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Cobalt-Catalyzed Asymmetric Hydrovinylation

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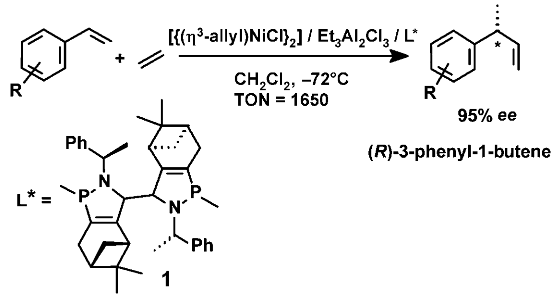
cobalt · 1,3-dienes · enantioselectivity · homogeneous catalysis · hydrovinylation

The transition-metal-catalyzed codimerization of 1,3-dienes with alkenes, also called hydrovinylation, offers great potential for practical synthetic applications. The hydrovinylation reaction was first reported by Alderson et al.[1] in 1965. They used rhodium and ruthenium salts under high ethene pressure with a range of substrates. Since then, a number of other metals such as iron, cobalt, nickel, and palladium have been used.[2] Most studies have focused on nickel and palladium. Styrene has been used as a benchmark substrate in many studies, especially for asymmetric variants of the reaction, which until very recently were almost exclusively carried out with nickel and palladium catalysts.[2]

The asymmetric nickel-catalyzed hydrovinylation reaction was pioneered by Wilke, Bogdanovic, and co-workers. In these early studies 1,3-cyclooctadiene, norbornene, and norbornadiene were codimerized with ethene by using $[\{(\eta^3\text{-allyl})NiCl\}_2]/Et_3Al_2Cl_3$ in combination with chiral monodentate phosphines derived from monoterpenes.[3] Enantioselectivity of up to 70 % *ee* was reached with cyclooctadiene. A real breakthrough was achieved by Wilke with the introduction of the azaphospholene ligand (*R*,*R*)-**1**, which gives rise to high *ee* values combined with high reaction rates for a range of vinylarene substrates. Styrene was converted into (*R*)-3-phenyl-1-butene in up to 95 % *ee* at −72 °C with a turnover number of 1650 (Scheme 1).[4] It was noted early on that the counterion used in the active cationic nickel complexes has a profound influence on the performance of the catalyst. The most active and enantioselective nickel catalysts known to date are based on $[\{(allyl)NiX\}_2]$ (X = Cl, Br), activated by $NaBAr^F$ (BAr^F = tetrakis-[3,5-bis(trifluoromethyl)phenyl]borate), in combination with monodentate phosphoramidite ligands. These systems were introduced by Leitner and co-workers[5] and further optimized by Smith and RajanBabu,[6] which gave rise to *ee* values of > 95 % for a range of substrates. The highly active nickel catalysts have a high tendency for double-bond isomerization, thus lowering the selectivity of the chiral primary product, especially at high conversion. For this reason, reactions are typically carried out at low temperature.



Scheme 1. Hydrovinylation of styrene by using Wilke's azaphospholene **1**.[4]

The corresponding cationic palladium catalysts are usually derived from the dimeric $[\{(allyl)PdX\}_2]$ complexes by halide abstraction with a silver salt of a weakly coordinating anion. Those systems show a much lower activity than the nickel catalysts. This fact was used to advantage in the first example of an asymmetric palladium-catalyzed hydrovinylation, since the isomerization of the double bond in the chiral codimers occurred only after full conversion of the starting alkene. This led to high chemoselectivity also at room temperature. The application of a bulky, monodentate P-stereogenic ligand led to 3-phenyl-1-butene being obtained in up to 86 % *ee*.[7] Bulky phosphine ligands with planar chirality also gave high *ee* values of up to 92 %.[8]

However, a serious drawback of the nickel and palladium systems is the fact that they are limited to the use of monodentate ligands. Activities are usually very low for chelating ligands, as coordination sites needed for the simultaneous binding of the substrates are blocked. Consequently this led to the reconsideration of other metals that were reported to catalyze hydrovinylation reactions and that potentially allow higher coordination numbers. This would allow the use of bidentate ligands for fine-tuning. Iron and cobalt are particularly attractive in this respect because of their low costs.

Inspired by the work of Hilt et al. on the cobalt-catalyzed codimerization of a range of 1,3-dienes and alkenes,[9] we explored the cobalt-catalyzed hydrovinylation of styrene with ethene. The activation of $[CoX_2(phosphine)]$ complexes by alkylating agents, especially Et_2AlCl, gave very active catalysts with unprecedented high selectivity for the formation of the codimers. In most cases the codimer (3-phenyl-1-butene) was obtained with more than 99 % selectivity, without any

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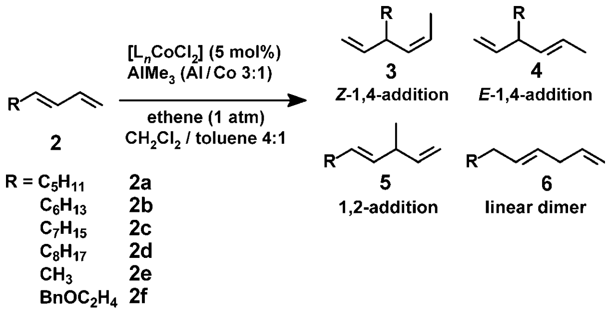
trace of double bond isomerization even at full conversion. For the first time asymmetric hydrovinylation was achieved with a cobalt system in up to 50% *ee* by using chiral diphosphine ligands.[10]

Following this lead, Sharma and RajanBabu very recently reported on the very efficient and highly selective hydrovinylation of a range of substituted 1,3-dienes with ethene (Scheme 2).[11] A number of mono- and diphosphines in the form of isolated complexes $[CoCl_2L_n]$ ($n=2$) were screened with different Lewis acids/alkylating reagents and (*E*)-1,3-nonadiene as the substrate. This led to the finding that the combination of DPPB (DPPB = 1,4-bis(diphenylphosphino)-butane and $AlMe_3$ was the best performing system.



Scheme 2. Cobalt-catalyzed hydrovinylation of 1,3-dienes.[11]

At −10 °C the *Z*-1,4 product **3a** was formed in 93% yield. The *E*-1,4 adduct **4a** was formed in 7% yield as the only other by-product. Interestingly, the product distribution was found to be strongly dependent on the nature of the ligand and on the temperature: Monodentate PPh_3 only gave polymeric products, while bis(diphenylphosphanyl)methane (DPPM) gave a mixture of the *E*-1,4- and *E*-1,2-addition products **4a** and **5a**, with preference for the latter (30% versus 67%, respectively). The intermediate ring-size chelate ligands bis(diphenylphosphanyl)ethane (DPPE) and bis(diphenylphosphanyl)propane (DPPP) gave a mixture of the branched and linear 1,4-addition products **3a** and **6a**, respectively, at low temperature (−10 to −20 °C). The product distribution changed for DPPP at higher temperature (23 °C), with only a mixture of *E*-1,4- and *E*-1,2-addition products **4a** and **5a** being obtained, again with the preferred formation of the *E*-1,2-addition product **5a** (26% versus 65%, respectively). This finding suggests that **3a** might be the kinetically controlled product.

The scope of the reaction was tested for a range of 4-substituted 1,3-dienes under the optimized reaction conditions. All the 4-substituted (*E*)-1,3-dienes were excellent substrates, and gave almost exclusively the *Z*-1,4-addition products **3** in yields higher than 90%. A benzyl ether functionality (**2f**) was also tolerated.

These exceptionally high selectivities with DPPB as the ligand led to a small number of classical chiral diphosphines with comparable chelate ring size being tested in the asymmetric hydrovinylation reaction (Table 1). High *ee* values of 90 to 99% were obtained with 4,5-bis(diphenylphosphanylmethyl)-2,2-dimethyl-1,3-dioxolane (DIOP) and 2,4-bis(diphenylphosphanyl)pentane(BDPP) for all the 4-alkyl-substituted 1,3-diene substrates tested. The products were isolated in excellent yields. However, the aryl-substituted 3-methyl-4-phenyl-1,3-butadiene gave essentially racemic product when (*S*,*S*)-BDPP was used as the ligand, but in a perfect yield of >99%. The corresponding 3-aryl-1-butene was obtained from 4-methylstyrene in 18% *ee* (*R*) when (*R*,*R*)-DIOP was used. These findings underline the great potential of this cobalt-catalyzed asymmetric hydrovinylation reaction.

Table 1: Cobalt-catalyzed asymmetric hydrovinylation of 1,3-dienes.[a]

R (**2**)	Ligand	Product **3** yield [%][b]	%*ee* (config.)
C_5H_{11} (**2a**)	(*R*,*R*)-DIOP	>99 (95)	95.0 (*S*)
C_5H_{11} (**2a**)	(*S*,*S*)-DIOP	>99 (96)	93.3 (*R*)
C_5H_{11} (**2a**)	(*S*,*S*)-BDPP	>99 (96)	97.1 (*R*)
C_6H_{13} (**2b**)	(*R*,*R*)-DIOP	>99 (96)	95.3 (*S*)
C_7H_{15} (**2c**)	(*R*,*R*)-DIOP	>99 (98)	95.4 (*S*)
C_8H_{17} (**2d**)	(*R*,*R*)-DIOP	>99 (95)	96.1 (*S*)
CH_3 (**2e**)	(*R*,*R*)-DIOP	>90[c]	90.1 (*S*)
CH_3 (**2e**)	(*S*,*S*)-DIOP	>90[c]	89.1 (*R*)
$BnOC_2H_4$ (**2f**)	(*R*,*R*)-DIOP	(40)[d]	99.0 (*S*)
$BnOC_2H_4$ (**2f**)	(*S*,*S*)-DIOP	(40)[d]	96.0 (*R*)

[a] 5 mol% $[CoCl_2(P^\wedge P)]$, Al/Co 3:1, ethene (1 atm), CH_2Cl_2/toluene (2.5 mL) 4:1, 0.4 mmol substrate, $T = -45$ °C, 6 h. [b] Determined by GC (yield of isolated product). [c] Volatile products. [d] Reaction at −20 °C, the rest is starting material.

A mechanism based on a cobalt(II) active species was proposed, in which the cobalt complex is alkylated by the alkyl aluminum compound and subsequently the remaining halide is abstracted by the Lewis acid to form a cationic cobalt(II) species with the generated aluminate as the counterion.

Certainly more detailed studies are needed on the mechanism of this catalyst system. Nevertheless, this simple protocol with extremely high selectivities and high *ee* values offers great potential for widening the scope of the reaction and for preparative (asymmetric) syntheses. The fact that one is not limited to monodentate ligands (although also monodentate ligands have been shown to be applicable[10]) makes the fine-tuning for a wide range of substrates especially feasible. Furthermore, a detailed understanding has to be gained on the influence of substituents that steer the reaction towards 1,4- or 1,2-addition. A lesson learned so far is that—like in many other catalytic transformations—different substrates might behave very differently and that so-called "standard conditions" do not apply. It will hence be advisable to screen the full parameter space for each class of substrates. This also calls for the development of in situ catalyst systems, in which the ligands can be varied more easily than with the pre-isolated catalyst precursor complexes currently used.

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

[2] a) T. V. RajanBabu, *Synlett* **2009**, 853–885; b) T. V. RajanBabu, *Chem. Rev.* **2003**, *103*, 2845–2860.

[3] a) B. Bogdanocic, B. Henc, B. Meister, H. Pauling, G. Wilke, *Angew. Chem.* **1972**, *84*, 1070–1071; *Angew. Chem. Int. Ed. Engl.* **1972**, *11*, 1023–1024; b) G. Wilke, B. Bogdanovic, *Angew. Chem.* **1973**, *85*, 1013–1023; *Angew. Chem. Int. Ed. Engl.* **1973**, *12*, 954–964.

[4] G. Wilke, *Angew. Chem.* **1988**, *100*, 189–211; *Angew. Chem. Int. Ed. Engl.* **1988**, *27*, 185–206.

[5] G. Franciò, F. Faraone, W. Leitner, *J. Am. Chem. Soc.* **2002**, *124*, 736–737.

[6] C. R. Smith, T. V. RajanBabu, *Org. Lett.* **2008**, *10*, 1657–1659.

[7] R. Bayersdörfer, B. Ganter, U. Englert, W. Keim, D. Vogt, *J. Organomet. Chem.* **1998**, *552*, 187–194.

[8] U. Englert, R. Härter, D. Vasen, A. Salzer, E. B. Eggeling, D. Vogt, *Organometallics* **1999**, *18*, 4390–4398.

[9] a) G. Hilt, F.-X. du Mesnil, S. Lüers, *Angew. Chem.* **2001**, *113*, 408–410; *Angew. Chem. Int. Ed.* **2001**, *40*, 387–389; b) G. Hilt, M. Arndt, D. F. Weske, *Synthesis* **2010**, 1321–1324.

[10] a) M. M. P. Grutters, C. Müller, D. Vogt, *J. Am. Chem. Soc.* **2006**, *128*, 7414–7415; b) M. P. Grutters, J. I. van der Vlugt, Y. Pei. A. M. Mills, M. Lutz, A. L. Spek, C. Müller, C. Moberg, D. Vogt, *Adv. Synth. Catal.* **2009**, *351*, 2199–2208.

[11] R. K. Sharma, T. V. RajanBabu, *J. Am. Chem. Soc.* **2010**, *132*, 3295–3297.