

Chemoselective Reactions of (*E*)-1,3-Dienes: Cobalt-Mediated Isomerization to (*Z*)-1,3-Dienes and Reactions with Ethylene

Yam N. Timsina, Souvagya Biswas, and T. V. RajanBabu*

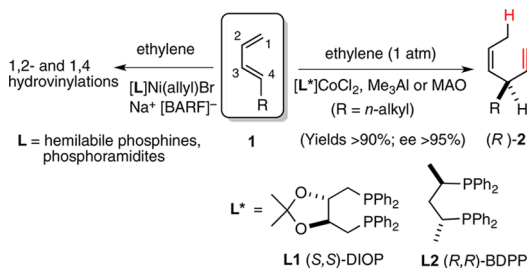
Department of Chemistry and Biochemistry, The Ohio State University, Columbus, Ohio 43210, United States

Supporting Information

ABSTRACT: In the asymmetric hydrovinylation (HV) of an *E/Z*-mixture of a prototypical 1,3-diene with (*S,S*)-(DIOP)CoCl₂ or (*S,S*)-(BDPP)CoCl₂ catalyst in the presence of Me₃Al, the (*E*)-isomer reacts significantly faster, leaving behind the *Z*-isomer intact at the end of the reaction. The presumed [LCo–H]⁺-intermediate, especially when L is a large-bite angle ligand, similar to DIOP and BDPP, promote an unusual isomerization of (*E/Z*)-mixtures of 1,3-dienes to isomerically pure *Z*-isomers. A mechanism that involves an intramolecular hydride addition via an [η^4 -(diene)(LCo–H)]⁺ complex, followed by π – σ – π isomerization of the intermediate Co(allyl) species, is proposed for this reaction.

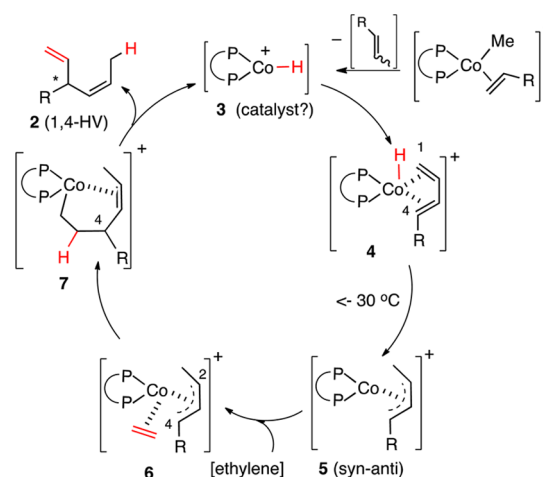
We recently reported a new protocol for a highly enantioselective Co(II)-catalyzed asymmetric hydrovinylation (HV) of unactivated 1,3-dienes that involves the use of a [1,*n*-bis-diphenylphosphinoalkane]CoCl₂ and Me₃Al (Scheme 1).^{1,2}

Scheme 1. Ni(II)- and Co(II)-Catalyzed Hydrovinylation of 1,3-Dienes



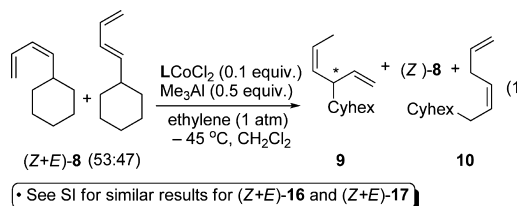
In order to explain the improved selectivity in the Co-catalyzed reactions as compared to the corresponding Ni-catalyzed reactions³ (Scheme 1), we invoked^{1a} an η^4 -cobalt-hydride complex 4 that restricts the conformations of the reactive intermediates in the former (Scheme 2). Complex 4 subsequently forms an allyl-cobalt intermediate 5, which undergoes ethylene insertion and β -hydride elimination to regenerate the presumed [LCo–H]⁺ catalyst 3⁺ to complete the catalytic cycle. When an *E/Z*-mixture of a prototypical 1,3-diene was subjected to our standard HV conditions (except for the presence of ethylene), the terminal (*Z*)-1,3-diene was found to be mostly unreactive at low temperature. The attendant implication is that the (*Z*)-isomer is unreactive toward [LCoH]⁺ or the equivalent catalyst. Since such hydride species

Scheme 2. Working Hypothesis on the Mechanism of Co(II)-Catalyzed Hydrovinylation



are also known to be capable of isomerization of alkenes, we wondered if conditions can be found to maximize the *Z*-isomer from an *E/Z*-mixture under kinetic conditions.^{5,6} The results of these studies are described in this paper.

The enantioselectivity in the asymmetric HV of a mixture of (*E*)-8 and (*Z*)-8 (*Z*:*E* = 53:47) using [(*S,S*)-DIOP]CoCl₂/Me₃Al (TMA) was found to depend on the conversion, with the (*E*)-isomer reacting at a significantly faster rate (eq 1, Table 1).^{6,7}



At low conversions (entries 1–3, Table 1), only *E*-8 undergoes hydrovinylation giving a maximum of ~83% ee. As conversion increases, the proportion of *Z*-8 increases, leaving behind, at 23 h, essentially pure (*Z*)-8 (*Z*:*E* = 49:1, entry 5). A minor product (<5%), tentatively identified as a linear hydrovinylation product (10), is also formed at higher conversions. A similar behavior is

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Table 1. Chemoselectivity in the Asymmetric HV of (Z/E)-8^a

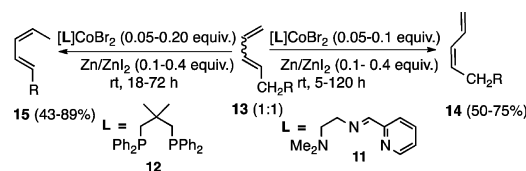
entry	time (h)	% (9)	ee % ^b (9)	% (8)	Z:E ^b (8)	10
(S,S)-DIOP ^c						
1	0.5	16	80	84	2.1:1.0	—
2	1.2	23	81	77	2.7:1.0	—
3	3	26	83	71	3.4:1.0	3
4	6	31	82	65	4.4:1.0	4
5	23	49	84	46	49:1	5
(S,S)-BDPP ^d						
6	1	21	85	79	1.9:1.0	<1
7	2	30	85	70	2.6:1.0	<1
8	5.2	42	82	49	7.1:1.0	9
9	8	47	77	43	13.3:1.0	10
10	23	61	73	25	49:1	13

^aSee eq 1 for procedure. ^bDetermined by GC. See Supporting Information for chromatograms. ^cAt −45 °C. (S)-9 major. ^dAt −15 °C. (R)-9 major.

observed with (S,S)-2,4-BDPP ligand, except a notable decrease in enantioselectivity (from 85% ee at 21% conversion to 73% ee at 61% conversion, entries 6–10) results. These results are most readily rationalized if one assumes that the (Z)-isomer is a reluctant partner in the HV reaction, while the (E)-isomer undergoes a fast reaction giving the (S)-9 [with (S,S)-DIOP] as the major product. With the more reactive BDPP complex, at higher temperatures (−15 °C), upon complete conversion of the (E)-isomer, the (Z)-isomer undergoes the reaction, giving enantiomeric product, along with 10. The (DIOP)CoCl₂ complex shows much more discrimination in the reactions of the (Z)- and (E)-isomers of the starting diene, leaving behind almost all of the (Z)-isomer unreacted (46%, Z:E = 49:1, entry 5) at the end of the reaction (entry 5, compared to 25% in entry 10 using 2,4-BDPP). The lower enantioselectivity at higher conversions using the BDPP ligand (entries 9 and 10) also suggests that the 1,4-HV of the (Z)-8 gives predominantly the opposite enantiomer.⁶ Implicit in these observations is also the striking *absence of the isomerization of the (Z)-(8) into the thermodynamically favored (E)-isomer in the presence of the presumed Co(II)-hydride intermediates*. Since (E)-8 appears to readily engage the [LCo-H]⁺ in the facile hydrovinylation, in the absence of ethylene, under proper conditions, kinetic control might prevail in the (E)–(Z)-isomerization of 8, and if so, using ligand effects could one make the (Z)-isomer?⁵ These expectations have indeed been borne out, and here we report the details of these investigations. While there are excellent methods for the formation of the (E)-1,3-diene isomer,⁸ there is a dearth of methods for the synthesis of isomerically pure (Z)-1,3-dienes,⁹ and in many biologically important compounds this configuration is important.¹⁰

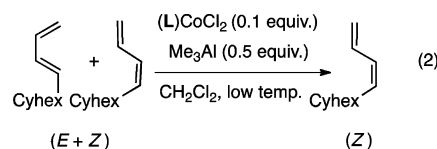
Before we describe our results, attention should be drawn to a related paper by Hilt et al., who documented a distinctly different protocol for the E/Z isomerization of 1,3-dienes.^{5d} In this report (Scheme 3), a Co(I) complex prepared under reducing conditions from a tridentate pyridine-imine ligand (11), CoBr₂, Zn, and ZnI₂ gave moderate yields of (Z)-1,3-dienes (14) from a 1:1 mixture of (Z)- and (E)-dienes (13). Behavior of the 1,3-diene was found to be highly dependent on the ligand, with a *bis*-phosphine-CoBr₂ under identical conditions (i.e., with Zn/ZnI₂) giving modest yields of a product (15), arising via a 1,5-hydrogen migration. The difference between Hilt's [*bis*-phosphine]Co-chemistry and

Scheme 3. Co(I)-Catalyzed Isomerization Reactions



the [*bis*-phosphine]CoCl₂/Me₃Al-mediated reactions described in this paper is highlighted by the *total absence* of the 1,5-hydrogen migration in the latter and the higher yields of Z-isomerization products obtained.

The initial scouting experiments were carried out on a mixture of (Z)- and (E)-8 using CoCl₂ complexes of chelating *bis*-diphenylphosphinoalkane ligands under conditions similar to the HV except for the presence of ethylene (eq 2).



The composition of isomers and identification of the product(s) were determined by ¹H and ¹³C NMR spectroscopy and gas chromatography.⁶ The results are presented in Table 2.

Table 2. Isomerization of 1,3-Diene (Z/E)-8: Ligand Effects^a

entry	start mat (Z):(E)-8	ligand	bite angle	temp (°C)/time (h)	product (Z):(E)-8
1	33:67	[DPPM]	72	−15/14	37:63
2	33:67	[DPPE]	85	−10/14	74:26
3	33:67	[DPPP]	91	−16/22	82:18
4	33:67	[DPPP] ^b	91	−4/16	33:67
5	33:67	[DPPB]	98	−15/14	>99:<1
6	33:67	[DPPpent] ^c	—	−15/14	>99:<1
7	33:67	(S,S)-DIOP	98	−10/12	100:0 ^d

^aSee eq 2 for procedure. ^bUsing CoBr₂. ^c*Bis*-1,5-diphenylphosphinopentane. ^dIsomeric product not seen in GC or NMR.

As shown in Table 2, the Z/E composition of the products is highly dependent on the ligand. A Co-complex containing ligand with a small bite angle,¹¹ 1,1-*bis*-diphenylphosphino-methane (DPPM, bite angle β = 72), showed little tendency to effect the isomerization (entry 1), whereas complexes of large bite angle ligands, 1,4-*bis*-diphenylphosphinobutane (entry 5, β = 98), 1,5-*bis*-diphenylphosphinopentane (entry 6), and DIOP (entry 7, β = 98), gave quantitative conversion to the (Z)-isomer at low temperature. *Bis*-diphenylphosphinopropane (DPPP, bite angle 91) gave up to 82% of the (Z)-isomer at −15 °C (entry 3). The reaction is specific for the chloride complex; as shown in the entry 4, the corresponding bromide complex is ineffective for the isomerization reaction.

We have examined the isomerizations of the mixtures of a number of 1,3-dienes under the optimized conditions (eq 2), and the most significant results are listed in Table 3. An expanded list of complexes and their effect on the isomerization of each of the dienes is included in the Supporting Information. As can be seen in entries 1–9, the isomerization reaction is broadly applicable giving excellent yields of the (Z)-isomers of most dienes. As inferred from the scouting studies (Table 2), ligands with relatively large bite angles, DPPB and DPPpent,

Table 3. Co(II)-Catalyzed Isomerization of (Z)- and (E)-1,3-Dienes^a

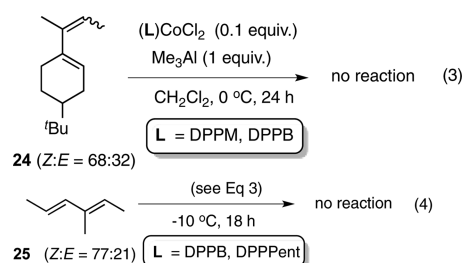
entry	(E+Z)- 1,3-diene	Z:E	L in [L]CoCl ₂	temp (°C) time (h)	yield (%)	Z:E
1.		33:67	DPPM DPPB DPPent	-15/14 -15/14 -15/14	>90 ^b >90 ^b >90 ^b	37:63 >99:<1 >99:<1
2.		46:54	DPPM DPPB	-18/14 -10/12	>90 ^b >90 ^b	50:50 >99:<1
3.		47:53	DPPB DPPent	-15/14 -15/14	92 >95	97:3 97:3
4.		51:49	DPPM DPPB	0/24 0/24	95 97	57:43 97:3
5.		60:40	DPPB DPPent	-12/13 -12/13	>99 >99	80:20 >99:<1
6.		67:33	DPPB DPPent	-12/14 -12/14	>99 >99	72:28 >99:<1
7.		66:34	DPPB DPPent	0/24 0/24	>90 >90	93:7 93:7
8.		53:47	DPPB	0/24	>95 ^c	98:2
9.		45:55	DPPB	-15/16	85 ^b	>99:<1

^aSee eq 2 for procedure. For an expanded list of ligand effects for each substrate, see Supporting Information. ^bYield of volatile products were estimated from NMR and GC. ^cProduct contains an unidentified impurity from the starting material.

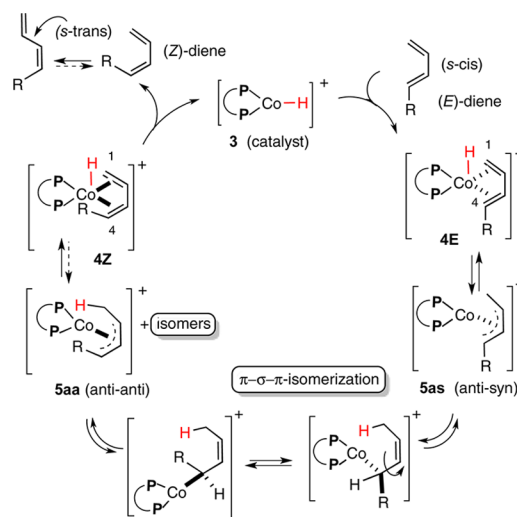
were found to be the most generally applicable for this reaction. For substrates where the diene is conjugated to an aromatic moiety (entries 5, 6, and 7), DPPent is the ligand of choice, giving excellent conversion to the expected (Z)-isomer. DPPB leads to slightly lower selectivities. The isomerization reaction gives satisfactory results even in substrates that contain Lewis basic centers (entries 6 and 7). A preparative scale experiment (3 mmol) using **16** as the starting material gave 91% isolated yield of the expected product.⁶

The isomerization reaction appears to be limited to terminal 1,3-dienes as illustrated by the examples shown in eqs 3 and 4. Substrates **24** and **25** failed to undergo the reaction under a variety of conditions using the ligands discussed previously. The starting material was recovered virtually unchanged.

The experiments listed in previous sections suggest that one reason for the poor reactivity/selectivity of the Z-substrates might be their reluctance to form an η^4 -complex.¹² A plausible explanation for the observed results, based on the assumption that the initial [LCo-H]⁺ addition to the 1,3-diene is reversible, is shown in Scheme 4. An intramolecular hydride delivery via an η^4 -complex **4E** gives the *syn-anti*-Co(allyl)-complex **5as**.¹³ This species could undergo the familiar π - σ - π isomerization¹⁴ to give, among others, an *anti-anti* complex (**5aa**). Hydride elimination from this species would generate a diene complex **4Z**, which for steric reasons, might dissociate to give the (Z)-diene. The (Z)-diene, once formed, will most likely exist in the (*s*)-*trans*



Scheme 4. Plausible Mechanism for the E- to Z-Isomerization of a 1,3-Diene



conformation, precluding any further η^4 -complexation with the Co(II)-catalyst.¹⁵

In summary, attempts to effect asymmetric hydrovinylation of a mixture of (Z)- and (E)-1,3-dienes using (P ~ P)CoCl₂/Me₃Al reveal that there is a significant difference in the relative rates of ethylene incorporation, with the (E)-isomer reacting significantly faster. In the absence of ethylene, under otherwise identical conditions, this Co-catalyst promotes an unusual isomerization of an (E)/(Z)-mixture of 1,3-dienes almost exclusively to the (Z)-isomer. This result is strikingly different from the related reaction mediated by the reagent combination [(P ~ P)CoBr₂/Zn/ZnI₂], where a product of 1,5-hydrogen shift is the major.^{5d,16} A mechanism that involves an intramolecular hydride addition via an η^4 -complex and subsequent π - σ - π isomerization of the intermediate Co(allyl) species is proposed for this reaction.

■ ASSOCIATED CONTENT

Supporting Information

Experimental details and characterization data. This material is available free of charge via the Internet at <http://pubs.acs.org>

■ AUTHOR INFORMATION

Corresponding Author

rajanbabu.1@osu.edu

Notes

The authors declare no competing financial interest.

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- (7) At higher temperatures (-10°C , 1 atm ethylene) (DPPB) CoCl_2/MAO converts both (Z)- and (E)-**8** to racemic **9** in quantitative yield. See Supporting Information for details.
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- (12) We have carried out Co-catalyzed asymmetric HV of E/Z-mixtures of **16** and **17** and observed results similar to what is documented in Table 1 for E/Z-**8**. See Supporting Information for details.
- (13) Kinetic preference for the formation of an anti-crotyl- η^3 -complex, and its subsequent isomerization to the more stable syn-isomer is known in $\{[\text{P}(\text{OEt})_3]_4\text{Ni-H}\}^+$ additions. See: Tolman, C. A. *J. Am. Chem. Soc.* **1970**, *92*, 6777.
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- (15) We have carried out high-level DFT calculations (Gaussian 09, geometries optimized with the 6-31G* basis set in conjunction with the B3LYP) on two of the dienes (**8**) and (**16**). Not surprisingly, the E-isomer is the more stable one ($K_{E/Z} = 3924$ and 24.8, respectively, 298 K), and both isomers exist almost exclusively in the s-trans form. The (Z)-isomer, once generated, will also exist exclusively in the s-trans conformation ($K_{s\text{-trans}/s\text{-cis}} = 1998$ and 612, respectively), preventing a stable η^4 -coordination to Co(II). See Supporting Information for details of these calculations and references to experimental data on E/Z-isomerization of 1,3-pentadiene.
- (16) We have also observed up to 69% conversion of a (Z/E)-mixture (46:54) of **16** to a product of 1,5-H-shift (**15**, $\text{R} = \text{C}_7\text{H}_{14}$) by using $(\text{DPPE})\text{CoBr}_2$ (20 mol%)/ Zn/ZnI_2 (40 mol%) for 72 h (see Supporting Information for details).