Diastereoselective Reduction of Chiral α-Ketoamides Derived from (*S*)-Proline Esters with Sodium Borohydride. Preparation of Optically Active α-Hydroxy Acids[1]

Kenso Soai* and Hitoshi Hasegawa
Department of Applied Chemistry, Faculty of Science, Science University of Tokyo, Kagurazaka, Shinjuku-ku, Tokyo, 162 Japan

Diastereoselective reductions of chiral α-ketoamides (**3**) derived from (*S*)-proline esters (**2**) with sodium borohydride were examined. Hydrolysis of the reduction products afforded optically active α-hydroxy acids (**5**) in good enantiomeric excesses (e.e.). The most influential factor of the asymmetric induction was the effect of using a mixed hydroxylic and non-hydroxylic solvent. The degree of asymmetric induction varied considerably with the ratio of alcohol and tetrahydrofuran (THF) in the mixed solvent. With aromatic ketoamides (**3**), higher asymmetric induction occurred in a mixed alcohol–THF solvent than in the corresponding individual solvents.

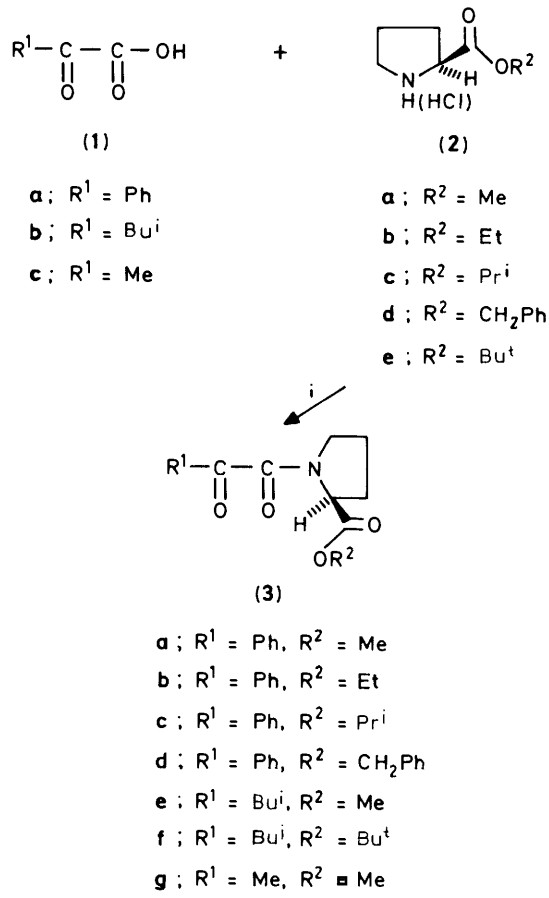
Although asymmetric additions of Grignard reagents to chiral α-ketoesters have been widely examined, there are fewer reports on the asymmetric reduction of chiral α-ketoamides with complex metal hydrides.[2] Furthermore, the optical yields reported, for example for the asymmetric reduction of chiral α-ketoamides using sodium borohydride ($NaBH_4$), are low to moderate (<44% e.e.).[2–4] It is accepted that the solvent is one of the most important factors affecting the degree of asymmetric induction.[5] However, there are only a few reports of the use of mixed solvents in asymmetric syntheses.[6]

As part of our study of reductions with $NaBH_4$, we have already reported the effect of a small amount of MeOH on the reactivity and chemoselectivity of complex borohydride.[7] We describe here the asymmetric reduction with $NaBH_4$ of chiral α-ketoamides derived from (*S*)-proline esters and an investigation of the effect of the reaction conditions: *i.e.* solvent, temperature, nature of reducing agent, nature of the ester, and nature of the acyl substituent of the α-ketoamide.

The chiral α-ketoamides (**3a**—**g**) were synthesized in 49—85% yield by the condensation of the corresponding α-ketoacids (**1a**—**c**) and the hydrochlorides of the (*S*)-(−)-proline esters (**2a**—**d**) or (*S*)-proline t-butyl ester (**2e**) using dicyclohexylcarbodi-imide (DCC) [and triethylamine or dicyclohexylamine for (**2a**—**d**)] in dichloromethane[8] (Scheme 1).

The first compound investigated, (**3a**), was reduced by $NaBH_4$ (0.5 mmol) at 0 °C for 3 h in various solvents (4 ml). The reductions were quenched by the addition of 1M-hydrochloric acid. N.m.r. analysis of the resulting mixture (**4a**) showed that the ketone carbonyl group of (**3a**) had been reduced selectively. The mixture (**4a**) was then hydrolysed by heating at 120 °C (bath temp.) in 2M-sulphuric acid for 2 h. Purification on preparative t.l.c. followed by bulb-to-bulb distillation afforded optically active mandelic acid (**5a**). The total yields of (**5a**) were in the range 61—82%, from (**3a**—**d**).

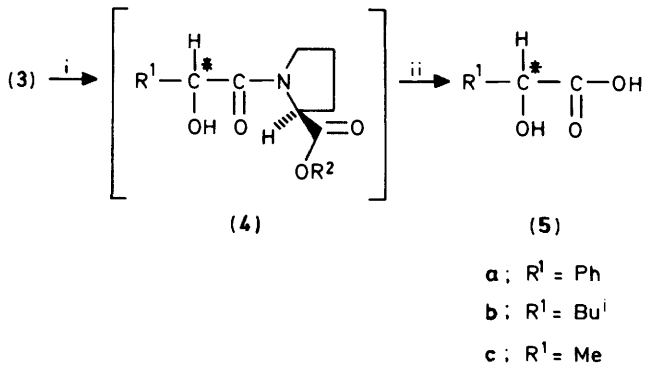
The direction and degree of the diastereoselectivity of the $NaBH_4$ reductions were determined by the values of the optical rotations of the purified product (**5a**). In some cases, the diastereoselectivity was also determined by ^1H n.m.r. (100 MHz) analysis of the unpurified reaction mixture (**4a**), the pair of singlets due to the benzylic methine proton (*ca.* 5.0 p.p.m.) showing the ratio of the diastereoisomers (**4a**). In one case, where a sample of (**4a**) of 50% d.e. [determined by n.m.r., derived from (**3a**)] was hydrolysed, the optical purity (determined by the optical rotation) of the mandelic acid (**5a**) obtained was found to be 45% {$[\alpha]_D^{25}$ +71.0° (*c* 1.2, H_2O); lit., $^9[\alpha]_D$ 158° (H_2O)};



Scheme 1. *Reagents*: i, DCC (Et_3N)

thus any racemisation that occurred was within the limits of experimental error in the hydrolysis step from (**4a**) to (**5a**).

The effect of using a mixed solvent, tetrahydrofuran (THF)–methanol (MeOH), on the diastereoselective reduction of compound (**3a**) with $NaBH_4$ is shown in the Figure. With $NaBH_4$ in MeOH (4 ml) as described above, the asymmetric induction was found to be only 4%. The same reduction in THF (4 ml) also resulted in a low (36%) asymmetric induction.



Scheme 2. *Reagents*: i, $NaBH_4$; ii, 2M-H_2SO_4

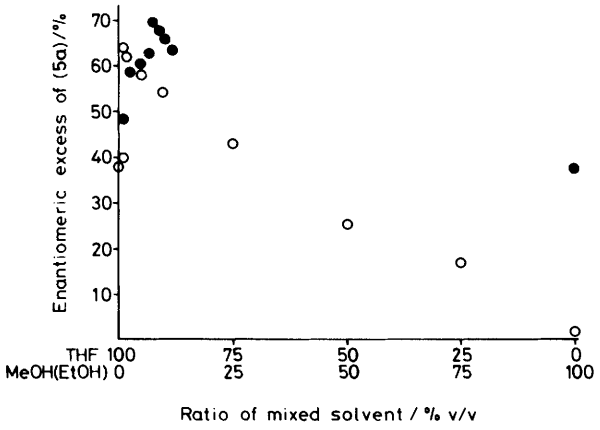


Figure. Plot of the enantiometic excess of compound (**5a**) against the volumetric ratio of THF-MeOH (○) or THF–EtOH (●) for the reduction of compound (**3a**) with $NaBH_4$ at 0 °C

However, when compound (**3a**) was reduced in THF–methanol (99:1, v/v; 4 ml), the optical yield of the product (**5a**) was raised to 64% e.e.; *i.e. the use of a mixed solvent resulted in a much higher asymmetric induction than with each individual solvent*, an unprecedented effect. We then investigated the effect of the ratio of the components of the mixed solvent (THF–MeOH). We found that the presence of a small amount of MeOH (*ca.* 1% volume) in THF increased the degree of asymmetric induction from 36% e.e. (THF alone) to 64% e.e. for the reduction of compound (**5a**) with $NaBH_4$. The combination of hydroxylic and non-hydroxylic solvents was also found to affect the asymmetric reduction (Table 1). As shown in Table 1, THF is a better non-hydroxylic solvent than diethyl ether or acetonitrile (entries 3, 6, and 7); ethanol and methanol are effective hydroxylic solvents, but the presence (1%) of propan-2-ol in THF gave similar results to THF alone (entries 1 and 5). When compound (**3a**) was reduced in THF–EtOH (92:8, v/v), (*S*)-(+)-mandelic acid (**5a**) was obtained in 85% yield [from (**3a**)] with an optical purity of 69% e.e. (entry 4) (The results obtained from THF–EtOH are also shown in the Figure). To the best of our knowledge, this degree of asymmetric induction is the highest yet reported for the diastereoselective reduction of chiral α-keto amides or α-ketoesters with $NaBH_4$. Water was also an effective co-solvent, though less so than MeOH or EtOH, the degree of asymmetric induction increasing from 38 to 51% when the solvent was changed from THF to THF–water (98:2, v/v) (entries 1 and 2). A similar effect was also observed when (**3d**) instead of (**3a**) was reduced in THF–water (entries 7 and 8).

The effect of temperature on the diastereoselectivity was found to be small (Table 2). The degree of asymmetric induction did not increase when the reduction was carried out at low temperature.

In order to examine the effect of the structure of the reducing agent, sodium tri-isopropoxyborohydride [$NaBH(OPr^i)_3$] in diethylene glycol dimethyl ether (diglyme) was used.[10] The effect of the alkoxy substituent was found to be small, the reduction of compound (**3a**) with $NaBH_4$ and $NaBH(OPr^i)_3$ in diglyme affording (*S*)-(**5a**) in 15 and 13% e.e. respectively (Table 3). It was also found that potassium tri-s-butylborohydride (K-Selectride), a well known stereoselective reducing reagent,[11] gave only low (17—36% e.e.) asymmetric induction even at low temperatures (−78 °C). Interestingly, the opposite configuration [(*R*)-(−)-] of the product (**5a**) was obtained from the reductions with K-Selectride, than from $NaBH_4$.

The effect of the structure of the ester and of the acyl substituent of compound (**3**) was then examined (Table 4). The methyl and isopropyl esters (**3a**) and (**3c**) gave the highest asymmetric induction (entries 1 and 3) of those investigated. The reduction of the acetyl derivative (**3g**) in THF–MeOH

Table 1. Effect of a mixed (hydroxylic and non-hydroxylic) solvent on the asymmetric reduction of compounds (3)

				(*S*)-(**5a**)	
Entry	Compound	Solvent	Ratio (v/v)	Yield (%)	E.e. (%)[a]
1	(**3a**)	THF	100	95	36
2	(**3a**)	THF–H_2O	98:2	82	51
3	(**3a**)	THF–MeOH	99:1	62	64
4	(**3a**)	THF–EtOH	92:8	85	69
5	(**3a**)	THF–Pr^iOH	99:1	61	38
6	(**3a**)	Et_2O–MeOH	99:1	82	42
7	(**3a**)	MeCN–MeOH	99:1	79	25
8	(**3d**)	THF	100	63	28
9	(**3d**)	THF–H_2O	99:1	35	37

[a] Enantiomeric excess, based on the reported value of the specific rotation for (*S*)-(+)-(**5a**), $[\alpha]_D$ +158° (H_2O): see ref. 9.

Table 2. Effect of temperature on the asymmetric reduction of compound (**3a**) with $NaBH_4$

		(*S*)-(**5a**)	
Solvent (v/v)	Temp. (°C)	Yield (%)	E.e. (%)[a]
THF–H_2O (99:1)	−30	96	32
	0	82	45
	+30	75	26
THF–MeOH (99:1)	0	62	64
	−78	78	60

[a] See footnote [a] of Table 1.

Table 3. Effect of the structure of the reducing agent on the diastereoselective reduction of compound (**3a**)

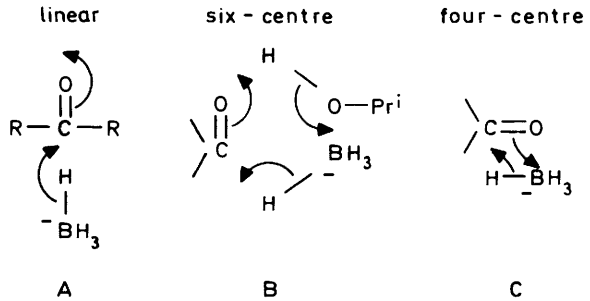
			Mandelic acid (**5a**)	
Reducing agent	Solvent	Temp. (°C)	Yield (%)	E.e. (%)[a]
$NaBH_4$	Diglyme[b]	0	73	15[c]
$NaBH(OPr^i)_3$	Diglyme	−30	73	13[c]
$KBH(Bu^s)_3$	THF	−78	80	36[d]
	Et_2O	−78	70	17[d]
	Toluene	−78	71	1[d]
$NaBH_3CN$	THF–aq.HCl	R.t.	39	0

[a] See footnote [a] of Table 1. [b] Diethylene glycol dimethyl ether. [c] (*S*)-Configuration. [d] (*R*)-Configuration.

Table 4. Effect of the structure of the ester and the acyl substituent of compound (3) on the asymmetric induction

			Compound (5)		
Entry	Compound	Solvent	Product (%)	$[\alpha]_D^{25}$(°) (*c*, solvent)	E.e. (%)
1	(**3a**)	THF–1% H_2O	(**5a**) (82)	+71.0 (1.2, H_2O)	45[a]
2	(**3b**)		(**5a**) (29)	+58.4 (0.8, H_2O)	37[a]
3	(**3c**)		(**5a**) (57)	+72.0 (1.9, H_2O)	46[a]
4	(**3d**)		(**5a**) (35)	+57.7 (0.6, H_2O)	37[a]
5	(**3e**)	THF–1% MeOH	(**5b**) (59)	−15.3 (1.4, 1M-NaOH)	56[b]
6	(**3f**)		(**5b**) (82)	−16.3 (1.5, 1M-NaOH)	60[b]
7	(**3g**)		(**5c**) (41)	−7.4 (2.9, 1.5M-NaOH)	55[c]

[a] See footnote [a] of Table 1. [b] Based on the value for (*S*)-(−)-(**5b**) of $[\alpha]_D$ −27.2° (1M-NaOH); M. Winitz, L. B-Frakenthal, N. Izumiya, S. M. Birnbaum, C. G. Baker, and J. P. Greenstein, *J. Am. Chem. Soc.*, 1956, **78**, 2423. [c] Based on the value for (*S*)-(−)-(**5c**) of $[\alpha]_D^{20}$ −13.5° (*c* 2.5, 1.5-M-NaOH); 'Aldrich Catalog Handbook of Fine Chemicals,' Aldrich Chemical Co. Inc., Milwaukee, 1980.



Scheme 3.

(99:1, v/v) afforded, after acidic hydrolysis, (*S*)-(+)-lactic acid (**5c**) in 55% e.e.

We do not have any physical proof for a rationalisation of these effects of the solvent on the diastereoselective reduction of compounds (**3**) with $NaBH_4$. Therefore, the following discussion is only our working hypothesis and is only one of the many possible mechanisms.

Although the solvent effect is not related to the structure of compound (**3**), there seem to be two factors which do affect the asymmetric induction; the mechanism of the $NaBH_4$ reduction, and chelation between compound (**3**) and the sodium cation from $NaBH_4$.

The transition state geometry (*i.e.* mechanism) of the $NaBH_4$ reduction of ketones has been a subject of much controversy.[12] Two recent papers revealed that the reduction mechanism differs according to the type of solvent (*e.g.* hydroxylic or non-hydroxylic). It has been demonstrated that during ketone reduction in alcoholic solvents, the alkoxyborate anion intermediate contains the solvent alkoxide rather than that of the product, suggesting a six-centre or linear transition state geometry (mechanism A or B, Scheme 3).[13] On the other hand, in the absence of protic solvents, the tetra-alkoxyborate anion contains the product alkoxide, suggesting a four-centre transition state geometry (mechanism C).[14]

Chelation between the Na^+ of $NaBH_4$ and the oxygen atoms of the amide and/or ester carbonyl may reduce the number of possible conformations of compound (**3**), and may therefore increase the diastereoselectivity of the reduction. A greater degree of chelation is expected in the THF than in MeOH, because MeOH is a more polarised solvent than THF.

It is reasonable that the mechanism and the stereochemical course of the $NaBH_4$ reductions of compound (**3**) depend on the composition of the solvent. In THF, the chelated structure between Na^+ and compound (**3**) is probably rather rigid, and reduction mechanism C may predominate. As the proportion of MeOH increases, the degree of chelation between Na^+ and (**3**) decreases, and the predominant mechanism becomes A or B. Since carbonyls are reduced with $NaBH_4$ much faster in alcohols than in ethereal solvents,[15] it is reasonable to assume that the presence of a small amount of MeOH in the THF will change the major reduction mechanism from C to A or B.

Thus, the diastereoselective reduction of chiral α-ketoamides derived from (*S*)-proline esters with $NaBH_4$ affords α-hydroxy acids in good enantiomeric excess. The degree of asymmetric induction is highly dependent on the ratio of hydroxylic and non-hydroxylic solvents used.

Experimental

I.r. spectra, high resolution mass spectra, and optical rotations were recorded respectively with a Hitachi 260—10 spectrophotometer, a Hitachi M-80 mass spectrometer, and a JASCO DIP-181 polarimeter. ^1H N.m.r. spectra were recorded with either a Varian EM-360A, a JEOL JNM-PMX-60, or a JEOL JNM-FX100 spectrometer. Solvents were distilled and/or dried over molecular sieves. Sodium borohydride ($NaBH_4$) and (*S*)-proline were used as purchased. Benzoylformic acid (**1a**) was recrystallised from toluene. 4-Methyl-2-oxopentanoic acid (**1b**) was distilled. Hydrochlorides of the (*S*)-proline esters (**2a—d**) and (*S*)-proline t-butyl ester (**2e**) were synthesised according to the literature procedures.[16] Compound (**3g**) was synthesised according to the literature procedure.[8]

General Procedure for the Syntheses of Alkyl (S)-N-*Benzoylformylprolinates* (**3a—d**).—To a mixture of benzoylformic acid (**1a**) (105 mmol) and the alkyl-(S)-prolinate hydrochloride (**2a—d**) (103 mmol) in dichloromethane (60 ml) was added triethylamine (10.157 g, 100.4 mmol) dissolved in CH_2Cl_2 (20 ml) during 30 min at −20 °C under argon. Then dicyclohexylcarbodi-imide (DCC) (20.700 g, 100.3 mmol) in CH_2Cl_2 (35 ml) was added during 80 min. After the mixture had been stirred at −20 °C for 4 h, the cooling bath was removed and the temperature was allowed to reach room temperature. Stirring was continued overnight, and a white precipitate was filtered off. The filtrate was washed successively with 3M-hydrochloric acid (10 ml × 2), saturated aqueous sodium hydrogen carbonate (10 ml × 2), and water (10 ml × 3), and then dried (Na_2SO_4). The solvent was evaporated on a rotary evaporator under reduced pressure (20—25 mmHg). Purification on silica gel column with CH_2Cl_2 as eluant gave the product (**3a—d**) as an oil: *methyl* (S)-N-*benzoylformylprolinate* (**3a**) (80%); $[\alpha]_D^{18}$ −18.4° (*c* 5.1, $CHCl_3$); $\nu_{max.}$ 2 960, 1 750, 1 685, 1 650, 1 600, 1 445, 1 245, 1 210, and 1 185 cm^{-1}; δ($CDCl_3$) 1.66—2.60 (4 H, m), 3.40—4.00 (5 H, m), 4.50—4.85 (1 H, m), 7.16—7.66 (3 H, m), and 7.80—8.20 (2 H, m) *m/z* (EI)

261.1016 (Calc. for $C_{14}H_{15}O_4N$: *M* 261.100) (Found: C, 64.3; H, 5.9; N, 5.3. $C_{14}H_{15}O_4N$ requires C, 64.36; H, 5.79; N, 5.36%).

Ethyl (S)-N-*benzoylformylprolinate* (**3b**) (49%); $[\alpha]_D^{25}$ −18.7° (*c* 8.5, $CHCl_3$); $\nu_{max.}$ 2 960, 2 870, 1 735, 1 670, 1 635, 1 595, 1 575, 1 430, 1 230, and 1 170 cm^{-1}; δ($CDCl_3$) 0.90—1.42 (3 H, m), 1.52—2.50 (4 H, m), 3.42—4.80 (3 H, m), 7.12—7.70 (3 H, m), and 7.92—8.16 (2 H, m) (Found: C, 65.4; H, 6.3; N, 5.1. $C_{15}H_{17}O_4N$ *requires* C, 65.44; H, 6.22; N, 5.09%).

Isopropyl (S)-N-*benzoylformylprolinate* (**3c**) (85%); $[\alpha]_D^{24}$ −20.4° (*c* 5.7, $CHCl_3$); $\nu_{max.}$ 2 960, 1 740, 1 720, 1 680, 1 650, 1 600, 1 440, 1 380, 1 200, 1 180, and 1 100 cm^{-1}; δ($CDCl_3$) 0.96—1.35 (6 H, m), 1.50—2.52 (4 H, m), 3.26—3.83 (2 H, m), 4.60—5.30 (2 H, m), 7.16—7.50 (3 H, m), and 7.86—8.06 (2 H, m) (Found: C, 66.25; H, 6.7; N, 4.9. $C_{16}H_{19}O_4N$ requires C, 66.42; H, 6.62; N, 4.84%).

Benzyl (S)-N-*benzoylformylprolinate* (**3d**) (57%); $[\alpha]_D^{26}$ −21.4° (*c* 7.5, $CHCl_3$); b.p. 194—205 °C/4 × 10^{-3} mmHg; $\nu_{max.}$ 3 070, 3 040, 2 960, 1 740, 1 685, 1 650, 1 600, 1 440, 1 250, and 1 180 cm^{-1}; δ($CDCl_3$) 1.56—2.46 (4 H, m), 3.42—3.70 (2 H, m), 4.56—5.22 (3 H, m), 7.20—7.72 (8 H, t), and 7.86—8.22 (2 H, m) (Found: C, 71.25; H, 5.7; N, 4.2. $C_{20}H_{19}O_4N$ requires C, 71.20; H, 5.68; N, 4.15%).

Methyl (S)-N-(3-*Methylbutanoyl*)*formylprolinate* (**3e**).—4-Methyl-2-oxopentanoic acid (0.653 g, 5.02 mmol) was condensed with (*S*)-proline methyl ester hydrochloride (0.887 g, 5.36 mmol) in DCC at 0 °C as described for compound (**3a**). After bulb-to-bulb distillation (bath temp. 180 °C, 2.5 mmHg), the *product* (**3e**) (0.922 g, 76%) was obtained, $[\alpha]_D^{26}$ −74.6° (*c* 5.1, $CHCl_3$); $\nu_{max.}$ 2 960, 1 750, 1 720, 1 650, 1 440, 1 220, and 1 180 cm^{-1}; δ($CDCl_3$) 0.86—1.02 (6 H, dd), 1.62—2.56 (5 H, m), 2.70—2.90 (2 H, q), 3.52—4.90 (5 H, m), and 4.40—5.00 (1 H, m) Found: C, 59.8; H, 7.9; N, 5.8. $C_{12}H_{19}O_4N$ requires C, 59.73; H, 7.94; N, 5.81%).

t-Butyl (S)-N-(3-*Methylbutanoyl*)*formylprolinate* (**3f**).—To a mixture of (*S*)-proline t-butyl ester (0.911 g, 5.34 mmol) and 4-methyl-2-oxopentanoic acid (0.689 g, 5.29 mmol) in CH_2Cl_2 was added DCC (1.123 g, 5.44 mmol) dissolved in CH_2Cl_2 (2 ml) during 17 min at −30 °C under argon. After the mixture has been stirred at −30 °C for 5 h, the cooling bath was removed and the mixture was allowed to reach room temperature. Stirring was continued overnight, and the white precipitate was filtered off. The filtrate was washed successively with 10% citric acid, aqueous sodium hydrogen carbonate, and water and then dried (Na_2SO_4). The solvent was evaporated to give a yellowish oil, bulb-to-bulb distillation (bath temp. 180 °C, 2.5 mmHg) of which gave *compound* (**3f**) (0.934 g, 62.3%) as a yellowish oil; $[\alpha]_D^{18}$ −62.4° (*c* 6.2, $CHCl_3$); $\nu_{max.}$ 2 960, 1 740, 1 720, 1 650, 1 440, 1 400, and 1 240 cm^{-1}; δ($CDCl_3$) 0.86—0.96 (6 H, d), 1.4 (9 H, s), 1.60—2.52 (5 H, m), 2.66—2.86 (2 H, t), 3.51—3.82 (2 H, m), and 4.32—4.84 (1 H, m) (Found: C, 63.6; H, 8.85; N, 4.9. $C_{15}H_{25}O_4N$ requires C, 63.58; H, 8.89; N, 4.94%).

General Procedure for the Reduction of Compounds (**3**) *with Sodium Borohydride* ($NaBH_4$). *Preparation of the α-Hydroxy Acids* (**5**).—The reactions were carried out under argon. Sodium borohydride (0.5 mmol) was suspended in the solvent (1 ml), and a solution (2 ml) of the α-ketoamide (0.5 mmol) was added during 14 min at 0 °C. The mixture was stirred for 3 h, and then the reaction was quenched with 1M-HCl (5 ml), extracted with dichloromethane (5 ml × 5), and dried (Na_2SO_4). The solvent was evaporated to give a yellowish oil, 2M-H_2SO_4 (5 ml) was added, and the mixture was refluxed for 2 h, then extracted with diethyl ether (5 ml × 8) and dried (Na_2SO_4). The solvent was evaporated to give white crystals which were purified by bulb-to-bulb distillation (bath temp. 170 °C, 2.5 mmHg) and/or silica gel t.l.c. (CH_2Cl_2–MeOH–AcOH, 20:1:1) to give (*S*)-(+)-mandelic acid (**5a**) in yields of 29—87%.

Reduction of the α-Ketoamide (**3a**) *with Sodium Triisopropoxyborohydride* [$NaBH(OPr^i)_3$].—To a 0.28M-diglyme solution (3.7 ml) of $NaBH(OPr^i)_3$ (1.04 mmol), compound (**3a**) (0.129 g, 0.49 mmol) in diglyme (2 ml) was added at −30 °C under argon. After the mixture had been stirred for 3 h, the reduction was quenched with 1M-HCl. Then the mixture was extracted with CH_2Cl_2 (5 ml × 6) and the extracts were dried (Na_2SO_4). The solvent was evaporated, 2M-H_2SO_4 (5 ml) was added, and the mixture was refluxed for 2 h, then extracted with diethyl ether (5 ml × 15) and dried (Na_2SO_4). The solvent was evaporated under reduced pressure (20—25 mmHg). Bulb-to-bulb distillation (170 °C, 2.5 mmHg) gave (*S*)-mandelic acid (**5a**) (0.053 g, 71%), $[\alpha]_D^{25}$ +20.8° (*c* 1.1, H_2O), 13% e.e.

Reduction of the α-Ketoamide (**3a**) *with Sodium Borohydride in diglyme*.—The reduction was carried out under the same conditions as the general procedure. $NaBH_4$ (0.021 g, 0.54 mmol) and the α-ketoamide (0.139 g, 0.53 mmol) in diglyme (2 ml) gave (*S*)-(**5a**) (0.059 g, 73%), $[\alpha]_D^{25}$ +23.3° (*c* 0.8, H_2O), 15% e.e.

Acknowledgements

This work was partially supported by a Grant-in-aid (No. 57740272) from the Ministry of Education, Science, and Culture.

References

1 Preliminary communication; K. Soai, K. Komiya, Y. Shigematsu, H. Hasegawa, and A. Ookawa, *J. Chem. Soc., Chem. Commun.*, 1982, 1282.
2 J. D. Morrison and H. S. Mosher, 'Asymmetric Organic Reactions,' ed. N. J. Englewood-Cliffs, 1972, ch. 2.
3 T. Munegumi and K. Harada, *Chem. Lett.*, 1983, 1225.
4 J. K. Whitesell, D. Deyo, and A. Bhattacharya, *J. Chem. Soc., Chem. Commun.*, 1983, 802.
5 Y. Inouye, 'Asymmetric Organic Reaction,' Kagakudojin, Kyoto, 1977, p. 41—43.
6 (*a*) K. Soai and T. Mukaiyama, *Chem. Lett.*, 1978, 491; (*b*) T. Mukaiyama, K. Soai, and S. Kobayashi, *Chem. Lett.*, 1978, 219; (*c*) T. Mukaiyama, K. Soai, T. Sato, H. Shimizu, and K. Suzuki, *J. Am. Chem. Soc.*, 1979, **101**, 1455; (*d*) K. Tomioka, K. Ando, Y. Takemasa, and K. Koga, *J. Am. Chem. Soc.*, 1984, **106**, 2718; (*e*) Y. Inouye, S. Inamasu, M. Horiike, M. Ohno, and H. M. Walborsky, *Tetrahedron*, 1968, **24**, 2907.
7 (*a*) K. Soai, H. Oyamada, and A. Ookawa, *Synth. Commun.*, 1982, **12**, 463; (*b*) K. Soai, H. Oyamada, M. Takase, and A. Ookawa, *Bull. Chem. Soc. Jpn.*, 1984, **57**, 1948; (*c*) K. Soai, H. Oyamada, and M. Takase, *ibid.*, 1984, **57**, 2327; (*d*) K. Soai and H. Oyamada, *Synthesis*, 1984, 605; (*e*) K. Soai, A. Ookawa, H. Oyamada, and M. Takase, *Heterocycles*, 1982, **19**, 1371; (*f*) K. Soai, A. Ookawa, and H. Hayashi, *J. Chem. Soc., Chem. Commun.*, 1983, 668.
8 *Cf.* B. W. Bycroft and G. R. Lee, *J. Chem. Soc., Chem. Commun.*, 1975, 988.
9 T. Kamaishi and S. Mitsui, *Nippon Kagaku Zasshi*, 1965, **86**, 623.
10 H. C. Brown, E. J. Mead, and C. J. Shoaf, *J. Am. Chem. Soc.*, 1956, **78**, 3616.
11 A. Hajos, 'Complex Hydride,' Akademiai Kiado, Budapest, 1979.
12 For a review, D. C. Wigfield, *Tetrahedron*, 1979, **35**, 449.
13 D. C. Wigfield and F. W. Gowland, *Tetrahedron Lett.*, 1976, 3373.
14 M. M. Kayser and S. Eliev, *Tetrahedron Lett.*, 1983, 1015.
15 A. Viger, A. Marquet, D. H. R. Barton, W. B. Motherwell, and S. Z. Zard, *J. Chem. Soc., Perkin Trans. 1*, 1982, 1937.
16 (*a*) S. Guttmann, *Helv. Chim. Acta*, 1961, **44**, 721; (*b*) J. Ramachandran and C. H. Li, *J. Org. Chem.*, 1963, **28**, 173; (*c*) G. W. Anderson and F. M. Callahan, *J. Am. Chem. Soc.*, 1960, **82**, 3359.

Received 6*th July* 1984; *Paper* 4/1167