, *Angew. Chem.* **2002**, *114*, 3929–3932; *Angew. Chem. Int. Ed.* **2002**, *41*, 3775–3778; c) T. V. RajanBabu, *Chem. Rev.* **2003**, *103*, 2845–2860.

[2] For recent representative examples, see: a) H. Park, T. V. RajanBabu, *J. Am. Chem. Soc.* **2002**, *124*, 734–735; b) G. Franciò, F. Faraone, W. Leitner, *J. Am. Chem. Soc.* **2002**, *124*, 736–737; c) Z. J. He, C. S. Yi, W. A. Donaldson, *Org. Lett.* **2003**, *5*, 1567–1569; d) R. Kumareswaran, M. Nandi, T. V. RajanBabu, *Org. Lett.* **2003**, *5*, 4345–4348; e) A. Zhang, T. V. RajanBabu, *Org. Lett.* **2004**, *6*, 1515–1517; f) A. Zhang, T. V. RajanBabu, *J. Am. Chem. Soc.* **2006**, *128*, 54–55; g) W. J. Shi, Q. Zhang, J. H. Xie, S. F. Zhu, G. H. Hou, Q. L. Zhou, *J. Am. Chem. Soc.* **2006**, *128*, 2780–2781; h) A. Zhang, T. V. RajanBabu, *J. Am. Chem. Soc.* **2006**, *128*, 5620–5621; i) M. M. P. Grutters, C. Müller, D. Vogt, *J. Am. Chem. Soc.* **2006**, *128*, 7414–7415.

[3] T. Alderson, E. L. Jenner, Jr. R. V. Lindsey, *J. Am. Chem. Soc.* **1965**, *87*, 5638–5645.

[4] C. S. Yi, Z. J. He, D. W. Lee, *Organometallics* **2001**, *20*, 802–804.

[5] a) M. G. Barlow, M. J. Bryant, R. N. Haszeldine, A. G. Mackie, *J. Organomet. Chem.* **1970**, *21*, 215–226; b) A. Grabulosa, G. Muller, J. I. Ordinas, A. Mezzetti, M. Á. Maestro, M. Font-Bardia, X. Solans, *Organometallics* **2005**, *24*, 4961–4973.

[6] G. Muller, J. I. Ordinas, *J. Mol. Catal. A: Chem.* **1997**, *125*, 97–108.

[7] $BArF^-$ = tetrakis[3,5-bis(trifluoromethyl)phenyl]borate.

[8] Oligomers = the oligomerization products of substrate with more than one ethylene molecule.

[9] dppe = 1,2-bis(diphenylphosphino)ethane.

[10] S. Poulain, N. Noiret, L. Fauconnot, C. Nugier-Chauvin, H. Patin, *Tetrahedron* **1999**, *55*, 3595–3604.

[11] T. Kametani, K. Kawamura, M. Tsubuki, T. Honda, *Chem. Pharm. Bull.* **1985**, *33*, 4821–4828.

[12] M. C. Lu, L. B. Shih, H. S. Jae, J. E. Gearien, E. B. Thompson, *J. Med. Chem.* **1987**, *30*, 424–427.