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Enantioselective hydrogenation of α-ketoamides over Pt/Al_2O_3 modified by cinchona alkaloids †

G.-Z. Wang, T. Mallat and A. Baiker *

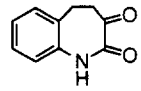
Department of Chemical Engineering and Industrial Chemistry, Swiss Federal Institute of Technology, ETH-Zentrum, CH-8092 Zürich, Switzerland

Abstract: Pyruvamide and its N-alkylated derivatives have been synthesised and hydrogenated enantioselectively to the corresponding alcohols over an alumina-supported Pt catalyst chirally modified by adsorbed cinchonidine. Depending on the substrate structure and reaction conditions, this catalyst system afforded ees up to 60%. This is the highest ee achieved hitherto with a solid catalyst in α-ketoamide hydrogenation. © 1997 Elsevier Science Ltd

Introduction

Enantioselective hydrogenation of prochiral ketones is one of the most intensively studied areas in asymmetric catalysis.[1] Excellent results have been achieved using homogeneous chiral Rh and Ru catalysts. The most successful strategy in preparing solid asymmetric hydrogenation catalysts is the modification of known metal catalysts by strongly adsorbed chiral compounds of natural origin.[2] Supported platinum modified by cinchona alkaloids, since its first application by Orito for the hydrogenation of α-ketoesters,[3] has attracted much attention. Considerable effort has been made to gain a better understanding of the mechanism of chiral recognition,[4] including theoretical calculations.[5] In order to further elucidate the nature of interaction between modifier and substrate, we have previously focused on the synthesis of new chiral modifiers. As a result, naphthalene based, structurally simple aminoalcohols[6] and aminoesters[7] have been developed for the low pressure enantioselective hydrogenation of α-ketoesters.

In the past decade efforts to broaden the application range of cinchona-modified Pt have been made. Rather poor ees, only 20% or below, were obtained in the enantioselective hydrogenation of β-diketones, β-ketoesters, aryl-alkyl ketones and α-methoxy ketones.[8] Better results were achieved in the hydrogenation of α-diketones (33–38% ee),[9] ketopantolactone (79% ee)[10] and 2,2,2-trifluoroacetophenone (56% ee)[11] to the corresponding substituted alcohols. The hydrogenation of a cyclic ketoamide **1** provided 47% ee, but no details of the reaction were reported.[12]



1

The aim of the present work was to study the enantioselective hydrogenation of α-ketoamides and investigate the influence of substrate structure on the enantiodifferentiation. For this purpose a number of N-alkylated pyruvamides have been prepared and hydrogenated over Pt/Al_2O_3 modified by cinchonidine.

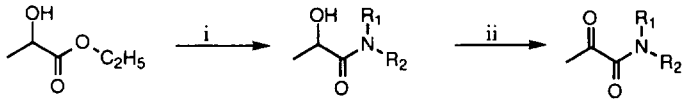
† Dedicated to Professor D. Seebach on the occasion of his 60th birthday

* Corresponding author. Email: baiker@tech.chem.ethz.ch

Results and discussion

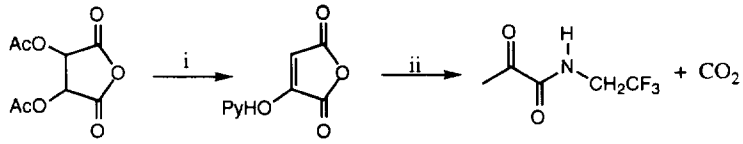
Synthesis of substrates

Most of the α-ketoamides were prepared by aminolysis of ethyl lactate followed by Jones oxidation, according to Scheme 1.



Scheme 1. (i) Alkyl- or arylamine, RT/reflux, 14–48 h, (ii) Jones reagent, acetone, 0°C–RT, 0.5 h.

However, ethyl lactate could not be aminolysed by $CF_3CH_2NH_2$, due to the low electron density on the nitrogen atom (pK_a=5.6, as compared to pK_a=10.7 for ethylamine).[13] Alternatively, N-2,2,2-trifluoroethyl pyruvamide was prepared starting from diacetyl tartaric anhydride according to a modified literature procedure,[14] as shown in Scheme 2.



Scheme 2. (i) Pyridine, 0°C, Py=pyridine, (ii) 1.15 eq. $CF_3CH_2NH_2$, CH_2Cl_2/pyridine, 0°C–RT.

In the original procedure the second step was performed in the pure amine. We found that using CH_2Cl_2 as solvent and conducting the reaction in the presence of pyridine provided better results. Since the reaction is exothermic, dilution of the substrate resulted in a mild reaction, and the presence of pyridine suppressed the possible formation of imine by shifting the substrate to its enolate form. Using this modifications, 2,2,2-trifluoroethyl pyruvamide was prepared in 87% yield and no significant side products could be detected by TLC and GC.

Enantioselective hydrogenation

The enantioselective hydrogenation of α-ketoamides was performed using a 5 wt-% Pt/Al_2O_3 catalyst and cinchonidine as modifier (Scheme 3). Other cinchona alkaloids, such as quinine and cinchonine, were also tested, but they afforded lower ees.

Scheme 3. Pt/Al_2O_3, cinchonidine, H_2, solvent, RT.

The solvent had a strong influence on the enantioselectivity. For example, the ees obtained in the hydrogenation of N-ethyl pyruvamide in ethanol and toluene were 34% and 23% respectively, much lower than that obtained in acetic acid under otherwise identical conditions (57.5%, see Table 3). For the same substrate in acetic acid the modifier/substrate ratio could be as low as 0.06 mol%, without significantly lowering the enantioselectivity (Table 1).

Unlike the hydrogenation of α-ketoesters, where enantioselectivity increases with ascending hydrogen pressure up to 70–100 bar,[2–4] the hydrogen concentration had no significant influence on the enantioselectivity of α-ketoamide hydrogenation. The influence of pressure on ee and reaction rate is illustrated in Table 2.

Since the reaction is faster at high pressure, the comparative hydrogenation of various ketoamides was performed at 60 bar and a substrate/modifier molar ratio of 400. As illustrated in Table 3,

Table 1. Influence of substrate/modifier mole ratio on the enantioselectivity of N-ethyl pyruvamide hydrogenation[a]

Substrate / modifier (mole/mole)	200	400	800	1600
Conversion (%)[b]	100	100	99	100
ee (%)[b]	57.5	57.5	56.0	52.5

a Standard reaction conditions except for substrate/modifier ratio; reaction time: 1 h. *b* Determined by GC; chemical selectivity > 98%; *(R)*-enantiomer is the major product as confirmed by comparison with the pure enantiomer.

Table 2. Effect of hydrogen pressure on the conversion and enantioselectivity in the hydrogenation of N-ethyl pyruvamide[a]

P_{H2} (bar)	1	5	10	60
Time (h)	2	2	1.5	1
Conversion (%)[b]	97	99	98	100
ee (%)[b]	50.0	57.0	57.5	57.5

a Standard reaction conditions except for hydrogen pressure. *b* Determined by GC, see Table 1.

pyruvamide and its N-mono-alkylated derivatives were hydrogenated to the corresponding α-hydroxylamides with 49–60% ee, depending on the steric and electronic properties of the substituents. However, rather low ees were obtained with N,N-dialkylated and N-arylated α-ketoamides. Both steric and electronic effects could account for the loss of enantioselection.

The hydrogenation of α-ketoamides, similarly to that of α-ketoesters, can be classified as "ligand-accelerated" reaction. In the hydrogenation of N-ethyl pyruvamide at 1 bar, the initial reaction rate of the modified reaction was about 2 times higher than that of the unmodified (racemic) reaction. This ratio is much lower than those reported for the enantioselective hydrogenation of α-ketoesters over chirally modified Pt catalysts (usually in the range of 5–20).[2–4] As a result, the relatively fast reaction may be one of the reasons for the observed lower enantioselectivity in the hydrogenation of α-ketoamides. From the molecular point of view, the replacement of the ethoxy group in ethyl pyruvate by an ethylamino group in N-ethyl pyruvamide results in an increase of electron density of the keto–carbonyl group. This electron density difference can be the ultimate reason for the difference in the ligand-rate accelerating factors and in the asymmetric induction, when comparing the hydrogenation of α-ketoesters and α-ketoamides under similar conditions. We have shown recently[11] that cinchona-modified Pt provides good enantioselectivity only for substrates possessing a strong electron-withdrawing substitutent in α-position to the carbonyl group.

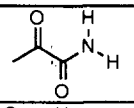
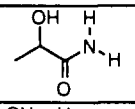
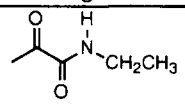
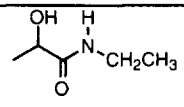
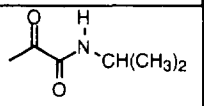
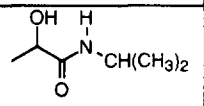
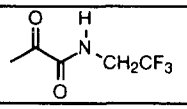
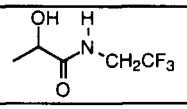
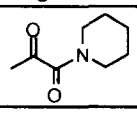
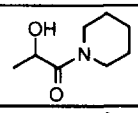
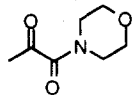
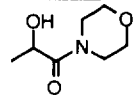
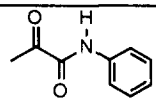
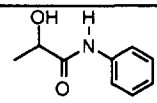
It is interesting to compare our results with those obtained recently[15] using homogeneous Rh-complex catalysts for the enantioselective hydrogenation of N-benzylbenzoylformamide. The ee varied in a broad range between 17 and 80% with bis(aminophosphanes), and between 74 and 89% with diphosphines as ligands.

In conclusion, a new class of activated ketones, none and N-mono alkylated α-amidoketones, can be enantioselectively hydrogenated to the corresponding alcohols even at low hydrogen pressure over Pt/Al_2O_3 in the presence of adsorbed cinchonidine. Optimisation of the reaction conditions may further improve enantioselectivities for this type of substrates. The variation of both electronic and steric factors of the substrates provides an experimental basis for theoretical calculations aiming at a better understanding of the substrate–modifier interaction.

Experimental

All amines were purchased from Fluka and distilled before use. DL-Lactamide was purchased from Aldrich. ^1H and ^{13}C NMR spectra were recorded on a Bruker Avance DPX 300 operating at 300 MHz and 75MHz, respectively, with chemical shifts related to TMS (δ=0). IR spectra were recorded on a

Table 3. Enantioselective hydrogenation of α-ketoamides over Pt/Al_2O_3 modified by cinchonidine[a]

Eentry	Substrate	Product	Time (h)	Conversion (%)[b]	ee (%)[b]
1			1	94	53.5
2			1 1	100 100	57.5 56.5[c,d]
3			1	100	49.0[c]
4			1	100	60.0[e]
5			2	73	1.0
6			2	100	4.0
7			1	90	14.0

a The reactions were conducted under standard conditions unless otherwise noted. *b* Determined by gas chromatography; chemical selectivity > 98%. *c (R)*-enantiomers are the major product as confirmed by using the pure enantiomers. *d* The reaction was conducted using 8 mmol substrate in 4 ml acetic acid. *e* Derivatized to its benzoate and analysed by gas chromatography.

Perkin Elmer 2000 IR-FT in $CHCl_3$ with s, m, w and vw indicating strong, moderate, weak and very weak bands respectively. Specific optical rotations were recorded on a Perkin Elmer 241 polarimeter at 25°C. EtOAc was the eluent for both TLC and column chromatography, if not otherwise stated.

Synthesis of lactamide derivatives

General procedure

11.8 g (0.1 mol) of ethyl lactate and 0.15 mol of the corresponding amine were placed in a 50 ml Schlenk tube. The reaction mixture was briefly degassed and stirred or heated for a certain time in nitrogen. The reaction was monitored by TLC. The excess of amine and the formed ethanol were removed under vacuum, and purified by column chromatography on silica gel.

(S)-N-Ethyl lactamide

It was prepared according to the general method starting with (*S*)-ethyl lactate and 6.8 g of ethyl amine. After stirring at RT for 14 h, TLC showed complete conversion. 11.5 g of colorless oil was obtained (98% yield). Rf=0.29. Anal. cal.: C, 51.26; H, 9.46; N, 11.96; found: C, 51.22; H, 9.25; N, 11.87. $[\alpha]_D^{25} = -21.2$. (C 1.0, $CHCl_3$). IR (cm^{-1}, $CHCl_3$): 3676, 3611 (O–H, w), 3422 (O–H, N–H, br. s), ca. 3000 (C–H, m), 1662 (C=O, s). ^1H NMR ($CDCl_3$): 6.64 (br.s, 1H), 4.20 (q, 6.8Hz, 1H),

3.31 (quintet, 7.2 Hz, 2H), 1.42 (d, 6.8Hz, 3H), 1.16 (t, 7.2Hz, 3H). ^{13}C NMR ($CDCl_3$): 175.3 (C=O), 67.9 (CH), 33.8 (CH_2), 20.8 (CH_3), 14.4 (CH_3).

(S)-N-Isopropyl lactamide

It was prepared according to the general method starting with (*S*)-ethyl lactate and 8.6 g of isopropyl amine. After refluxing for 48 h, a small amount of ethyl lactate was still detectable. After column chromatography 12.2 g colorless oil was obtained (93% yield). Rf=0.30. Anal. cal.: C, 54.94; H, 9.99; N, 10.67; found: C, 54.32; H, 9.66; N, 10.34. $[\alpha]_D^{25} = -19.2$. (C 1.1, $CHCl_3$). IR (cm^{-1}, $CHCl_3$): 3677, 3600 (O–H, w), 3410 (O–H, N–H, br. s), ca 3000 (C–H, m), 1659 (C=O, s). ^{1}H NMR ($CDCl_3$): 6.34 (br.s, 1H), 4.18 (q, 6.8Hz, 1H), 4.07 (oct. 6.6 Hz, 2H), 2.84 (br.s, 1H), 1.42 (d, 6.8Hz, 3H), 1.16 (t, 6.6Hz, 6H). ^{13}C NMR ($CDCl_3$): 173.5 (C=O), 68.3 (CH), 41.1 (CH), 22.7 (CH_3), 21.4 (CH_3).

N-Phenyl lactamide

It was prepared according to the general method starting with ethyl lactate and 14 g of aniline. After refluxing for 48 h, a small amount of ethyl lactate was still detectable. After column chromatography 13.3 g colorless oil was obtained (80% yield). Rf=0.47. Anal. cal.: C, 65.44; H, 6.71; N, 8.48; found: C, 65.09; H, 6.74; N, 8.56. IR (cm^{-1}, $CHCl_3$): 3618 (O–H, w), 3384 (O–H, N–H, br. s), ca. 3000 (C–H, m), 1714 (C=O, s). ^{1}H NMR ($CDCl_3$): 8.41 (br. s, 1H), 7.56 (d, J=8.4 Hz, 2H), 7.33 (t, J=7.5 Hz, 2H), 7.12 (t, J=7.4 Hz, 1H), 4.37 (q, J=6.8 Hz, 1H), 2.70 (br.s, 1H), 1.53 (d, J=6.8 Hz, 3H). ^{13}C NMR ($CDCl_3$): 174.0 (C=O), 137.1 (CH), 128.8 (CH), 124.5 (CH), 120.1 (CH), 68.4 (CH), 20.6 (CH_3).

N,N-Tetramethylene-4-oxo-lactamide

It was prepared according to the general method starting with ethyl lactate and 13 g of morpholine. After refluxing for 48 h, a trace of ethyl lactate was still detectable. After column chromatography 14.2 g colorless oil was obtained (88% yield). Rf=0.30. Anal. cal.: C, 52.82; H, 8.23; N, 8.80; found: C, 52.79; H, 7.98; N, 9.02. IR (cm^{-1}, $CHCl_3$): 3671 (O–H, w), 3455 (O–H, br. s), ca. 3000 (C–H, m), 1644 (C=O, s). ^{1}H NMR ($CDCl_3$): 4.44 (quintet, 6.8Hz, 1H), 3.78 (d, J=7.2 Hz, 1H),3.7 (m, 6H), 3.43 (m, 2H), 1.33 (d, 6.8Hz, 3H). ^{13}C NMR ($CDCl_3$): 173.7 (C=O), 66.7 (CH_2), 66.3 (CH_2), 64.0 (CH), 45.3 (CH_2), 42.7 (CH_2), 21.2 (CH_3).

N,N-Hexamethylene lactamide

It was prepared according to the general method starting with 5.9 g of ethyl lactate and 6.4 g of piperidine. After refluxing for 48 h, a small amount of ethyl lactate was still detectable. After column chromatography 13.3 g colorless oil was obtained (80% yield). Rf=0.43. Anal. cal.: C, 61.12; H, 9.62; N, 8.91; found: C, 61.23; H, 9.77; N, 8.32. IR ($CHCl_3$): ^{1}H NMR ($CDCl_3$): 4.44 (q, J=6.6, 1H), 3.59 (m, 2H), 3.33 (m, 2H), 2.41 (s, 3H), 1.73–1.52 (m, 6H),1.32 (d, J=6.8, 3H). ^{13}C NMR ($CDCl_3$): 173.3 (C=O), 64.0 (CH), 45.8 (CH_2), 43.6 (CH_2), 26.1 (CH_2), 25.4 (CH_2), 24.3 (CH_2), 21.4 (CH_3).

Synthesis of α-ketoamides

General procedure

80 mmol of alkyl lactamide was dissolved in 50 ml acetone and cooled to 0°C. A solution containing 26 g (87 mmol) sodium dichromate dihydrate dissolved in 50 ml water and 15 ml sulphuric acid was added via dropping funnel. The reaction mixture was warmed to room temperature and stirred for 30 min. TLC indicated complete conversion. The reaction mixture was diluted with diethyl ether and the two phases were separated. The aqueous phase was extracted 5 times with 30 ml diethyl ether and the combined organic phase was stirred with solid sodium sulphite for 1 h to reduce the unreacted dichromate. After filtration the solvent was evaporated under vacuum, and the product further purified by column chromatography.

N-Ethyl pyruvamide

It was prepared according to the general method starting with 9.4 g of N-ethyl lactamide. After column chromatography 7.9 g colorless oil was obtained, which upon standing gave a microcrystalline solid with 86% yield. The compound was further purified by crystallisation from ether/pentane. MP: RT. Rf=0.56. Anal. cal.: C, 52.16; H, 7.88; N, 12.17; found: C, 51.97; H, 8.03; N, 12.01. IR (cm^{-1}, $CHCl_3$): 3410 (N–H,m), 3025–2935 (C–H, w), 1719 (C=O, m), 1684 (C=O, s). (^1H NMR ($CDCl_3$): 7.28 (br.s, 1H), 3.34 (d×q, J=7.3×6.0), 2.48 (s, 3H), 1.20 (t, J=7.3, 3 H). ^{13}C NMR ($CDCl_3$): 197.2 (C=O), 159.9 (C=O), 34.2 (CH_2), 24.3 (CH_3), 14.4 (CH_3).

N-Isopropyl pyruvamide

It was prepared according to the general method starting with 10.3 g of N-isopropyl lactamide. After column chromatography 8.8 g colorless oil was obtained, which upon standing gave a microcrystalline solid (87% yield). The compound was further purified by crystallisation from ether/pentane. MP: 48–49°C. Rf=0.61. Anal. cal.: C, 55.80; H, 8.58; N, 10.84; found: C, 55.51; H, 8.35; N, 10.67. IR (cm^{-1}, $CHCl_3$): 340 (N–H, m), 3026–2930 (C–H, w), 1722 (C=O, m), 1683 (C=O, s). ^1H NMR ($CDCl_3$): 7.29 (br.s, 1H), 4.04 (oct, J=6.5, 1H), 2.47 (s, 3H), 1.20 (d, J=6.5, 6 H). ^{13}C NMR ($CDCl_3$): 197.5 (C=O), 159.3 (C=O), 41.6 (CH), 24.4 (CH_3), 22.4 (CH_3).

N-Phenyl pyruvamide

It was prepared according to the general method starting with 13.2 g of lactanilide. After column chromatography 11.7 g white plates were obtained (90% yield). The compound was further purified by crystallisation from ethanol/water. Rf=0.68. MP: 104–105°C. Anal. cal.: C, 66.25; H, 5.56; N, 8.58; found: C, 65.97; H, 5.74; N, 8.77. IR (cm^{-1}, $CHCl_3$): 3377 (N–H,m), ca. 3029 (C–H, w), 1722 (C=O, m), 1695 (C=O, s). ^1H NMR ($CDCl_3$): 8.71 (br.s, 1H), 7.63 (d, J=8.2H, 2H), 7.37 (t, J=8.4Hz, 2H), 7.17 (t, J=7.4Hz, 1H), 2.56 (s, 3H). ^{13}C NMR ($CDCl_3$): 197.3 (C=O), 157.6 (C=O), 136.3 (CH), 129.2 (CH), 125.3 (CH), 119.7 (CH), 24.0 (CH_3).

Pyruvamide

It was prepared according to the general method starting with 7.1 g of lactamide. After column chromatography 3.5 g of colorless oil was obtained (51% yield). Rf=0.46. MP: 106–107°C. Anal. cal.: C, 41.38; H, 5.79; N, 16.09; found: C, 41.90; H, 5.67; N, 15.52. IR (cm^{-1}, $CHCl_3$): 3516 (N–H, m), 3400 (N–H,m), 3025–2935 (C–H, w), 1707 (2C=O, s). ^1H NMR ($CDCl_3$): 6.87 (br.s, 1H), 6.13 (br.s, 1H), 2.47 (s, 3H). ^{13}C NMR ($CDCl_3$): 196.5 (C=O), 162.3 (C=O), 24.2 (CH_3).

N,N-(Tetramethylene-4-oxo) pyruvamide

It was prepared according to the general method starting with 12.7 g of morpholinyl lactamide. After column chromatography 12 g light yellow oil was obtained (96% yield). Rf=0.45. Anal. cal.: C, 53.49; H, 7.05; N, 8.91; found: C, 53.37; H, 7.16; N, 9.03. IR (cm^{-1}, $CHCl_3$): 3014–2864 (C–H, w), 1713 (C=O, m), 1643 (C=O, s). ^1H NMR ($CDCl_3$): 3.76–3.62 (m, 8H), 3.55–3.50 (m, 2H), 2.44 (s, 3H). ^{13}C NMR ($CDCl_3$): 198.0 (C=O), 164.7 (C=O), 66.8 (CH_2), 66.5 (CH_2), 46.1 (CH_2), 41.9 (CH_2), 27.7 (CH_3).

N,N-Hexamethylene pyruvamide

It was prepared according to the general method starting with 3.2 g (20 mmol) of piperidinyl lactamide. After column chromatography 2.6 g colorless oil was obtained (85% yield). Rf=0.57. Anal. cal.: C, 61.91; H, 8.44; N, 9.03; found: C, 61.37; H, 8.26; N, 8.91. IR (cm^{-1}, $CHCl_3$): 3011–2862 (C–H, w), 1719 (C=O, m), 1635 (C=O, s). ^1H NMR ($CDCl_3$): 3.56 (m, 2H), 3.37 (m, 2H), 2.41 (s, 3H), 1.71–1.53 (m, 6H). ^{13}C NMR ($CDCl_3$): 199.0 (C=O), 165.4 (C=O), 46.8 (CH_2), 42.4 (CH_2), 27.8 (CH_3), 26.4 (CH_2), 25.3 (CH_2), 24.3 (CH_2).

Synthesis of N-2,2,2-trifluoroethyl pyruvamide

The first step of the synthesis (Scheme 2) was performed according to a known process.[10] Under nitrogen, 1.93 g (10 mmol) of pyridinium oxymaleic anhydride was dissolved in 20 ml dry methylene chloride containing 1 ml pyridine precooled to 0°C. 1.14 g of 2,2,2-trifluoroethyl amine was added. Gas evolved slowly during reaction. The reaction mixture was stirred for 1h at 0°C, warmed up to room temperature and stirred for 2 h. 8 ml of 10% HCl was added. The organic phase was separated and washed with 5 ml water, dried over anhydrous K_2CO_3. After filtration the solvent was evaporated under reduced pressure, followed by column chromatography. 1.47 g of colorless liquid was obtained (87% yield). Rf=0.66. Anal. cal.: C, 35.51; H, 3.58; N, 8.28; found: C, 35.29; H, 3.74; N, 8.49. IR (cm^{-1}, $CHCl_3$): 3411 (N–H, m), ca. 3000 (C–H, vw), 1705 (2×C=O, s). ^1H NMR ($CDCl_3$): 7.37 (br.s, 1H), 3.95 (d×q, J=6.78×8.872 H), 2.51 (s, 3H). ^{13}C NMR ($CDCl_3$): 194.7 (C=O), 159.2 (C=O), 122.8 (q, J=278.3, CF_3), 39.8 (q, J=35.4, CH_2), 23.3 (CH_3).

Enantioselective hydrogenation of α-ketoamides

100 mg 5 wt-% Pt/Al_2O_3 (Engelhard 4759) was prereduced in flowing hydrogen in a fixed bed reactor for 2 h at 400°C. The Pt dispersion was 0.27 after heat treatment, as determined from TEM images. Hydrogenations were performed in a 100 ml stainless steel autoclave (Baskerville) with magnetic stirring. A 50 ml glass liner with a PTFE cap and stirrer were used to keep the system inert. Under standard conditions, 2.94 mg (0.01 mmol) cinchonidine (modifier), 4 mmol α-ketoamide and 2 ml AcOH (solvent). The reactions were performed at room temperature and 60 bar hydrogen pressure. After filtering off the catalyst the product was directly analysed by gas chromatography (Chiralsil DEX CB, Chrompack). Before analysis, the N-2,2,2-trifluoroethyl lactamide was transferred to its benzoate derivative according to conventional method and analysed without purification by the same column. The absolute configurations were determined by gas chromatography using the authentic samples.

For the isolation of N-2,2,2-trifluoroethyl lactamide and lactamide, the reaction mixture was diluted with 5 ml of ethyl acetate, and 2 g of Na_2CO_3 was added to neutralise the acetic acid. After filtration the product was purified by column chromatography.

Lactamide

NMR and IR spectra corresponding to commercial product. Rf=0.64 (EtOH), $[\alpha]_D^{25}$=+8.9 (C 0.96, MeOH).

N-2,2,2-Trifluoroethyl lactamide

Rf=0.41 (EtOAc). $[\alpha]_D^{25}$=+8.4. (C 1.1, $CHCl_3$). IR (cm^{-1}, $CHCl_3$): 3671, 3612 (O–H, w), 3420 (O–H, N–H, br. s), ca. 3000 (C–H, m), 1689 (C=O, s). ^1H NMR ($CDCl_3$): 7.32 (br.s, 1H), 4.28 (q, 6.8Hz, 1H), 3.90 (m, 3H), 1.42 (d, 6.8Hz, 3H). ^{13}C NMR ($CDCl_3$): 175.7 (C=O), 123.9 (q, $^1J_{C-F}$=551.2, CF_3), 68.3 (CH), 40.2 (q, $^2J_{C-F}$=35.0, CH_2), 20.8 (CH_3).

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