Reduction of Five-Membered α,β-Unsaturated Lactones and Related Compounds with the Ni^{2+}/BH_4^- System

Nobuhiro ABE,* Fumiko FUJISAKI, Kunihiro SUMOTO,* and Seiji MIYANO

Faculty of Pharmaceutical Sciences, Fukuoka University, Nanakuma, Jonan-ku, Fukuoka 814-01, Japan. *Received November 7, 1990*

The reductions of an α,β-unsaturated lactone (5) and lactam (7) with the Ni^{2+}/BH_4^- system resulted in the formation of *cis*-hydrogenated products (8a and 9a) with high stereoselectivity. The *cis* products (8a and 9a) were easily isomerized to the corresponding *trans* isomers (8b and 9b, respectively) by refluxing with sodium methoxide in anhydrous methanol. Isotope labeling studies with methyl cinnamate as the substrate indicated that the reduction with this reducing system poceeds stepwise *via* a carbon–nickel intermediate.

Keywords Ni^{2+}/BH_4^-; reduction; hydrogenation; α,β-unsaturated 5-membered lactone; α,β-unsaturated lactam; isotope labeling study; methyl cinnamate

Reducing systems consisting of sodium borohydride ($NaBH_4$) with a transition metal halide such as $CoCl_2$, $NiCl_2$, or $CuCl_2$ have been employed in hydrogenation of various organic functional groups.[1-7] However, to our knowledge, no application of this reducing system to the stereoselective *cis* hydrogenation of C=C functionalities has been reported so far.[8] Quite recently, we have found that the reaction of the α,β-unsaturated 5-membered lactone (**1**) with Ni^{2+}/BH_4^- in MeOH affords only the *cis*-hydrogenated compound (**2**) in good yield[9] (Chart 1). It seems likely that the nature of the reducing system is responsible for such high stereoselectivity.

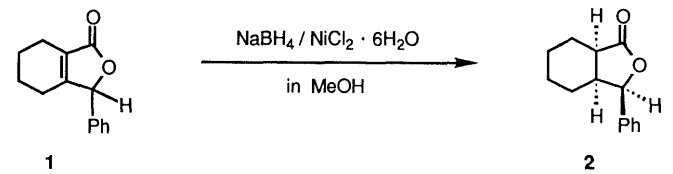
In order to investigate further the above reducing system, we carried out some experiments with the five-membered α,β-unsaturated lactone (**5**) and lactam (**7**), as well as an isotope labeling study with methyl cinnamate.

We wish to report here that the Ni^{2+}/BH_4^- reducing system possesses a high stereoselectivity in the hydrogenation of the C=C bond in a five-membered α,β-unsaturated lactone/lactam system. A homogeneous borohydride-containing complex[10,11] was suggested as the most probable reducing species in these reductions.

Results and Discussion

The starting α,β-unsaturated lactone (**5**) and lactam (**7**) were prepared by the procedures described previously and their structures were confirmed by spectroscopic and elemental analysis (see Chart 2 and Experimental).

The reduction of the lactone (**5**) with the Ni^{2+}/BH_4^- system in MeOH gave a stereoisomeric mixture [*cis*/*trans* (**8a**/**8b**) = 3/1] separable by high-performance liquid chromatography (HPLC). However, the reduction of the lactam (**7**) with this system resulted in the formation of the *cis* hydrogenated derivative (**9a**) with no formation of the *trans* isomer (**9b**) (Chart 3). The stereochemistry of these products was established from the ^{13}C-nuclear magnetic resonance (^{13}C-NMR) spectroscopic data, compared with the ^{13}C-resonance behavior of known 1,2-dimethylcyclopentanes.[12] Thus, the two methyl signals at higher magnetic field (2.5—3.8 ppm) were assigned to the isomers having *cis* configuration (**8a** and **9a**). Both *cis* products (**8a** and **9a**) were isomerized to the corresponding *trans* isomers (**8b** and



1 2

Chart 1

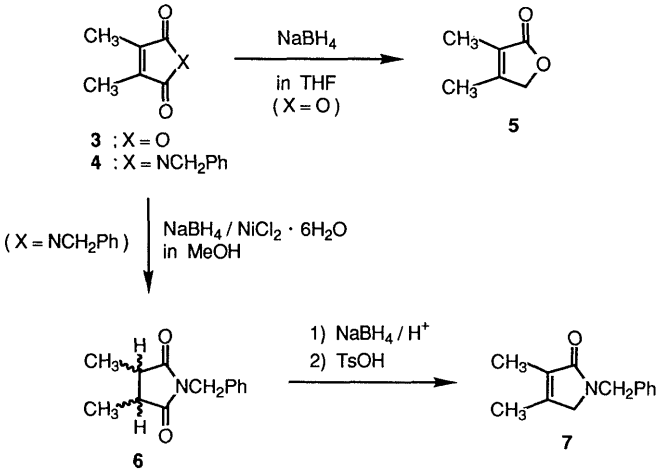


Chart 2

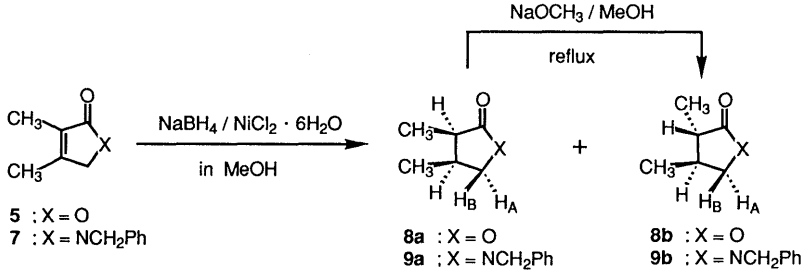


Chart 3

Table I. Isotope Labeling Study with Methyl Cinnamate

	Reagent/solvent	Metal	t_R (min)	Number of deuterium atoms per mole of methyl 3-phenylpropionate			
				β Position		α Position[c]	
				MS[a]	^{1}H-NMR[b]	MS	^{1}H-NMR
Run 1	$NaBH_4$/MeOD	Ni_2B	90	0.07	0.0	0.8	0.96
Run 2	$NaBH_4$/MeOD	$NiCl_2$	20	0.20	0.17	0.26	0.31
Run 3	$NaBD_4$/MeOH	$NiCl_2$	30	0.84	0.9	0.54	0.47

a) Calculated from the relative abundances of the benzyl fragment ion and the molecular ion. Relative abundances were corrected, using the $(M+1)^+$ ion in the authentic undeuterated sample. *b*) The deuterium incorporation was evaluated from the result of integration of the signals due to the α and β methylene units (δ 2.71—2.52 and 3.06—2.87 ppm) relative to that of the methyl group (δ 3.663 ppm). *c*) No significant H/D exchange was observed at the α position in methyl 3-phenylpropionate.

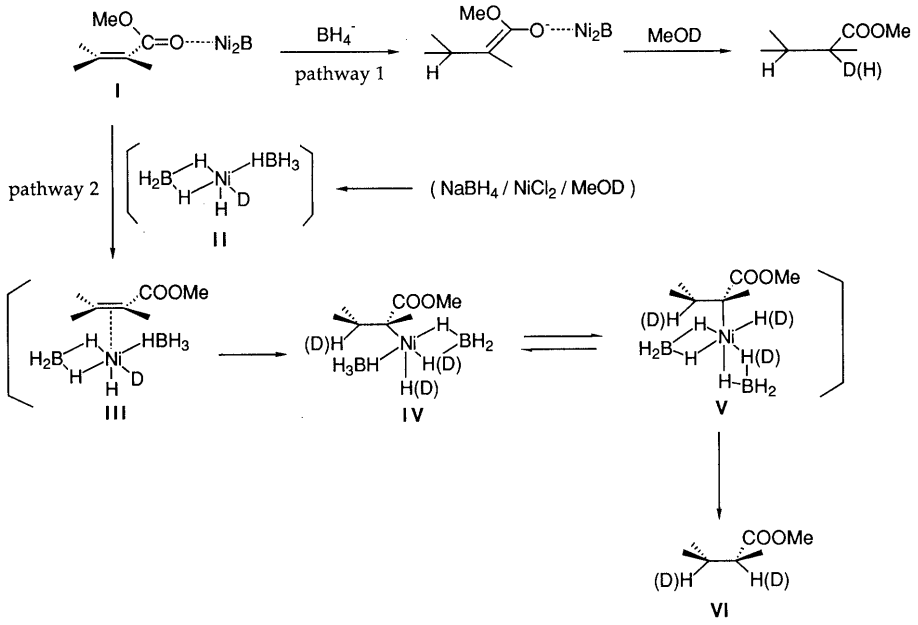


Chart 4

9b, respectively) in good yields by refluxing with sodium methoxide in anhydrous methanol, which also supports the above assignments. The fact of the formation of the thermodynamically unstable *cis* isomer (**8a** or **9a**) apparently indicates that these reductions take place in a *cis* fashion.

In order to elucidate the reduction mechanism,[2,5-7,13,14] isotope labeling studies with methyl cinnamate as the substrate were carried out. The ratios of incorporation determined by mass and ^{1}H-NMR spectral techniques are summarized in the table.

The reaction under heterogeneous conditions with preformed Ni_2B (run 1 in Table I)[6,15] resulted in the exclusive incorporation of a deuterium atom at the α position. This apparently indicates hydride addition from uncoordinated BH_4^-[14] (pathway 1 in Chart 4) and little contribution of a heterogeneous catalytic hydrogenation process. On the other hand, under the usual conditions, where the formation of a black precipitate (Ni_2B) occurred *in situ* (run 2 in Table I), no significant specificity was observed regarding the incorporation of a deuterium atom at the α position. These results require that homogeneous species play some significant part in the reduction of methyl cinnamate with this system. The parallel experiment employing $NaBD_4$ and $NiCl_2$ in MeOH under the usual conditions led to methyl 3-phenylpropionate with about 84—90% deuterium at the β position and only about 47—54% deuterium at the α position (run 3 in Table I). The results obtained from runs 2 and 3 suggest that the hydrogen added to the β position arises directly from the starting sodium borohydride. From the outcome of the isotope labeling studies shown in the table, we consider that the overall hydrogenation with this reducing system proceeds stepwise through the following two stages: (a) formation of the carbon–nickel intermediate from the reaction of the olefin I and illustrated five-coordinate Ni complex II as the active species (I→III→IV), and then (b) reductive cleavage of the carbon–nickel bond in this intermediate (IV⇄V) yielding the product (V→VI). These stages are illustrated in Chart 4.

In the reduction of **5** or **7** with this reducing system, the *cis* stereoselectivities may be explained through the mechanism of pathway 2 shown in Chart 4. The nickel boride (Ni_2B) formed *in situ* would contribute to an initial activation of α,β-unsaturated carbonyl group in the substrates.[16]

Further synthetic applications of this mild reducing system are being examined and the details will be reported in separate papers.

Experimental

Infrared (IR) spectra were obtained on a Hitachi 250 spectrometer. ^{1}H- and ^{13}C-NMR spectra were recorded on a JEOL GX-400 spectrometer with a 5 mm probe and tetramethylsilane (TMS) as an internal standard

at 25 °C in $CDCl_3$ equipped with a G MHD 80R (JEOL) computer system. ^{1}H-NMR spectra in isotope labeling studies were obtained with a Hitachi R-90H spectrometer using TMS as an internal standard. High-resolution mass spectra (MS) were measured on a JEOL D-300 spectrometer with electron impact ionization at an ionizing potential of 70 eV. High-performance liquid chromatographic analyses were performed by using a Waters M-45 or 501 solvent delivery system equipped with a U-6K injector and R-401 differential refractometer (Waters μ-Porasil, 3.9 × 300 mm or YMC-pack S-043 I-15 sil. 20 × 250 mm).

3,4-Dimethyl-2(5*H*)-furanone (**5**)[17] was prepared from 2,3-dimethylmaleic anhydride according to the method reported previously.[18] The preparation of the lactam (**7**), according to the route shown in Chart 2, is described below.

1-Benzyl-3,4-dimethyl-1*H*-pyrrole-2,5-dione (4) This compound was prepared from 2,3-dimethylmaleic anhydride and benzylamine by the method described previously.[19] The yield was 90%, mp 44—45 °C (hexane). *Anal.* Calcd for $C_{13}H_{13}NO_2$: C, 72.54; H, 6.09; N, 6.51. Found: C, 72.72; H, 6.10; N, 6.21. IR (KBr): 1774, 1710 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.27 (5H, m, aromatic protons), 4.61 (2H, s, $-CH_2-$Ph), and 1.94 (6H, s, 2 × CH_3). ^{13}C-NMR ($CDCl_3$) δ: 171.5 [C(2) and C(5)], 137.1 and 136.6 [C(3) and C(4)], 128.3, 127.5 (aromatic carbons), 41.3 (a benzylic carbon), 8.5 (methyl carbons).

1-Benzyl-1,5-dihydro-3,4-dimethyl-2*H*-pyrrol-2-one (7) $NaBH_4$ (0.38 g, 0.01 mol) was added portionwise to a stirred solutions of 1-benzyl-3,4-dimethyl-1*H*-pyrrole-2,5-dione (**4**) (2.15 g, 0.01 mol) and $NiCl_2 \cdot 6H_2O$ (0.24 g, 0.001 mol) in methanol at -10 °C. After neutralization of the reaction mixture with aqueous HCl (5%), the solvent was removed under reduced pressure. The resulting residue was dissolved in H_2O (10 ml) and the solution was extracted with dichloromethane. The extract was dried over anhydrous magnesium sulfate. Evaporation of the solvent gave an oily mixture of two stereoisomers of 1-benzyl-3,4-dimethyl-2,5-pyrrolidinedione (**6**) (2.12 g, 97.7%). This mixture was used in the next step. For the transformation to the α,β-unsaturated lactam (**7**) from the 2,5-pyrrolidinedione ring system, the procedure reported by Hubert *et al.*[20] was employed. The oily product was obtained in 89% yield, and was purified by column chromatography on alumina with diethyl ether and then ethyl acetate as eluants. The purified oily material (**7**) was extremely hygroscopic. MS *m/z*: 201 (M^+). IR (KBr): 1675 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.26 (5H, m, aromatic protons), 4.60 (2H, s, $=NCH_2$Ph), 3.61 [2H, s, C(5)-H], 1.90 [3H, s, C(3)-CH_3], and 1.83 [3H, s, C(4)-CH_3]. ^{13}C-NMR ($CDCl_3$) δ: 172.38 (C-2), 128.3, 127.7, 127.2 (aromatic carbons), 145.7 (C-4), 137.5 (C-3), 53.5 (C-5), 45.9 (a benzylic carbon), 12.9 [C(4)-CH_3], 8.6 [C(3)-CH_3]. *Anal.* Calcd for $C_{13}H_{15}NO \cdot 0.35H_2O$: C, 75.22; H, 7.62; N, 6.75. Found: C, 75.26; H, 7.51; N, 6.55.

Reduction of the α,β-Unsaturated Lactone (5) $NaBH_4$ (0.81 g, 21.4 mmol) was added portionwise to a stirred solution of α,β-unsaturated lactone (**5**) (0.6 g, 5.4 mmol) and $NiCl_2 \cdot 6H_2O$ (0.63 g, 2.7 mmol) in methanol at 15 °C. The black precipitate was filtered off and the filtrate was acidified with aqueous HCl (10%). The solvent was removed under reduced pressure and the resulting residue was diluted with H_2O. The mixture was extracted with Et_2O and the extract was washed with brine and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave an oily mixture of **8a** and **8b**, in 91% yield. The isomeric ratio of the products [**8a**/**8b**] was 3/1 as determined by HPLC using 60% ether/hexane as the eluant. The retention times for the two isomers (**8a** and **8b**) were 4.0 and 5.1 min, respectively. *Anal.* Calcd for $C_6H_{10}O_2$: C, 63.14; H, 8.83. Found: C, 62.99; H, 9.11. Purification of this mixture by preparative HPLC afforded an analytical sample of *cis*-dihydro-3,4-dimethyl-2(3*H*)-furanone (**8a**). MS *m/z*: 114 (M^+). IR (KBr): 1775 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 4.30 [1H, dd, $J_{C(5)\text{-H}(gem)}$ = 9.0 Hz, $J_{C(4)\text{-H},C(5)\text{-H}_A}$ = 6.0 Hz, C(5)-H_A], 3.93 [1H, dd, $J_{C(5)\text{-H}(gem)}$ = 9.0 Hz, $J_{C(4)\text{-H},C(5)\text{-H}_B}$ = 3.0 Hz, C(5)-H_B], 2.68 [qd, 1H, $J_{C(3)\text{-CH}_3,C(3)\text{-H}}$ = 7.0 Hz, $J_{C(4)\text{-H},C(3)\text{-H}}$ = 8.0 Hz, C(3)-H], 2.62 [1H, m, C(4)-H], 1.17 [3H, d, $J_{C(3)\text{-H},C(3)\text{-CH}_3}$ = 7.0 Hz, C(3)-CH_3], 1.02 [3H, dd, $J_{C(4)\text{-H},C(4)\text{-CH}_3}$ = 7.0 Hz, $J_{C(5)\text{-H}_A,C(4)\text{-CH}_3}$ = 1.0 Hz, C(4)-CH_3]. ^{13}C-NMR ($CDCl_3$) δ: 179.686 (C-2), 72.948 (C-5), 38.254 (C-3), 33.837 (C-4), 13.349 [C(4)-CH_3], 9.798 [C(3)-CH_3].

Isomerization of the *cis* Lactone (8a) A mixture of the *cis* lactone (**8a**) with 100% isomeric purity (0.14 g, 1.25 mmol) and sodium methoxide (0.12 g, 2 mmol) in anhydrous methanol was refluxed for 3.5 h. The resulting solution was concentrated under reduced pressure, diluted with water, and acidified with HCl (10%). The mixture was extracted with ether, and the extract was washed with aqueous sodium carbonate, and dried over anhydrous magnesium sulfate. Evaporation of the solvent afforded the *trans* lactone (**8b**) with 95% isomeric purity [by HPLC using 60% ether/hexane as the eluant]. Purification of the product by preparative HPLC gave a pure sample of *trans*-4,5-dihydro-3,4-dimethyl-2(3*H*)-furanone (**8b**). MS *m/z*: 114 (M^+). IR (KBr): 1778 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 4.37 [1H, ddd, $J_{C(5)\text{-H}(gem)}$ = 9.0 Hz, $J_{C(4)\text{-H},C(5)\text{-H}_B}$ = 7.5 Hz, C(5)-H_B], 3.72 [1H, ddd, $J_{C(5)\text{-H}(gem)}$ = 9.0 Hz, $J_{C(4)\text{-H},C(5)\text{-H}_A}$ = 10.0 Hz, $J_{C(4)\text{-CH}_3,C(5)\text{-H}_A}$ = 0.5 Hz, C(5)-H_A], 2.18 [1H, m, C(4)-H], 2.11 [1H, qd, $J_{C(3)\text{-CH}_3,C(3)\text{-H}}$ = 6.5 Hz, $J_{C(4)\text{-H},C(3)\text{-H}}$ = 11.0 Hz, C(3)-H], 1.24 [3H, d, $J_{C(3)\text{-H},C(3)\text{-CH}_3}$ = 6.0 Hz, C(3)-CH_3], 1.15 [3H, dd, $J_{C(4)\text{-H},C(4)\text{-CH}_3}$ = 6.0 Hz, $J_{C(5)\text{-H}_A,C(4)\text{-CH}_3}$ = 0.5 Hz, C(4)-CH_3]. ^{13}C-NMR ($CDCl_3$) δ: 179.579 (C-2), 72.432 (C-5), 41.820 (C-3), 38.709 (C-4), 15.550 [C(4)-CH_3], 13.061 [C(3)-CH_3].

Reduction of the α,β-Unsaturated Lactam (7) $NaBH_4$ (0.95 g, 25 mmol) was added portionwise to a stirred solution of α,β-unsaturated lactam (**7**) (1.11 g, 5 mmol) and $NiCl_2 \cdot 6H_2O$ (0.6 g, 2.5 mmol) in methanol at 15 °C. The black precipitate was filtered off and the filtrate was acidified with aqueous HCl (10%). The methanol was removed under reduced pressure and the resulting material was diluted with H_2O. After extraction with Et_2O, the ether extract was washed with brine, and dried over anhydrous magnesium sulfate. Evaporation of the solvent afforded the oily *cis*-1-benzyl-3,4-dimethyl-2-pyrrolidinone (**9a**) with 100% isomeric purity in 99.2% yield. An analytical sample was obtained by HPLC (AcOEt/hexane/Et_2O = 1/4/5 as the solvent). The product was extremely hygroscopic. *Anal.* Calcd for $C_{13}H_{17}NO \cdot 0.25H_2O$: C, 75.14; H, 8.49; N, 6.74. Found: C, 75.11; H, 8.48; N, 6.61. MS *m/z*: 203 (M^+). IR (KBr): 1682 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.342—7.207 (5H, m, aromatic protons), 4.485 (1H, d, J = 14.5 Hz, NCH_2Ph), 4.392 (1H, d, J = 14.5 Hz, NCH_2Ph), 3.269 [1H, dd, $J_{C(5)\text{-H}(gem)}$ = 9.5 Hz, $J_{C(4)\text{-H},C(5)\text{-H}_A}$ = 7 Hz, C(5)-H_A], 2.766 [1H, dd, $J_{C(5)\text{-H}(gem)}$ = 9.5 Hz, $J_{C(4)\text{-H},C(5)\text{-H}_B}$ = 5 Hz, C(5)-H_B], 2.557 [1H, dq, $J_{C(4)\text{-H},C(3)\text{-H}}$ = 7.0 Hz, $J_{C(3)\text{-CH}_3,C(3)\text{-H}}$ = 7.5 Hz, C(3)-H], 2.419 [1H, dddq, $J_{C(3)\text{-H},C(4)\text{-H}}$ = 7 Hz, $J_{C(5)\text{-H}_A,C(4)\text{-H}}$ = 7.0 Hz, $J_{C(5)\text{-H}_B,C(4)\text{-H}}$ = 5.0 Hz, $J_{C(4)\text{-CH}_3,C(4)\text{-H}}$ = 7 Hz, C(4)-H], 1.113 [3H, d, $J_{C(3)\text{-H},C(3)\text{-CH}_3}$ = 7.5 Hz, C(3)-CH_3], 0.925 [3H, d, $J_{C(4)\text{-H},C(4)\text{-CH}_3}$ = 7.0 Hz, C(4)-CH_3]. ^{13}C-NMR ($CDCl_3$) δ: 177.014 (C-2), 136.781, 128.510, 128.252, 128.130, 127.356 (aromatic carbons), 52.065 (C-5), 46.419 (NCH_2Ph), 40.485 (C-3), 30.286 (C-4), 14.062 [C(4)-CH_3], 10.298 [C(3)-CH_3].

Isomerization of the *cis* Lactam (9a) A mixture of the *cis* lactam (**9a**) with 100% isomeric purity (0.2 g, 1 mmol) and sodium methoxide (0.12 g, 2 mmol) in anhydrous methanol was refluxed for 20 h. The resulting solution was concentrated under reduced pressure, diluted with water, and extracted with ether. The extract was washed with brine, and dried over anhydrous magnesium sulfate. Evaporation of the solvent afforded the *trans* lactam (**9b**) with 85% isomeric purity (by HPLC using AcOEt/hexane/Et_2O = 1/4/5 as the eluant) in 75% yield. The retention times of the two isomers [**9a** and **9b**] were 9.8 and 12.4 min, respectively. Separation by HPLC afforded the pure *trans*-1-benzyl-3,4-dimethyl-2-pyrrolidinone (**9b**). MS *m/z*: 203 (M^+). IR (KBr): 1677 (C=O) cm^{-1}. ^{1}H-NMR ($CDCl_3$) δ: 7.338—7.206 (5H, m, aromatic protons), 4.462 (1H, d, J = 14.5 Hz, NCH_2Ph), 4.413 (1H, d, J = 14.5 Hz, NCH_2Ph), 3.242 [1H, dd, $J_{C(5)\text{-H}(gem)}$ = 8.0 Hz, $J_{C(4)\text{-H},C(5)\text{-H}_B}$ = 9.5 Hz, C(5)-H_B], 2.758 [1H, dd, $J_{C(5)\text{-H}(gem)}$ = 8.0 Hz, $J_{C(4)\text{-H},C(5)\text{-H}_A}$ = 9.0 Hz, C(5)-H_A], 2.042 [1H, dq, $J_{C(4)\text{-H},C(3)\text{-H}}$ = 10 Hz, $J_{C(3)\text{-CH}_3,C(3)\text{-H}}$ = 7 Hz, C(3)-H], 1.909 [1H, dddq, $J_{C(3)\text{-H},C(4)\text{-H}}$ = 10 Hz, $J_{C(5)\text{-H}_A,C(4)\text{-H}}$ = 9.0 Hz, $J_{C(5)\text{-H}_B,C(4)\text{-H}}$ = 9.5 Hz, $J_{C(4)\text{-CH}_3,C(4)\text{-H}}$ = 7 Hz, C(4)-H], 1.213 [3H, d, $J_{C(3)\text{-H},C(3)\text{-CH}_3}$ = 6.83 Hz, C(3)-CH_3], 1.077 [3H, d, $J_{C(4)\text{-H},C(4)\text{-CH}_3}$ = 6.83 Hz, C(4)-CH_3]. ^{13}C-NMR ($CDCl_3$) δ: 176.893 (C-2), 136.660, 128.555, 128.009, 127.371 (aromatic carbons), 52.034 (C-5), 46.525 (NCH_2Ph), 44.598 (C-3), 35.901 (C-4), 17.325 [C(4)-CH_3], 14.381 [C(3)-CH_3].

Isotope Labeling Study with Methyl Cinnamate Run 1: $NaBH_4$ (0.38 g, 10 mmol) was added in three portions to a stirred solution of $NiCl_2$ (0.32 g, 2.5 mmol) and D_2O (0.4 g, 20 mmol) in MeOD (over 99.5%, 25 ml). Gas evolution, followed by the formation of a black precipitate of Ni_2B was observed. After 10 min, the supernatant was decanted, and the black precipitate was washed with MeOD, until no Ni^{2+} could be detected in the washings. Then $NaBH_4$ (0.188 g, 5 mmol) was added portionwise to a mixture of the black precipitate and methyl cinnamate (0.4 g, 2.5 mmol) in MeOD (25 ml) at 10 °C over a period of 90 min. The mixture was filtered and the filtrate was acidified with aqueous HCl (10%). The solvent was removed under reduced pressure and the residue was taken up in H_2O (5 ml). The mixture was extracted with Et_2O and the extract was washed with brine and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave 0.37 g (91.4%) of methyl 3-phenylpropionate.

Run 2: $NaBH_4$ (0.2 g, 5.3 mmol) was added portionwise to a stirred solution of $NiCl_2 \cdot 6D_2O$ (0.6 g, 2.5 mmol) and methyl cinnamate (0.4 g, 2.5 mmol) in MeOD (25 ml) at 10 °C over a period of 20 min. The mixture was filtered and the filtrate was acidified with aqueous DCl (20%). The

solvent was removed under reduced pressure and the residue was taken up in D_2O (5 ml). The mixture was extracted with Et_2O and the extract was washed with brine and dried over anhydrous magnesium sulfate. Evaporation of the solvent gave 0.35 g (86.4%) of methyl 3-phenylpropionate.

Run 3: Reduction of methylcinnamate (0.4 g, 2.5 mmol) was carried out in the same manner as in run 2, using $NaBD_4$ (0.35 g, 9 mmol) and MeOH (25 ml) instead of $NaBH_4$ and MeOD (reaction time, 30 min). The results on the incorporation of deuterium into methyl 3-phenylpropionate are summarized in the table.

References and Notes

1) T. Satoh, S. Suzuki, Y. Suzuki, Y. Miyazi, and Z. Imai, *Tetrahedron Lett.*, **1969**, 4555.
2) T. Satoh, K. Nanba, and S. Suzuki, *Chem. Pharm. Bull.*, **19**, 817 (1971).
3) A. Nose and T. Kudo, *Chem. Pharm. Bull.*, **32**, 2421 (1984).
4) A. Nose and T. Kudo, *Chem. Pharm. Bull.*, **29**, 1159 (1981).
5) S.-K. Chung, *J. Org. Chem.*, **44**, 1014 (1979).
6) S. W. Heinzman and B. Ganem, *J. Am. Chem. Soc.*, **104**, 6801 (1982).
7) J. A. Cowan, *Tetrahedron Lett.*, **27**, 1205 (1986).
8) Jacobi *et al.* proposed that the hydrogenation of 5,6,7,7a-tetrahydro-3-methyl-2,4-benzofurandione with Ni^{2+}/BH_4^- would produce the *cis* isomer initially, though the isolated product was the *trans* isomer [see, P. A. Jacobi, T. A. Craig, D. G. Walker, B. A. Arrick, and R. F. Frechette, *J. Am. Chem. Soc.*, **106**, 5585 (1984)].
9) S. Miyano, N. Abe, F. Fujisaki, and K. Sumoto, *Heterocycles*, **26**, 1813 (1987).
10) R. C. Wade, D. G. Holah, A. N. Hughes, and B. C. Hui, *Catal. Rev.-Sci, Eng.*, **14**, 211 (1976).
11) W. Strohmeier and H. Steigerwald, *Z. Naturforsch*, **32b**, 111 (1977).
12) M. Christl, H. J. Reich, and J. D. Roberts, *J. Am. Chem. Soc.*, **93**, 3463 (1971).
13) N. Satyanarayana and M. Periasamy, *Tetrahedron Lett.*, **25**, 2501 (1984).
14) J. O. Osby, S. W. Heinzman, and B. Ganem, *J. Am. Chem. Soc.*, **108**, 67 (1986).
15) In order to rule out the homogeneous reaction, Ni_2B was previously washed out with MeOD till no Ni^{2+} was detected in the washings (see reference 7).
16) We confirmed that the reduction of **5** did not take place under heterogeneous conditions [10 mol eq of $NaBH_4$ + 1 mol eq of preformed Ni_2B] or under homogeneous conditions in the absence of a black precipitate [at −10 °C, 3 mol eq of $NaBH_4$ + 1 mol eq of $NiCl_2 \cdot 6H_2O$]. In addition, we observed that under the latter homogeneous conditions the reduction was initiated by the formation of a black precipitate (Ni_2B).
17) W. W. Epstein and A. C. Sonntag, *J. Org. Chem.*, **32**, 3390 (1967).
18) D. M. Bailey and R. E. Johnson, *J. Org. Chem.*, **35**, 3574 (1970).
19) R. Brettle and D. P. Cummings, *J. Chem. Soc., Perkin Trans. 1*, **1977**, 2385.
20) J. C. Hubert, J. B. P. A. Wijnberg, and W. N. Speckamp, *Tetrahedron*, **31**, 1437 (1975).