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[15] Computations were carried out using a Silicon Graphics Octane workstation and the modeling software SYBYL 6.7 (Tripos Assoc., St. Louis, USA, **2001**). Important parameters for the *ams* calculation: geometries of the catalyst fragments without the phosphorus and iridium substituents are based on X-ray structures of **3**[6c] and of the $\mathrm{IrCl_2}$ complex of **9** (C. W. Lehmann, M.-A. Schneider, S. Oevers, W. C. Kaska, M. W. Haenel, unpublished results). Systematic search about the $\mathrm{P{-}C_{alkyl}}$ bonds with 5° and the $\mathrm{C_{alkyl}{-}C_{methyl}}$ bonds with 30° (**3**, **6**) or 60° (**4**, **7**) torsion angle increments. All conformations with $E <$ 3 $\mathrm{kcal\,mol^{-1}}$ (force field: TAFF, no charges) higher than the energy minimum are superimposed according to Figure 2, forming a "super-molecular" fragment. The *ams* was determined using Connolly's method[16] analogous to the previously published procedure[14] by "rolling" a sphere of 1.8 Å diameter over the Ir part of the molecular surface of these super-molecular fragments.

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Nickel-Catalyzed Homoallylation of Aldehydes in the Presence of Water and Alcohols**

Masanari Kimura, Akihiro Ezoe, Shuji Tanaka, and Yoshinao Tamaru*

By virtue of their high polarity, a wide variety of allylic metal and metalloid (e.g., B, Si, Sn) complexes can serve as nucleophilic reagents toward carbonyl compounds;[1] some allylations can be successfully performed even in the presence of water under Barbier conditions.[2] On the other hand, because of their low polarity, the homoallylic metals that are capable of undergoing a nucleophilic addition reaction are likely to be limited to some electropositive main group metals (e.g., Li, Mg).[3] Accordingly, reactions with these homoallylic metals should be performed with care under strictly water-free conditions and could be applied effectively to those compounds that do not possess an acidic hydrogen.

Here, we disclose that even in the presence of water and alcohols, nickel complexes serve as a catalyst to promote homoallylation of aldehydes with 1,3-dienes. The reaction proceeds under essentially the same conditions as those reported recently from these laboratories for a nickel-catalyzed homoallylation of carbonyl compounds with dienes in the presence of a stoichiometric amount of $\mathrm{Et_3B}$.[4–6] These two reactions, that is, in the presence and in the absence of water, provide bishomoallyl alcohols in comparable yields

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[*] Prof. Dr. Y. Tamaru, Dr. M. Kimura, A. Ezoe, Dr. S. Tanaka
Department of Applied Chemistry, Faculty of Engineering
Nagasaki University
1-14 Bunkyo-machi, Nagasaki 852-8521 (Japan)
Fax: (+81) 95-847-9008
E-mail: tamaru@net.nagasaki-u.ac.jp

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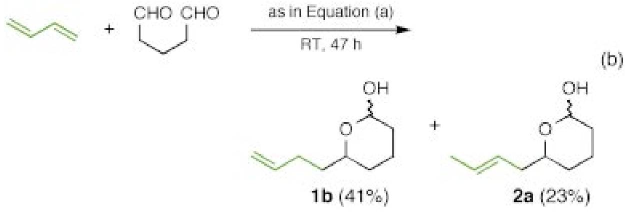
with the same sense of stereoselectivity and regioselectivity. For example, isoprene (4.0 mmol) reacted with glutaraldehyde (1.0 mmol) regioselectively at the C1 position and stereoselectively to provide **1a** in 57% yield as a single

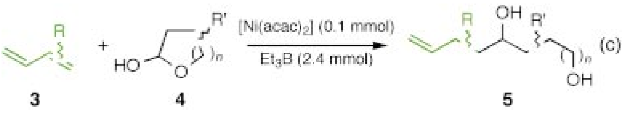
isomer, which is 1,3-*anti* with respect to a tetrahydropyranyl oxygen and a methyl group, when exposed to $[Ni(acac)_2]$ (0.1 mmol, acac = acetylacetonato) and Et_3B (2.4 mmol) in THF (5 mL) at room temperature for 40 h [Eq. (a)]. Glutaradehyde is stable in water and commercially available as an aqueous solution.[7] In the above reaction, a 50% aqueous solution was used as received; it follows that the homoallylation could be performed successfully in the presence of about six equivalents of water.

Butadiene reacted with glutaraldehyde (50% aqueous) similarly well and provided the expected homoallylation product **1b** in reasonable yield [Eq. (b)]; however, as noted



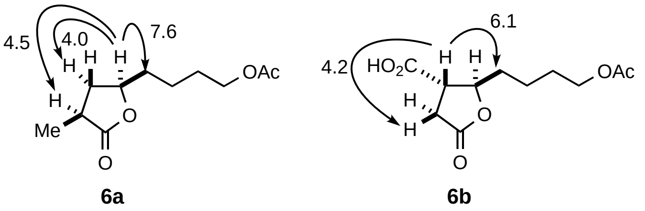
previously,[4] butadiene was the only exception among the dienes examined so far that furnished such an allylation product as **2a** as a minor component.

Encouraged by the compatibility of the $[Ni(acac)_2]/Et_3B/$diene/aldehyde system with water, we next examined the applicability of the system to the homoallylation of cyclic hemiacetals **4** [Eq. (c)]. To achieve homoallylation of cyclic



hemiacetals with a homoallylic metal, one would anticipate that two equivalents of the reagent would be required; the first equivalent to abstract the hydrogen atom, the second to effect a nucleophilic addition to the aldehyde of ω-metalloxyaldehyde, which might be present as a component of an equilibrium mixture with 2-metalloxy-1-oxacycloalkane. To our surprise, the homoallylation of cyclic hemiacetals proceeded successfully under identical conditions to those for the homoallylation of aldehydes,[4] that is, use of extra amounts of $[Ni(acac)_2]$, Et_3B, and dienes was not necessary (Table 1). Furthermore, unsymmetrical dienes, such as isoprene (**3b**) and methyl sorbate (**3d**), reacted regioselectively at the C1 and C2 positions, respectively. The stereoselectivity was also excellent; **3b** provided 1,3-*anti* isomers **5b** and **5e** exclusively (Table 1, runs 2 and 5) and **3d** afforded 1,2-*anti* isomers **5d** and **5g** as a single diastereomer (Table 1, runs 4 and 7), irrespective of the ring size of **4**. The reactivity decreases in the order of 2-hydroxytetrahydrofuran (**4a**), 2-hydroxytetrahydropoyran (**4b**), and 2-hydroxy-5,6-benzo-1-oxacyclohexane (**4c**) (cf., Table 1, runs 3, 6, and 8). Indeed, a small amount of **4c** (13%) remained unchanged even after 78 h at room temperature (Table 1, run 8).

Reduction of **1a** with $NaBH_4$ afforded a diol **5e**, the IR and ^1H NMR spectra of which were identical in all respects to those of the product obtained in run 5, Table 1. The 1,3-*anti* structure of **5e** was derived from that of a lactone derivative **6a** on the basis of NOE experiments (Figure 1, See Experimental Section). The 1,2-*anti* structure of **5g** was also established based on that of the lactone derivative **6b** (Figure 1).



6a **6b**

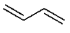
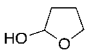
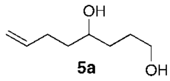
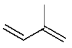
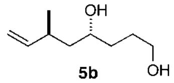
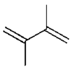
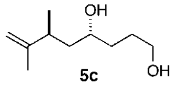
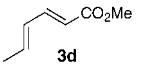
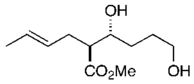
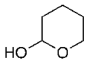
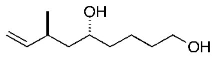
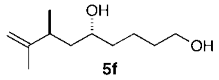
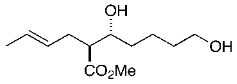
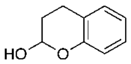
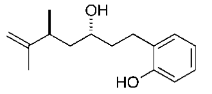
Figure 1. Selected NOE data (% increment) of **6a** and **6b** derived from **5e** and **5g**, respectively.

In conclusion, we have demonstrated that a catalytic system of $[Ni(acac)_2]$/diene/Et_3B efficiently promotes homoallylation of a 50% aqueous solution of glutaraldehyde and cyclic hemiacetals at room temperature. Unsymmetrical dienes react regio- and stereoselectively and provide bishomoallyl alcohols with excellent 1,2- and 1,3-asymmetric induction. These reaction features may be ideal for modification of sugars and greatly contribute to carbohydrate and related chemistry. The low toxicity and low cost of the reagents and the mild reaction conditions are of particular interest from an environmental and an economic point of view.

Experimental Section

anti-5-Hydroxy-7-methyl-8-nonen-1-ol (**5e**) (run 5, Table 1): Into a flask containing $[Ni(acac)_2]$ (25.7 mg, 0.1 mmol) purged with N_2 were successively added dry THF (5 mL), isoprene (400 μL, 4.0 mmol), 2-hydroxytetrahydrofuran (102.1 mg, 1.0 mmol),[8] and Et_3B (2.4 mmol, 1 M hexane) by syringe. The homogeneous mixture was stirred at room temperature for 62 h. After dilution with EtOAc, the mixture was washed with 2 M HCl, saturated $NaHCO_3$, and then with brine. The aqueous phases were combined and saturated with NaCl, and then extracted three times with EtOAc. The combined organic phase was dried ($MgSO_4$) and concentrated in vacuo. The residue was purified by column chromatography over silica gel (hexane/EtOAc, 2/1, v/v) to provide **5e** (108.5 mg, 63%). IR (neat film): $\tilde{\nu} = 3332$ (s), 1639 (m), 1057 (m), 995 (m), 910 (s) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz, TMS): $\delta = 1.02$ (d, $J = 6.6$ Hz, 3 H), 1.36–1.63 (m, 10 H), 2.33 (m, 1 H), 3.65 (t, $J = 6.2$ Hz, 2 H), 4.94 (dd, $J = 1.5$, 10.3 Hz, 1 H), 5.03 (br dd, $J = 1.5$, 17.2 Hz, 1 H), 5.78 (ddd, $J = 7.7$, 10.3, 17.2 Hz, 1 H); ^{13}C NMR ($CDCl_3$, 100 MHz, TMS): $\delta = 20.3$, 21.7, 32.7, 35.6, 37.3, 44.5, 62.9, 70.4, 112.9, 145.2; HRMS calcd for $C_{10}H_{20}O_2$:172.1463; found m/z (%): 172.1462 ([M^+], 6), 157 (3), 154 (3), 129 (13), 116 (100); elemental analysis calcd (%) for $C_{10}H_{20}O_2$: C 69.72, H 11.70; found: C 69.32, H 11.52.

Table 1. Et$_3$B-promoted, Ni^0-catalyzed homoallylation of cyclic hemiacetals **4a–c** with 1,3-dienes **3a–d**.[a]

Run	Diene **3**	Hemiacetal **4**	t [h]	Product **5**	Yield [%]
1	 **3a**	 **4a**	24	 **5a**	63[b]
2	 **3b**	**4a**	22	 **5b**	83
3	 **3c**	**4a**	23	 **5c**	88
4	 **3d**	**4a**	46	 **5d**	64
5	**3b**	 **4b**	62	 **5e**	63
6	**3c**	**4b**	40	 **5f**	99
7	**3d**	**4b**	72	 **5g**	51
8	**3c**	 **4c**	78	 **5h**	82[c]

[a] Reaction conditions: A homogeneous solution of **3** (4 mmol), **4** (1 mmol), [Ni(acac)$_2$] (0.1 mmol), and Et$_3$B (2.4 mmol in 1M hexane) in THF (5 mL) was stirred under N$_2$ at room temperature for the period of time indicated. [b] In addition to **5a**, an allylation product, *trans*-6-octene-1,4-diol, was isolated in 23% yield. [c] Yield based on 87% conversion of **4c**.

cis-γ-(4-Acetoxybutyl)-α-methyl-γ-butyrolactone (**6a**): A solution of **5e** (86.1 mg, 0.5 mmol) in dichloromethane (5 mL) was cooled to −78 °C, and ozone was bubbled through until a blue color appeared (ca. 10 min). The excess of ozone was removed by a flow of N$_2$. The mixture was allowed to warm to room temperature. Into this solution were added AcOH (2 mL), H$_2$O (0.2 mL), concentrated H$_2$SO$_4$ (0.2 mL), and 30% H$_2$0$_2$ (1 mL). The mixture was stirred at room temperature for 1 h and then at 60 °C for 5 h. The mixture was diluted with EtOAc, washed with saturated NaHCO$_3$ and then brine, and dried (MgSO$_4$) and concentrated in vacuo. The residue was purified by column chromatography over silica gel (hexane/EtOAc, 8/1, v/v) to provide **6a** (61.1 mg, 57%). IR (neat film): $\tilde{\nu} = 2939$ (s), 1755 (s), 1737 (s), 1244 (s), 1168 (s), 1002 (m), 927 (m) cm^{-1}; ^{1}H NMR (CDCl$_3$, 400 MHz, TMS): $\delta = 1.27$ (d, $J = 7.0$ Hz, 3H), 1.51 (td, $J = 12.5$, 10.6 Hz, 1H), 1.42–1.80 (m, 6H), 2.05 (s, 3H), 2.49 (ddd, $J = 5.3$, 8.8, 12.5 Hz, 1H), 2.68 (ddq, $J = 8.8$, 12.5, 7.0 Hz, 1H), 4.07 (t, $J = 6.6$ Hz, 1H), 4.34 (ddt, $J = 7.7$, 10.6, 5.3 Hz, 1H); ^{13}C NMR (CDCl$_3$, 100 MHz): $\delta = 15.1$, 20.9, 22.0, 28.4, 35.2, 35.9, 37.4, 64.1, 78.2, 171.1, 179.3; HRMS calcd for C$_{11}$H$_{18}$O$_4$: 214.1205; found m/z (%): 214.1227 ([M^+], 17), 196 (59), 125 (72), 95 (100).

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