etherate and titanium tetrachloride were obtained from Aldrich and were used without purification.

Dimethyl 1α,3-Dimethyl-5β-phenyl-8-[(trimethylsilyl)-methyl]-2-azabicyclo[2.2.2]oct-2-ene-4,6α-dicarboxylate (5). To a solution of 3.0 g (0.01 mol) of 1 and 22.8 g (0.2 mol) of allyltrimethylsilane in 75 mL of chloroform cooled to 0–10 °C under nitrogen was added dropwise via syringe 5.7 g (0.03 mol) of titanium tetrachloride over 20 min. The reaction mixture was then stirred at 0–10 °C for 3 h during which time the color darkened and some precipitate became apparent. The reaction mixture was then poured onto ice, and this neutralized with saturated sodium bicarbonate solution. This was extracted with 3 × 75 mL of chloroform, and the combined organics were washed with brine and dried over sodium sulfate. Solvent removal on the rotary evaporator afforded a yellow oil that was purified by flash chromatography on silica gel (230–400 mesh), eluting with 2% methanol/chloroform. Eluting from the column were 2.95 g (71%) of **5** [R_f 0.5, white, crystalline solid, mp 152–155 °C] and 0.29 g (10%) of **6** [R_f 0.4, mp 131–133 °C]: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 0.078 (9 H, s), 0.27 (1 H, dd, J = 13.9, 12.7 Hz, H_{9a}), 0.47 (1 H, dd, J = 14.0, 1.5 Hz, H_{9b}), 0.83 (1 H, br dd, J = 13.0, 3.4 Hz, H_{7a}), 1.56 (3 H, s), 2.46 (1 H, dd, J = 13.1, 9.4 Hz, H_{7b}), 2.55 (3 H, s, allylic CH_3), 2.60 (1 H, r d, J = 6.9 Hz, H_6), 2.76 (1 H, m, H_8), 3.58 (3 H, s, CO_2CH_3), 3.74 (1 H, d, J = 7 Hz, H_5), 3.74 (3 H, s, CO_2CH_3), 7.0–7.35 (5 H, m, aromatic); mass spectrum, m/e 415 (M^+), 400, 384, 374, 356, 342, 314, 302, 270, 261, 242, 238. Anal. Calcd for $C_{23}H_{33}NO_4Si$: C, 66.46; H, 8.00; N, 3.37. Found: C, 66.43; H, 8.23; N, 3.59.

Dimethyl 1α,3-Dimethyl-5β,8-diphenyl-2-azabicyclo-[2.2.2]oct-2-ene-4,6α-dicarboxylate (8). To a solution of 1.0 g (3.3 mmol) of 1 and 6.86 g (66 mmol) of styrene dissolved in 60 mL of chloroform and cooled to 0–10 °C under nitrogen was added 10 mmol of boron trifluoride etherate via syringe over 20 min. The resulting clear, yellow solution was stirred at 0–10 °C for 3 h, and the reaction mixture was then quenched by pouring on ice. This was neutralized with saturated sodium bicarbonate solution, and the aqueous phase was extracted with 3 × 75 mL portions of chloroform. The combined organic extracts were washed with brine and dried over sodium sulfate, and the solvent was stripped on the rotary evaporator to give a yellow oil. This material was purified by flash chromatography on silica gel (230–400 mesh), eluting with 10% isopropyl alcohol/hexane. The desired cycloadduct 8 was eluted from the column, R_f 0.5, to afford after solvent removal a white, crystalline solid: mp 138–139 °C; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 1.49 (1 H, ddd, J = 13.8, 6.1, 2.0 Hz, H_{7a}), 1.59 (3 H, s, CH_3), 2.30 (3 H, s, allylic CH_3), 2.62 (1 H, dd, J = 13.8, 10.1 Hz, H_{7b}), 2.66 (1 H, dd, J = 6.8, 1.9 Hz, H_6), 3.36 (3 H, s, CO_2CH_3), 3.70 (3 H, s, CO_2CH_3), 3.78 (1 H, dd, J = 10.1, 6.1 Hz, H_8), 3.88 (1 H, d, J = 6.8 Hz, H_5), 7.10 (3 H, m), 7.2 (7 H, m); mass spectrum, m/e 405 (M^+). Anal. Calcd for $C_{25}H_{27}NO_4$: C, 74.05; H, 6.71; N, 3.45. Found: C, 74.40; H, 6.81; N, 3.33.

X-ray Crystal Structure Analysis of 5. Suitable crystals of **5** ($C_{23}H_{33}NO_4Si$) for X-ray diffraction studies formed from a neat oil with space group symmetry of $P2_1/C$ and cell constants of a = 10.668 (1) Å, b = 26.569 (5) Å, c = 9.274 (1) Å, and β = 114.70 (1)° for Z = 4 and a calculated density of 1.15 g/cm^3. Of the 3211 reflections measured with an automatic four-circle diffractometer equipped with Cu radiation, 2791 were observed [$I > 3\sigma(I)$]. The structure was solved with a multisolution tangent formula approach and difference Fourier analysis and refined by full-matrix least-squares techniques.[1] Hydrogens were assigned isotropic temperature factors corresponding to their attached atoms. The function $\sum w(|F_o| - |F_c|)^2$ with $w = 1/[\sigma(F_o)]^2$ was minimized to give an unweighted residual of 0.062. No abnormally short intermolecular contacts were noted. Tables I containing the final fractional coordinates, temperature parameters, bond distances, and bond angles are available as supplementary material. Figure 1 (supplementary material) is a computer-generated perspective drawing of **5** from the final X-ray coordinates showing the relative stereochemistry.

Acknowledgment. We thank Dr. S. M. Pitzenberger for his analysis of NMR spectra, J. P. Moreau for elemental analysis, Dr. H. Ramjit for mass spectral determinations, and M. Banker for typing the manuscript. We also thank Dr. J. J. Baldwin for help and encouragement throughout the course of this work.

Registry No. 1, 70677-78-0; (±)-**5**, 105335-61-3; **6**, 77234-00-5; (±)-**8**, 105335-62-4; $H_2C{=}CHCH_2SiMe_3$, 762-72-1; $C_6H_5CH{=}CH_2$, 100-42-5.

Supplementary Material Available: ORTEP of **5** and listings of crystallographic data including atomic positional and thermal parameters, bond distances, and bond angles (5 pages). Ordering information is given on any current masthead page.

Homogeneous and Heterogeneous Catalytic Asymmetric Reactions. 1. Asymmetric Hydrogenation of the Prochiral C=C Bond on a Modified Raney Ni Catalyst

M. Bartók,* Gy. Wittmann, Gy. Göndös, and G. V. Smith†

Department of Organic Chemistry, József Attila University, Szeged, Hungary

Received January 30, 1985

The catalyst TA–MRNi (Raney Ni catalyst modified with (*R,R*)-tartaric acid) has been in use for the asymmetric hydrogenation of prochiral ketones since 1962.[1] An optical yield of 80–90% has been achieved in the case of prochiral ketones on the catalyst TA–NaBR–MRNi.[2] The efforts to carry out the enantioselective hydrogenation of the prochiral C=C bond on modified MRNi have proved practically ineffective.[3-5]

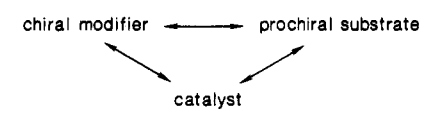
The literature data lead to the conclusion that there is a considerable difference between organic compounds containing C=O and C=C bonds as concerns enantioselective hydrogenation. The monographs referred to[4,5] did not pay any special attention to this difference.

In our opinion, the failure of C=C compounds to display enantioselectivity can be explained in that the examined substrates, in the absence of an appropriate binding site, could not form a complex with the catalyst or with the chiral group of the modifier. Setting out from this starting point, after a number of efforts, we selected the sodium salts of prochiral C=C containing carboxylic acids as model compounds for a study of enantioselective hydrogenation.

Results and Discussion

Some characteristic data relating to our experimental results are listed in Table I. It may be seen that an outstandingly high enantioselectivity was observed with sodium (*E*)-α-phenylcinnamate (1). The enantioselectivity was considerably lower for the *Z* isomer and for the free acids. We interpret these experimental results as follows.

The accepted view concerning the mechanism of action of the catalyst in question is that the occurrence of enantioselectivity demands the formation of a mixed ligand complex on the surface of the catalyst:[4,5,7]



The enantioselectivity is governed by the strength of the interactions between the components of this complex. The steric structure of the product formed during hydrogenation is determined by the adsorption of the substrate. The

† Department of Chemistry and Biochemistry, Southern Illinois University, Carbondale, IL 62901.

0022-3263/87/1952-1139$01.50/0

Table I. Experimental Results on Chiral Hydrogenation of Compounds 1-6 on TA-NaBr-MRNi[a] Catalysts

compd	p,[b] %	$[\alpha]^{20}_D$ (c, solv)	substrate/cat., mmol/g	rate, mL of H_2/(g of cat.)h
sodium (*E*)-α-phenylcinnamate (1)	17.03	−22.77° (14.273, acetone)	23.0226	884.9
sodium (*Z*)-α-phenylcinnamate (2)	0.47	−0.63° (11.543, acetone)	28.3129	309.5
sodium (*E*)-α-phenyl-4-methoxycinnamate (3)		−2.12° (14.808, EtOH)	21.1312	258.9
sodium (*Z*)-α-phenyl-4-methoxycinnamate (4)		−0.198° (12.827, EtOH)	16.3395	310.6
(*E*)-α-phenylcinnamic acid (5)	0.20	−0.28° (11.790, acetone)	24.3556[c]	44.3
(*E*)-α-phenyl-4-methoxycinnamic acid (6)	0		18.0455[d]	

[a] TA-NaBr-MRNi: Raney Ni modified with (*R,R*)-tartaric acid and NaBr. [b] p (%) = ($[\alpha]_{D\,measd}/[\alpha]_{D\,max}$)100. [c] The dissolution of Ni during modification is well-known.[6] We observed the dissolution of 7.05 mg of Ni during the hydrogenation. [d] No hydrogenation occurred; 9.03 mg of Ni dissolved.

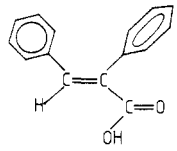


Figure 1. Structure of (*E*)-α-phenylcinnamic acid.

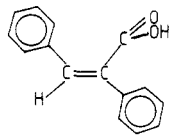


Figure 2. Structure of (*Z*)-α-phenylcinnamic acid.

enantioselectivity decreases in the event of a strong substrate adsorption, since the effect of the modifier can not be manifested.

The studied compounds (1–6) exhibit very characteristic differences as regards their stereochemical[8] and electronic[9] properties. In (*E*)-α-phenylcinnamic acid, the β-phenyl group and the carboxyl function are in conjugative interaction with the C=C bond and are in a coplanar arrangement (Figure 1). Consequently, the *E* acid **5** has $pK_s \sim 7$. At the same time, in (*Z*)-α-phenylcinnamic acid, the two phenyl groups are coplanar with the C=C bond, whereas the carboxyl group is deconjugated (Figure 2). As a result, the *Z* acids are stronger acids, with $pK_s \sim 5$, while their alkali metal salts are more ionic in character. The C=C bond in the *E* acid is less sterically hindered than that in the *Z* acid from the aspect of hydrogenation. The presence of the methoxy group modifies the above findings in that its electron-repelling effect leads to increases in the electron density and the size of the molecule.

Conclusions as to the interaction of the substrate and the modifier can be drawn from the literature data. The carboxylic acids are known to tend to intermolecular acid salt formation;[10,11] further, through the functional groups of TA they interact both with the carboxyl groups of the substrate and with the surface metal atoms;[4,5] finally, the C=C bond of the substrate is also coordinated to the surface metal ions.[12] Similar interactions may be assumed between 1 and the TA on the surface. One such possible linkage is shown in Figure 3.

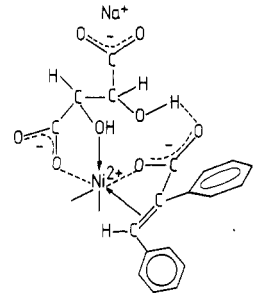


Figure 3. Interaction of TA and 1 on Ni.

It appears that in **1** both the geometry of the substrate and its interaction with TA are optimum from the aspect of enantioselectivity. In this experiment the optical yield and the reaction rate were highest. In the cases of **2** and **4**, the coplanarity means that extremely strong surface adsorption is probable; this weakens the directing effect of the modifier and also decreases the rate of the reaction, for product desorption is presumably the rate-determining step.

Although the steric arrangement of the *E* compound is favorable as concerns its interaction with TA in the hydrogenation of **3**, the methoxy group increases the strength of adsorption, as demonstrated by the lower enantioselectivity. In the *Z* compounds **2** and **4**, the steric position of the β-phenyl group probably has a disadvantageous effect on the interaction with TA. The main factor in the hydrogenation of the free acids **5** and **6** is the corrosion of the catalyst. In these experiments it is necessary to take into account the appreciable transformation of the surface and the displacement of the modifier from the surface.

At the present stage of our work, our experimental results do not permit an exact knowledge of the nature of the interaction between the substrate and the modifier. Nevertheless, it is highly probable that the interactions in these reactions are of a different type from those with ketone substrates.

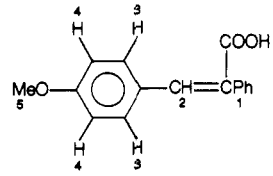
Experimental Section

α-Phenylcinnamic Acids. The compounds were prepared as described in the literature.[13] Various physical, analytical and spectroscopic data on the products are in Table II.

Sodium Salts of α-Phenylcinnamic Acids. The sodium salts were prepared from the purified acids in ethanolic solution by the addition of an ethanolic solution of sodium ethylate. After

(1) Izumi, Y.; Imaida, M.; Fukawa, H.; Akabori, S. *Bull. Chem. Soc. Jpn.* **1963**, *36*, 155.
(2) Tai, A.; Harada, T.; Hiraki, Y.; Murakami, S. *Bull. Chem. Soc. Jpn.* **1983**, *56*, 1414.
(3) Smith, G. V.; Musoiu, M. *J. Catal.* **1979**, *60*, 184.
(4) Klabunovskii, E. I.; Vedenyapin, A. A. *Asymmetricheskii Kataliz*, Nauka: Moskva, 1980.
(5) Izumi, Y.; Tai, A. *Stereo-Differentiating Reactions*; Kodansha Ltd.: Tokyo; Academic: New York, 1977. Izumi, Y. *Adv. Catal.* **1984**, *32*, 215.
(6) Hoek, A.; Sachtler, W. M. H. *J. Catal.* **1979**, *58*, 276.
(7) Groenewegen, J. A.; Sachtler, W. M. H. *J. Catal.* **1975**, *38*, 501.
(8) Zimmerman, H. E.; Ahramjian, L. J. *J. Am. Chem. Soc.* **1959**, *81*, 2086.
(9) Bowden, K.; Parking, D. C. *Can. J. Chem.* **1968**, *46*, 3909.
(10) Crawford, M. *J. Chem. Soc.* **1941**, 259.
(11) McGregor, D. R.; Speakman, J. C.; Lehmann, M. S. *J. Chem. Soc., Perkin Trans. 2* **1977**, 1740.
(12) Ugo, R. *Aspects of Homogeneous Catalysis*; Carlo Manfredi: Editore-Milano, 1970; Vol. 1.
(13) Fieser, L. F. *Experiments in Organic Chemistry*, 3rd ed., D. C. Heat: Boston, 1955.
(14) Ketcham, R.; Jambotkar, D. *J. Org. Chem.* **1963**, *28*, 1034.

Table II. Various Physical, Analytical, and Spectroscopic Data on Substrates



		Anal.					IR,[a] cm^{-1}		^1H NMR,[b] ppm				
		calcd		found			$C(---O)_2$	$C(---O)_2$					
compd	mp, °C	C	H	C	H	recryst solv	asym	sym	5-H	4-H	3-H	2-H	1-H
1	354-355	73.16	4.50	73.28	4.66	EtOH	1600	1390		7.15		7.65	7.34
2	303-310	73.16	4.50	72.89	4.81	EtOAc	1552	1412		7.23		7.63	6.42
3	304-306	69.56	4.74	68.94	4.40	EtOH	1560	1390	3.63	6.52[d]	6.88[d]	7.59	7.18
4	294-296	69.56	4.74	68.70	4.76	EtOH	1570	1414	3.72	6.77[e]	7.23[e]	6.35	7.57
5	172-174					benzene							
6	192-194[c]					benzene							

[a] IR spectra were recorded in KBr tablets on Unicam SP 200 instrument. [b] NMR spectra were recorded in Me_2SO in the presence of Me_4Si as internal standard on a JEOL C-60HL instrument. [c] 189-190 °C.[14] [d] J_{4-3} = 9 Hz. [e] J_{4-3} = 9 Hz.

evaporation of the resulting solution, the sodium salts were obtained by recrystallization from an appropriate solvent (see Table II). The yields were almost quantitative. Before use, the salts were dried at 120 °C and 0.1 torr for 2 h. Some data on the products are given in Table II.

Catalyst Preparation. Freshly prepared RNi was used in every experiment. The general method of preparation was as follows: 3 g of a 1:1 Ni-Al alloy (Carlo Erba Analyticals, Code 457675) was treated at 80 °C for 45 min with 60 mL of 20% NaOH solution. The resulting alloy was washed with 20 × 40 mL of distilled water.

Catalyst Modification. The modification involved a slight variation of the method of Izumi et al.[1] An aqueous solution (75 mL) of 1.6% D-TA (Janssen Chimica, No. T-10-9) and 10% NaBr was poured onto the catalyst prepared as above. After heating to 50 °C, the pH of the mixture was adjusted to 3.0 with 1 mL of NaOH. The mixture was kept at pH 3 and stirred intensively with a magnetic stirrer for 45 min, during the addition of an aqueous 5% D-TA + 10% NaBr solution, with continuous recording of the pH (Radiometer pH meter 22, Radelkis, Hungary). After treatment, the modifying solution was poured off the catalyst, which was then washed with 10 mL of water and 3 × 10 mL of absolute ethanol.

Hydrogenation. Hydrogenations were performed at 30 °C, in 20 mL of absolute ethanol, in a hydrogenation vessel operating at atmospheric pressure. The reaction vessel had a double wall. The reaction mixture was stirred magnetically. With the exception of **6**, the model compounds were hydrogenated with 100% conversion. After the uptake of the calculated quantity of hydrogen, the catalyst was filtered off, the filtrate was evaporated down, the residue was treated with dilute iced HCl and with ether (for **1**, **2**, and **5**) or EtOAc (for **3**, **4**, and **6**). The organic phase was separated, washed with 3 × 10 mL of water, dried over anhydrous Na_2SO_4, and evaporated, and the $[\alpha]^{20}_D$ value was determined (Polamat A, Carl Zeiss). The hydrogenated compounds obtained were checked for purity by means of their ^1H NMR and IR spectra and elementary analysis. The results of the hydrogenation experiments are in Table I. The optical yields in the case of 2,3-diphenylpropionic acid were calculated via the values given for the optically pure modifications[15,16] through the formula $p = 100[\alpha]_{D\,meas}/[\alpha]_{D\,max}$. (*R*)-2,3-Diphenylpropionic acid has $[\alpha]^{25}_D$ −133.7° (*c* 0.4905, acetone). The $[\alpha]_D$ for the optically pure modification of 2-phenyl-3-(*p*-methoxyphenyl)propionic acid is unknown.

The aluminium[17] and nickel[18] contents of the filtered catalyst were dissolved in concentrated HCl, the solution was diluted to a definite volume with water, and titrimetric determinations were carried out. The reaction rates were calculated from the initial, linear section of the hydrogen consumption curves.

Acknowledgment. We gratefully acknowledge MTA and NSF support for the US/Hungarian collaboration. We also acknowledge the support provided for this research by the Hungarian Academy of Sciences (Grant No. 319/82/1.3) and the Ministry of Culture (Grant No. 40/1981). We express our thanks to Dr. G. B. Bartók for the microanalyses, to Dr. J. T. Kiss for the IR recordings, and to Dr. G. Dombi for the ^1H NMR recordings.

Registry No. **1**, 15352-96-2; **2**, 15352-97-3; **3**, 106319-21-5; **4**, 106319-22-6; **5**, 91-48-5; **6**, 13938-24-4; (*R*)-$C_6H_5CH_2CHPhCO_2H$, 17040-62-9; (−)-4-$H_3COC_6H_4CH_2CHPhCO_2H$, 106319-23-7.

(15) Pettersson, K. *Ark. Kemi* **1954**, *7*, 339.
(16) Watson, M. B.; Youngson, G. W. *J. Chem. Soc. C* **1968**, 258.
(17) Sajó, I. *Acta Chim. Hung.* **1955**, *6*, 251.
(18) Kinnunen, J.; Merikanto, B. *Chem. Anal.* **1954**, *43*, 13.

Stereochemistry and Synthetic Applications of the Products of Yeast Reduction of 3-Hydroxy-3-methyl-5-phenylpent-4-en-2-one

Giovanni Fronza, Claudio Fuganti,*
Giuseppe Pedrocchi-Fantoni, and Stefano Servi

Dipartimento di Chimica del Politecnico, CNR Centro di Studio per le Sostanze Organiche Naturali, 20133 Milano, Italy

Received August 6, 1986

In recent years a growing number of chiral intermediates complementary or alternative to the components of the "pool of chirality"[1] have been produced by microbial transformations or by use of purified enzymes and have been used successfully in the synthesis of natural products. Among this set of compounds, species containing in a relatively small carbon framework chiral centres of type RR'CHOH or/and RR'R''CH are prominent and, due to its commercial availability and synthetic flexibility, bakers' yeast is the most widely used microbial system for making them.[2]

(1) Seebach, D.; Kalinowski, H. O. *Nachr. Chem. Tech.* **1976**, *24*, 415. Fischli, A. In *Modern Synthetic Methods*; Scheffold, R., Ed.; Salle und Sauerlander: Frankfurt am Main, 1980; Vol. 2, p 269.
(2) For recent representative examples of the use of purified enzymes and microbial transformations in organic synthesis, see: *Enzymes in Organic Synthesis*; CIBA Foundation Symposium 111; Pitman: London, 1985. *Enzymes as Catalysts in Organic Synthesis*; Schneider, M. P., Ed.; Nato ASI Series; D. Reidel Publishing Co., 1986; Series C, Vol. 178.

0022-3263/87/1952-1141$01.50/0