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Nickel-Catalyzed Intramolecular Homoallylation of ω-Dienyl Aldehyde

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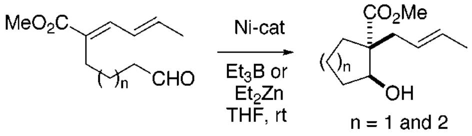
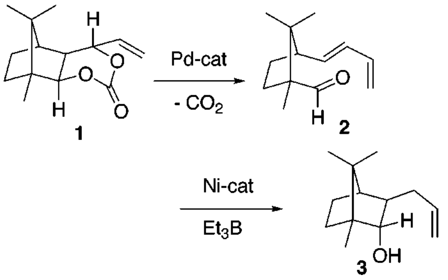
ABSTRACT



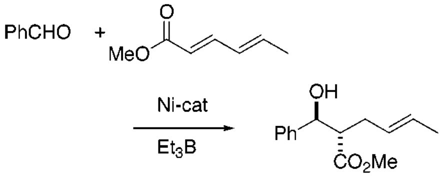
In the presence of a catalytic amount of Ni(acac)$_2$, Et$_3$B and Et$_2$Zn nicely promote a reductive homoallylic cyclization of ω-dienyl aldehydes and provide 2-allylcyclopentanols and -cyclohexanols with high stereoselectivity in excellent yield. The reaction requires only two kinds of commercially available, inexpensive reagents, Ni(acac)$_2$ and Et$_2$Zn or Et$_3$B, and completes at room temperature within 30 min with Et$_2$Zn and 1–2 days with Et$_3$B. No ligand additives (e.g., phosphine, nitrogen compounds) are required.

The most remarkable aspect of transition metal-catalyzed reactions is that they enable one to perform effectively the C−C bond formation and cleavage reactions that might be achieved with difficulty or through laborious steps by the use of organometallic reagents of main group metals.[1] Recently, we disclosed that palladium complexes nicely catalyzed a decarboxylative C−C bond cleavage reaction of bi- and tricyclic allylic carbonates (e.g., **1**) and provided ω-dienyl aldehydes and ketones (e.g., **2**) in excellent yields (Scheme 1).[2] We also reported that nickel complexes nicely catalyze a regio- and stereoselective homoallylation of aldehydes and ketones with a variety of 1,3-dienes, where Et$_3$B[3] and Et$_2$Zn[4] serve as a reducing agent, delivering a hydrogen atom at the allylic position closer to the nucleophilic termini of the dienes (Scheme 2).

Scheme 1. Pd-Catalyzed C−C Bond Cleavage Reaction and Formally Reverse Ni-Catalyzed C−C Bond Formation Reaction



Scheme 2. Ni-Catalyzed, Et$_3$B-Promoted Homoallylation of Benzaldehyde with Methyl Sorbate



By virtue of their high polarity, a wide variety of allylic metals and metalloids (e.g., B, Si, Sn)[5] can serve as a nucleophile toward carbonyl compounds. On the other hand, because of their low polarity, the kind of metals of homoallylic metals that are capable of undergoing nucleophilic addition is likely to be confined to some electropositive

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[1] Tsuji, J. *Transition Metal Reagents and Catalysts*; Wiley: Chichester, 2000.
[2] Harayama, H.; Kuroki, T.; Kimura, M.; Tanaka, S.; Tamaru, Y. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2352.
[3] Kimura, M.; Ezoe, A.; Shibata, K.; Tamaru, Y. *J. Am. Chem. Soc.* **1998**, *120*, 4033.
[4] Kimura, M.; Fujimatsu, H.; Ezoe, A.; Shibata, K.; Shimizu, M.; Matsumoto, S.; Tamaru, Y. *Angew. Chem., Int. Ed.* **1999**, *38*, 397.
[5] Yamamoto, Y.; Asao, A. *Chem. Rev.* **1993**, *93*, 2207.

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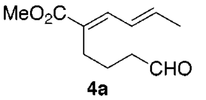
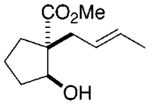
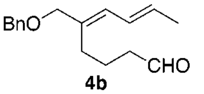
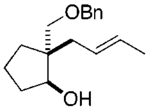
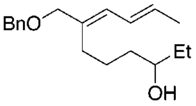
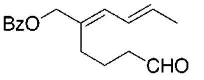
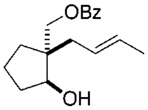
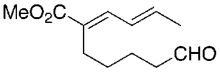
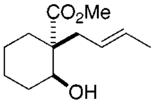
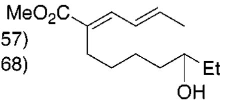
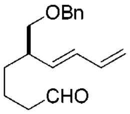
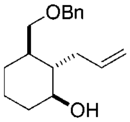
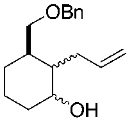
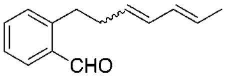
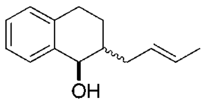
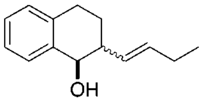
Table 1. Ni-Catalyzed Reductive Cyclization of ω-Dienyl Aldehydes **4** and **5**[a]

run	aldehydes **4** and **5**	reducing agent	temp, time	products **6** - **9** (% isolated) [cis:trans]
1	 **4a**	Et_2Zn	rt, 15 min	 **6a** (72)
2		Et_3B	rt, 34 h	**6a** (67)
3	 **4b**	Et_2Zn	rt, 15 min	 **6b** (64)  **8a** (22)
4		Et_3B	rt, 24 h	**6b** (80) **8a** (0)
5	 **4c**	Et_2Zn	rt, 30 min	 **6c** (66)
6		Et_3B	rt, 24 h; 40 °C, 40 h	**6c** (27)[b]
7	 **5a**	Et_2Zn	rt, 30 min	 **7a** (57)  **8b** (16)
8		Et_3B	rt, 24 h	**7a** (68) **8b** (0)
9	 **5b**	Et_2Zn	rt, 30 min	 **7b** (62)  **7b'** (10)
10		Et_3B	rt, 24 h	**7b** (62) **7b'** (8)
11	 **5c** (E:Z = 4.7:1)	Et_2Zn	rt, 5 min	 **7c** (74) [1:1]  **9a** (9) [1:1]
12		Et_3B	rt, 24 h	**7c** (61) [1:1.2] **9a** (7) [1:1]

[a] **4** or **5** (1 mmol), Et_2Zn (2.4 mmol, 1 M hexane) or Et_3B (2.4 mmol, 1 M hexane), and $Ni(acac)_2$ (0.1 mmol) in dry THF (5 mL). [b] **4c** was recovered in 29% yield.

elements (e.g., Li, Mg). In this Letter, we disclose that the above-mentioned Ni-catalyzed intermolecular homoallylation is applicable to an intramolecular version under essentially identical reaction conditions (**2** → **3**, Scheme 1). Scheme 1 clearly inidcates that of the same class of group 10 elements Pd serves as a catalyst for the C−C bond cleavage (**1** → **2**), while Ni promotes the formally reverse C−C bond formation reaction (**2** → **3**).

The reductive cyclization of **2** to **3** could be undertaken with great ease just by mixing **2**, $Ni(acac)_2$ (0.1 equiv, acac = acetylacetonato), and Et_3B (2.4 equiv) in THF at room temperature for 36 h. The reagents, $Ni(acac)_2$ and Et_3B (1 M hexane solution), are commercially available and were used as received. The isolated yield of **3** was moderate (47%); however, the stereoselectivity was excellent and **3** was obtained as a single isomer. Recently, a similar Ni-catalyzed intramolecular homoallylation of ω-dienals was reported by Mori et al.;[6] however, the reaction requires somewhat sophisticated conditions: $Ni(cod)_2$ (10 mol %, cod = 1,5-cyclooctadiene), PPh_3 (20 mol %), and $(i\text{-}Bu)_2Al(acac)$ (150 mol %).[7]

Results obtained for the intramolecular homoallylation of ω-dienyl aldehydes **4** and **5** forming five- and six-membered rings, respectively, are summarized in Table 1. For all substrates, the cyclization was examined under two different conditions, using either Et_2Zn or Et_3B as a reducing agent. With Et_2Zn all the reactions proceeded very fast, completing

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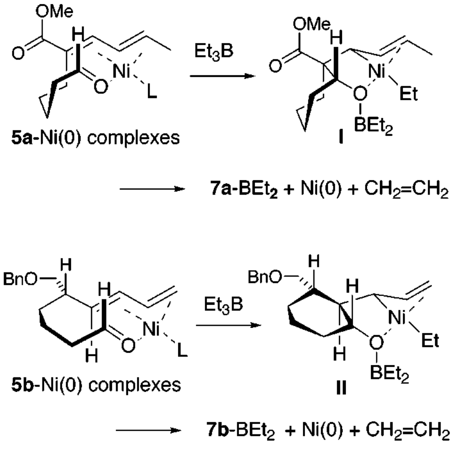
(6) Sato, Y.; Takimoto, M.; Mori, M. *J. Am. Chem. Soc*. **2000**, *122*, 1624.

(7) It may be pertinent to give a rationale to a difference between the present *homoallylation* and an Ni-promoted or -catalyzed *allylation* of ω-dienyl aldehydes reported by Mori et al. [(a) Sato, Y.; Takimoto, M.; Hayashi, K.; Katsuhara, T.; Takagi, K.; Mori, M. *J. Am. Chem. Soc*. **1994**, *116*, 9771]. As was suggested in our previous work[4] and also in Mori's recent work,[6] a catalytic homoallylation involves the formation of 5-vinyl-2-oxanickellacyclopentane (e.g., **I** and **II**, Scheme 3), followed by an ethyl group transfer from Et_3B or Et_2Zn in our case or an isobutyl group transfer form $(i\text{-}Bu)_2Al(acac)$ in the Mori's case,[6] where a hydrogen is delivered to the allylic carbon bound to Ni via a β-H elimination−reductive elimination sequence. Depending on the structure of substrates and reaction conditions, however, a hydrogen might be delivered to an alternative allylic position, furnishing an allylation product (e.g., **9a**, runs 11 and 12, Table 1). On the other hand, Mori's protocol for an allylation[7a] involves addition of Ni-H species to a diene, followed by an intramolecular nucleophilic allylation of aldehyde by the π-allylnickel thus-formed.

within half an hour at room temperature. One drawback of Et$_2$Zn is that in some cases it serves not only as a reducing agent but also as an ethyl nucleophile toward aldehyde and provides the ethylation product **8** in significant amounts (runs 3 and 7, Table 1). Et$_3$B requires a longer reaction time for completion of the reaction (1−2 days); however, with this reagent, no ethylation of aldehyde took place. Accordingly, the cyclization products **6b** and **7a** were obtained in much improved yields (cf. runs 3 and 4 and runs 7 and 8). ω-Dienal **4c** displayed contrasting reactivity depending on the kind of the reducing agents (runs 5 and 6). It underwent the cyclization as usual when exposed to Et$_2$Zn; however, it was reluctant and provided the expected product **6c** in poor yield with 29% recovery of the starting material when treated with Et$_3$B even under forcing conditions. This is probably because, under these conditions, the dienyl benzoate moiety of **4c** disturbs the catalytic activity of the Ni(0) species, e.g., by forming a π-allylnickel species.

As for the stereoselectivity, in every case no significant difference was observed between a pair of reactions with Et$_2$Zn and Et$_3$B. All of the substrates with a similar structure type, **4a**−**c** and **5a**, i.e., (*Z*)-ω-dienyl aldehydes, provided cyclization products with the same stereochemistry as that of single diastereomers, i.e., *cis* with respect to the hydroxyl group and 2(*E*)-butenyl group (runs 1−8, Table 1). The generation of quaternary carbon centers with excellent stereoselectivity is an interesting aspect to be noted in these reactions. This 1,2-*anti* mode of stereoselectivity is the same as that observed for the intermolecular homoallylation between benzaldehyde and methyl sorbate (Scheme 2)[3] and might be rationalized according to Scheme 3, illustrated for the reaction of **5a** and Et$_3$B as a representative example. A cooperative oxidative addition of the diene and the aldehyde moieties onto Ni(0) through **5a**−Ni(0) complexes,[8] and a subsequent ethyl group transfer from Et$_3$B to Ni(II),[9] might form the *cis*-fused 7-oxa-8-nickellabicyclo[4.3]nonane intermediate **I**, which undergoes β-H elimination of the Ni−Et bond and reductive elimination of the thus-formed NiH to generate **7a**−BEt$_2$, Ni(0) complexes, and ethylene.

Scheme 3 *cis*- (for **5a**) and *trans*-Selective (for **5b**) Intramolecular Reductive Homoallylation of ω-Dienyl Aldehydes



(*E*)-ω-Dienyl aldehyde **5b**, on the other hand, underwent the homoallylation in a quite different manner and furnished **7b**, bearing a hydroxyl group and an allyl group *trans* to each other (runs 9 and 10). Another diastereomer, **7b′**, was also isolated as a minor product, with the relative configuration of the substituents not being determined yet. The stereochemical outcome of **7b** may be rationalized in a similar manner to that for the reaction of **5a**−Ni(0) complexes; **5b**−Ni(0) complexes would furnish the *trans*-fused 7-oxa-8-nickellabicyclo[4.3]nonane intermediate **II**, where a BnOCH$_2$ group occupies a quasi-equatorial position of a chairlike cyclohexane ring to minimize steric repulsion (Scheme 3). It may be worth noting that both the **5a**− and **5b**−Ni(0) complexes share a characteristic coordination mode: η^4-transoid diene and aldehyde, extending the α-methylene carbon of the alkyl tether almost parallel to the internal double bond of the diene.

In sharp contrast to the above, benzaldehyde derivative **5c** did not show any correlation between the geometry of the diene and the stereochemistry of the cyclization product (runs 11 and 12); **5c** (*E*:*Z* = 4.7:1) provided a mixture of *cis*- and *trans*-**7c** in a ratio of ca. 1:1. Furthermore, a 1:1 mixture of allylation products, *cis*- and *trans*-**9a**, was obtained as a minor product.[10]

In summary, we have disclosed that our protocol for the intermolecular homoallylation of aldehydes with 1,3-dienes catalyzed by nickel complexes could be applied successfully to an intramolecular version of ω-dienyl aldehydes, which provided 2-allylcyclopentanols and -cyclohexanols with high stereoselectivity in a predictable way and in good yield. The reaction requires only two kinds of commercially available, inexpensive reagents, Ni(acac)$_2$ and Et$_2$Zn or Et$_3$B, and proceeds smoothly at room temperature within 30 min with Et$_2$Zn and 1−2 days with Et$_3$B. No ligand additives (e.g., phosphine, nitrogen compounds) are required.

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Supporting Information Available: Experimental procedures and characterization data for the new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) A similar mechanism was proposed for the Ni(cod)$_2$-catalyzed reductive cyclization of ω-ynals promoted by Et$_3$SiH: (a) Montgomery, J. *Acc. Chem. Res.* **2000**, *33*, 467. (b) Tang, X.-Q.; Montgomery, J. *J. Am. Chem. Soc.* **1999**, *121*, 6098.

(9) A related metathesis with R$_3$B or R$_2$Zn: (a) Kimura, M.; Shibata, K.; Koudahashi, Y.; Tamaru, Y. *Tetrahedron Lett.* **2000**, *41*, 6789. (b) Kimura, K.; Matsuo, S.; Shibata, K.; Tamaru, Y. *Angew. Chem., Int. Ed.* **1999**, *38*, 3386. (c) Giovannini, R.; Stüdemann, T.; Dussin, G.; Knochel, P. *Angew. Chem., Int. Ed.* **1998**, *37*, 2387. (d) Vettel, S.; Vaupel, A.; Knochel, P. *J. Org. Chem.* **1996**, *61*, 7473.

(10) All the products were appropriately characterized on the basis of ^{1}H NMR (400 MHz), IR, and high-resolution mass spectra and/or elemental analyses. The spectral data (^{1}H and IR) of **7b** were identical in all respects to those reported.[6]