Conjugate additions of organocuprates to a 3-methylene-6-isopropylidketopiperazine acceptor for the asymmetric synthesis of homochiral α-amino acids

Steven D. Bull, Stephen G. Davies,* A. Christopher Garner and Michael D. O’Shea

The Dyson Perrins Laboratory, University of Oxford, South Parks Road, Oxford, UK OX1 3QY. E-mail: steve.davies@chemistry.ox.ac.uk

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Addition of a range of organocuprates to (S)-N,N’-bis(p-methoxybenzyl)-3-methylene-6-isopropylidketopiperazine-2,5-dione 8 affords cis-3-isopropyl-6-alkylidketopiperazines in excellent yield and >95% de. Subsequent deprotection and hydrolysis of these cis-3-isopropyl-6-alkylidketopiperazines affords homochiral (S)-α-amino acids in excellent yield.

Introduction

Homochiral α-amino acids are important synthetic targets for the development of new methodologies for asymmetric synthesis.1 As a consequence, a large number of simple heterocyclic chiral auxiliaries have been developed, many of which are based on the diastereoselective alkylation of masked glycine enolate fragments.2 In order to address many of the problems associated with the scale-up of this class of auxiliary, we have recently reported on (S)-N,N’-bis(p-methoxybenzyl)-3-isopropylidketopiperazine-2,5-dione 1 as a new chiral relay for the preparation of homochiral (R)-α-amino acids.3 Alkylation of the enolate derived from 1 with a representative range of alkyl halides gave highly crystalline trans-alkylated products 2a–f in >90% de, which, after simple recrystallisation of the crude reaction products, afforded pure homochiral trans-alkylated diastereoisomers 2a–f in good yield (Scheme 1). The high diastereoselectivities observed have been interpreted to result from a chiral relay mechanism involving the conformational preference of the N-p-methoxybenzyl protecting groups (Fig. 1).3a,4 Deprotection of the trans-alkylated auxiliaries 2a or 2b to their constituent α-amino acids was easily achieved via oxidative removal of the p-methoxybenzyl groups using ceric ammonium nitrate in CH3CN–H2O, to afford 3a or 3b in good yield. Subsequent acid catalysed hydrolysis of these trans-diketopiperazines gave a mixture of the (R)-amino acids 4a or 4b and (S)-valine 5 which were separated by ion exchange chromatography to afford homochiral (R)-phenylalanine 4a and (R)-alanine 4b respectively, in good yield (Scheme 1).3a,b

While this methodology is ideally suited to the preparation of homochiral α-amino acids of known absolute configuration, situations often arise where both enantiomers of a target α-amino acid are required.5 Although both enantiomers of the target α-amino acid may be prepared separately via duplicate syntheses employing the same chiral auxiliary of opposite absolute configuration, this approach is tedious and inherently wasteful. An attractive alternative to this parallel synthesis approach would involve the preparation of both enantiomers of an α-amino acid from the same homochiral auxiliary via
stereodivergent approach. In this case the stereoselective synthesis of the cis-3-isopropyl-6-alkyl derivatives 6 from 1 would enable a complementary route to homochiral (S)-α-amino acids 7 to be achieved. For example, we have recently communicated that cis-alkyldiketopiperazine 6a may be obtained from 1 via an approach involving regioselective deprotonation–reprotonation of trans-(3S,6R)-3-isopropyl-6-benzylketopiperazine derivative 2a. Thus, treatment of 2a with n-BuLi in THF at −78 °C resulted in regioselective deprotonation at C6, affording an enolate which was stereoselectively reprotonated at C6 from the Re-face to afford cis-(3S,6S)-3-isopropyl-6-benzylketopiperazine 6a (92% de, 93% yield). Chromatographic purification of the reaction mixture afforded diastereomerically pure and homochiral 6a with no evidence of any racemisation at the C3 stereogenic centre, enabling deprotection of 6a to afford homochiral (S)-phenylalanine 7a in excellent yield (Scheme 2).6

In order to widen the range of substrates to which this stereodivergent approach may be applied we now report herein that a wide range of cis-3-isopropyl-6-alkylketopiperazines 6 may be prepared in excellent de, via a versatile synthetic approach involving 1,4-conjugate addition of organocuprates to the 6-methylene acceptor 8. Part of this work has been previously communicated.5

Results and discussion

Conjugate addition of organocuprates to (S)-3-methylene-6-isopropylketopiperazine acceptor 8

There have been many reports detailing the use of chiral auxiliaries to control the asymmetric 1,4-conjugate addition of nucleophiles to α,β-unsaturated acid fragments,5 however the use of this kind of strategy for the asymmetric synthesis of homochiral α-amino acids is less well investigated. Strategies involving the conjugate addition of chiral nucleophiles to α,β-unsaturated acceptors, or the addition of nucleophiles to chiral α,β-unsaturated acceptors have been reported, however these methodologies suffer from practical problems that affect either the yield or ee of the target α-amino acid.6 In order to address the synthetic problems associated with this conjugate addition methodology, we proposed that addition of organocuprates to (6S)-N,N′-bis(p-methoxybenzyl)-3-methylene-6-isopropylylketopiperazine-2,5-dione 8 (derived from methylation of 1), would afford an enolate fragment 9 which would be diastereoselectively reprotonated to afford cis-3-isopropyl-6-alkylketopiperazines 6 in excellent de. Subsequent deprotection and hydrolysis of cis-6, according to our previously published procedure, would afford the desired (S)-α-amino acids 7. The dehydroalanine derived acceptor 8 was easily prepared in 92% yield via deprotonation of 1 with n-BuLi in THF at −78 °C, quenching the resulting enolate with paraformaldehyde, and heating the crude reaction mixture for 1 hour prior to workup. The stereochemical integrity of the C3 stereocentre of 8 was confirmed to be >95% ee by comparison of the 500 MHz 1H NMR spectrum of homochiral 8 with that of an authentic sample of (±)-8 (prepared de novo from racemic valine) in the presence of the chiral solvating agent 2,2,2-trifluoro-1-(9H-fluoren-9-y1)ethanol.

Addition of Ph2CuCN to methylene acceptor 8, in THF at −78 °C, followed by quenching of the resulting enolate 9a with aqueous ammonium chloride, afforded a crude reaction mixture which contained the cis-(3S,6S)-3-isopropyl-6-benzylketopiperazine 6a as the only identifiable product. The diastereoselectivity of this reaction was confirmed as >95% by examination of the 1H NMR spectra of the crude reaction mixture which revealed the absence of any resonances corresponding to the known16 minor diastereoisomer trans-(3S,6R)-3-isopropyl-6-benzylketopiperazine 2a (Scheme 3, Table 1).

<table>
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<th>Product</th>
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<th>Cuprate conditions</th>
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<td>Ph</td>
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<td>6b</td>
<td>Bu</td>
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<tr>
<td>6f</td>
<td>Pr</td>
<td>2 PrMgBr–CuCN</td>
<td>88</td>
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*Table 1* Yields for organocuprate additions to methylene acceptor 8 to afford 6a–f

Purification of the crude reaction mixture via chromatography afforded the desired homochiral diastereoisomerically pure cis-(3S,6S)-3-isopropyl-6-benzylketopiperazine derivatives 6b–f were prepared via addition of the corresponding organocuprate to the methylene acceptor 8 in >95% de and in 88–92% isolated yield (Scheme 3, Table 1).

The excellent cis diastereoselectivity observed in these additions arises from highly selective Re-face protonation of enolate 9 resulting from the conjugate addition. We have proposed that the high degree of facial selectivity in alkylation of the unsubstituted parent auxiliary 1 is the result of a chiral relay involving the p-methoxybenzyl protecting groups operating within the system and the selectivity in the protonation of the metallated enolate 9a–f presumably derives from similar factors (Fig. 2).14 Notably the de obtained via reprotonation of the copper enolate 9a with aqueous ammonium chloride is superior to that obtained via direct deprotonation of trans-2a and reprotonation of the lithium enolate (92% de) utilising the hindered proton source, 2,6-di-tert-butylphenol.6 Indeed reprotonation of the lithium enolate derived from 2a with ammonium chloride gives 6a in 91% de while reprotonation of the copper enolates 9a–f with the same proton source leads to uniformly high diastereoselectivities.

Deprotection and hydrolysis of cis-3-isopropyl-6-alkylketopiperazines 6a–f to afford homochiral α-amino acids 7a–f

Deprotection of homochiral N,N′-bis(p-methoxybenzyl)-3-isopropyl-6-alkylketopiperazines 6a–f was achieved in good yield *via* a three step process. Oxidative removal of the
p-methoxybenzyl groups with ceric ammonium nitrate in CH₃CN⋅H₂O (3 : 1) followed by chromatographic purification over alumina to remove cerium salts afforded homochiral cis-3-isopropyl-6-alkyldiketopiperazines 10a-f in good yield. Hydrolysis of 10a-f, by refluxing in 6 M HCl, afforded a mixture of (S)-valine 5 and the desired (S)-α-amino acids 7a-f. Whilst these α-amino acids 7a-f could be separated from the valine chiral auxiliary via ion exchange chemistry over Dowex 50-XH, this approach proved tedious especially when carried out on a large scale. As a result, an alternative separation approach was adopted whereby treatment of the mixture of α-amino acids 5 and 7a-f with HCl–MeOH afforded a mixture of (S)-valine methyl ester 11 and (S)-α-aminoesters 12a-f The free aminoesters (S)-12a.b.d.e were easily separated from 11 by fractional distillation under vacuum, whilst the more volatile esters (S)-12c and (S)-12f were separated from (S)-valine methyl ester 11 via silica chromatography. Subsequent hydrolysis of (S)-12a-f to their corresponding homochiral α-amino acids (S)-7a-f was achieved by treatment with refluxing 6 M HCl. The enantiomeric excess of each α-amino acid (S)-7a-f was confirmed to be >99% ee by comparison with authentic racem samples using chiral HPLC analysis (Scheme 4, Table 2).

**Conclusion**

In conclusion, we have shown that conjugate addition of organocuprates to N,N′-bis(p-methoxybenzyl)-3-methylene-6-isopropylidiketopiperazine 8 provides simple access to cis-(3S,6S)-diketopiperazines 6 which may be deprotected to afford homochiral (S)-α-amino acids 7 in good yield. Importantly this methodology is more efficient than the previously described approach based on alkylation of the enolate of 1 and provides access to α-amino acids, such as 7b, previously unavailable from our methodology.

**Experimental**

**General**

Melting points (mp) were obtained using a Thermogalen™ III or Griffin Gallenkamp melting point apparatus and are uncorrected. Optical rotations were measured with a Perkin-Elmer 241 polarimeter with a thermally jacketed 10 cm cell at approximately 20 °C and are reported in units of 10⁻¹ deg cm² g⁻¹. Concentrations (c) are given in g per 100 ml. Infrared (IR) spectra were recorded as KBr discs on a Perkin-Elmer 1750 Fourier Transform spectrometer. Absorptions are reported in wavenumbers (cm⁻¹). Proton magnetic resonance spectra (¹H NMR) were recorded at 200 MHz on a Varian Gemini 200 or a Bruker AC200 spectrometer, at 300 MHz on a Bruker WH300, at 400 MHz on a Bruker AC400 and at 500 MHz on a Bruker AM500 spectrometer and are referenced to the residual solvent peak. The following abbreviations were used: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet and br, broad. Coupling constants (J) were recorded in hertz to the nearest 0.05 Hz. Carbon magnetic resonance spectra (¹³C NMR) were recorded at 50.3 MHz on a Varian Gemini 200 or Bruker AC200 spectrometer, at 100.6 MHz on a Bruker AC400 spectrometer and at 125.7 MHz on a Bruker AMX500 spectrometer using DEPT editing. Diastereomeric excesses were determined by peak integration of the ¹H NMR spectra of the crude reaction product. Low resolution mass spectra (m/z) were recorded on...
To a stirred solution of I (5.0 g, 12.6 mmol) in anhydrous THF (20 ml) at −78 °C was added a solution of n-butyllithium in hexanes (8.25 ml, 1.53 M) at −78 °C, over a period of two minutes. The resultant solution was allowed to stir at −78 °C for a further 15 minutes prior to the addition of solid paraformaldehyde (ca. 10 g) and subsequent removal of the cooling bath. The resultant suspension was then heated at 70 °C for one hour, cooled, water (3 ml) added and the mixture was partitioned between ether and water, extracted with ether and the organic phase dried (MgSO₄). The solvents were removed in vacuo. Filtration through a short stub of silica using ether as the eluent and removal of the solvents in vacuo afforded the title compound 8 as a thick, pale yellow coloured gum that was used directly as such in vacuum sublimation.

(3S,5S)-N,N'-Bis(4-methoxybenzyl)-3-isopropyl-6-isopropyldiketopiperazine-2,5-dione 8

To a stirred solution of 1 (1.25 M, 1.8 M in cyclohexane–ether) gave a crude reaction mixture which was chromatographed on silica gel using ethyl acetate–hexane (1:5) to afford the title compound 8 as a pale yellow oil (1.05 g, 88%). 

Table 2  Isolated yields for protection of 6a–f to 10a–f and α-amino acids 7a–7f (Scheme 4)
(1H, d, J 14.8, ArCH₂), 3.90 (1H, d, J 14.7, ArCH₃), 5.19 (1H, d, J 14.7, ArCH₂), 5.37 (1H, d, J 14.8, ArCH₃), 6.80–6.86 (4H, m, aromatic CH), 7.06–7.15 (4H, m, aromatic CH); δC (75 MHz, CDCl₃) 11.0, 19.6, 20.7, 27.4, 62.3, 47.1, 48.8, 153.3, 155.7, 160.6, 65.1, 114.2, 127.9, 128.0, 129.2, 129.4, 159.2, 165.9 (C=O), 167.2 (C=O); m/z (CI) 425 (MH⁺, 100%); Found: MH⁺, 425.2441. C₁₉H₁₄N₂O₄ requires 425.2440.

(53.65)-N’,N’-Bis-(4-methoxybenzyl)-3-isopropyl-6-n-pentyl-piperazine-2,5-dione 6d. Treatment of 8 according to general procedure I using butyltrimethylsilane (3.68 ml, 1.6 M in hexanes) gave a crude reaction mixture from which the title compound 6d was crystallised (ether-hexane) (1.04 g, 91%). Mp 70 °C; [α]D = [−186.7] (c 1.00, CHCl₃); νmax (KBr/cm⁻¹) 3438, 3198, 3091, 3038, 2961, 2930, 2878, 1669 (s, C=O), 1453; δH (500 MHz, DMSO-d₆) 0.27 (3H, d, J 6.8, CH₃CH₂), 0.66 (3H, d, J 7.1, CH₃CH₂), 1.71 (1H, dsep, J 4.5, 6.8, CH₃CH₂), 2.88 (1H, d, J 13.5, 5.0, CH₃CH₂), 3.16 (1H, dd, J 13.5, 4.3, 3.75), 3.51–3.59 (1H, m, 3H, C₃H₆), 4.70–4.73 (2H, m, aromatic CH), 7.23–7.28 (2H, m, aromatic CH), 7.92 (1H, br s, NH), 8.12 (1H, br s, NH); δC (50 MHz, DMSO-d₆) 16.1, 18.2, 31.0, 37.8, 55.2, 99.2, 125.7, 127.9, 130.3, 136.3, 166.4, 166.5; m/z (CI) 247 (MH⁺, 100%) (Found: MH⁺, 247.1440. C₁₈H₁₄N₂O₂ requires 247.1446).

(53.65)-N’,N’-Bis-(4-methoxybenzyl)-3-isopropyl-6-cyclohexylmethylpiperazine-2,5-dione 6e. Treatment of 8 according to general procedure I with cyclohexylmagnesium chloride (2.94 ml, 2 M in ether) gave a crude reaction mixture which was chromatographed on silica gel using 1:5 ethyl acetate–hexane to afford the title compound 6e as a clear oil (1.11 g, 92%). νmax (KBr/cm⁻¹) 3438, 3317, 3086, 2974, 1679 (s, C=O), 1457; δH (500 MHz, DMSO-d₆) 0.82 (3H, d, J 6.8, CH₃CH₂), 0.88 (9H, s, C₃H₉), 0.92 (3H, d, J 7.0, CH₃CH₂), 1.37 (1H, dd, J 14.1, 7.5, CH₂), 1.84 (1H, dd, J 14.1, 3.4, CH₂), 2.00–2.02 (1H, m, CH₂CH₂), 3.50–3.75 (1H, m, 3H, C₃H₆), 3.64–3.78 (1H, m, 6H, C₃H₆), 7.92 (1H, br s, NH), 8.08 (1H, br s, NH); δC (50 MHz, DMSO-d₆) 17.7, 18.8, 29.4 (30), 34.3, 52.1, 52.0, 59.8, 167.8 (C=O), 169.8 (C=O); m/z (CI) 227 (MH⁺, 100%) (Found: MH⁺, 227.1751. C₁₈H₁₄N₂O₂ requires 227.1759).

(53.65)-N’,N’-Bis-(4-methoxybenzyl)-3-isopropyl-6-isobutyl-piperazine-2,5-dione 6f. Treatment of 8 according to general procedure I with isopropylmagnesiumtribromide (2.94 ml, 2 M in THF) gave a crude reaction mixture which was chromatographed on silica gel using 1:5 ethyl acetate–hexane to afford the title compound 6f as a viscous oil (978 mg, 88%). νmax (KBr/cm⁻¹) 3438, 3321, 3198, 3091, 3038, 2961, 2876, 1665 (s, C=O), 1451; δH (500 MHz, DMSO-d₆) 0.83 (3H, d, J 6.9, CH₃CH₂), 0.85 (3H, t, J 7.4, CH₃CH₂), 0.94 (3H, d, J 7.1, CH₃CH₂), 1.69 (2H, m, CH₂CH₂), 2.17 (1H, m, CH₃CH₂), 3.68 (1H, m, 3H, C₃H₆), 3.79 (1H, m, 6H, C₃H₆), 8.00 (1H, br s, NH), 8.12 (1H, br s, NH); δC (125 MHz, DMSO-d₆) 9.2, 17.0, 18.5, 26.2, 31.0, 54.8, 59.3, 167.0, 167.8; m/z (CI) 185 (MH⁺, 100%) (Found: MH⁺, 185.1289. C₁₈H₁₄N₂O₂ requires 185.1290).

(53.65)-N’,N’-Bis-(4-methoxybenzyl)-3-isopropyl-6-ethyl-piperazine-2,5-dione 10c. Deprotection of 6f (870 mg, 2.05 mmol) by general procedure II using CAN (6.75 g, 12.3 mmol) gave the title compound 10c (339 mg, 90%). Mp 210 °C (sub); [α]D = −41.5 (c 1.00, AcOH); νmax (KBr/cm⁻¹) 3320, 3194, 3014, 2976, 2880, 1665 (s, C=O), 1451; δH (500 MHz, DMSO-d₆) 0.82–0.89 (6H, m, CH₂CH₂CH₂), 2.00–2.02 (1H, m, CH₂CH₂), 3.50–3.75 (1H, m, 3H, C₃H₆), 3.64–3.78 (1H, m, 6H, C₃H₆), 7.92 (1H, br s, NH), 8.08 (1H, br s, NH); δC (50 MHz, DMSO-d₆) 17.7, 18.8, 29.4 (30), 34.3, 52.1, 52.0, 59.8, 167.8 (C=O), 169.8 (C=O); m/z (CI) 227 (MH⁺, 100%) (Found: MH⁺, 227.1751. C₁₈H₁₄N₂O₂ requires 227.1759).

General procedure II: deprotection of 6a–f

To a solution of 6a–f (~1.0 g) in water (6 ml) and acetonitrile (18 ml) was added ceric ammonium nitrate (6 equiv.) in one portion. The resultant suspension was stirred at room temperature for one hour, neutral alumina added (ca. 1 g), the solvent removed in vacuo, and the crude residue applied to a column of neutral alumina (gradient elution EtOAc–EtOAc–EtOH 4:1) to afford 10a–f.
Deprotection of 6e (1.46 g, 2.97 mmol) by general procedure II using CAN (9.76 g, 17.8 mmol) gave the title compound 10e (748 mg, 91%). Mp 227°C (sub.; [a]_D^22.5 (c 1.10, AcOH); v_max (KBr/cm^-1) 3193, 3056, 2926, 2923, 2853, 1665 (s, C=O), 1449; δ_H (500 MHz, DMSO-d_6) 0.80–1.0 (2H, m, C(CH_3)_2), 1.11–1.30 (4H, m, 2 × CH_2), 1.45–1.81 (7H, m, 3 × CH_2 and CH(CH_3)CH_2), 0.89 (3H, d, J 6.8, CH(CH_3)CH_2), 0.99 (3H, d, J 7.0, CH_3CH_2CH_3), 2.10–2.20 (1H, m, CH_3CH(CH_3)CH_2), 3.64–3.68 (1H, m, 3-H), 3.82–3.86 (1H, m, 6-H), 8.06 (1H, br s, NH), 8.20 (1H, NH). 3287 J. Chem. Soc, Perkin Trans. 1, 2001, 3281–3287.

Deprotection of 6f (817 mg, 1.81 mmol) by general procedure II using CAN (5.94 g, 10.8 mmol) gave the title compound 10f (345 mg, 90%). Mp 212°C (sub.; [α]_D^22.5 = −55.1 (c 0.90, AcOH); v_max (KBr/cm^-1) 3276, 3196, 2938, 2874, 2875, 1666 (C=O), 1453; δ_H (500 MHz, DMSO-d_6) 0.85 (3H, d, J 6.9, CH(CH_3)CH_2), 0.87 (3H, d, J 6.8, CH(CH_3)CH_2), 0.89 (3H, d, J 7.0, CH_3CH_2CH_3), 1.00 (3H, d, J 6.9, CH(CH_3)CH_2), 1.45–1.52 (1H, m, CH_3), 1.68–1.73 (1H, m, CH_3), 1.80–1.85 (1H, m, CH_3CH(CH_3)CH_2), 2.10–2.15 (1H, m, CH_3CH(CH_3)CH_2), 3.65–3.70 (1H, m, 3-H), 3.76–3.80 (1H, m, 6-H), 8.20 (1H, br s, NH), 8.47 (1H, NH). General procedure III: isolation of amino acid hydrochloride salts

A solution of 10a-f (200–500 mg) was refluxed in 6 M HCl (60 ml) overnight and the solvent was removed in vacuo. The resultant mixture of amino acid hydrochloride acid salts was refluxed in methanolic HCl for 2 hours. The solvents were removed to afford a residue which was neutralised with NaHCO_3 (aq), extracted with CH_2Cl_2 (3 × 30 ml), dried (MgSO_4), and the solvents again removed in vacuo (Warning: amino acid methyl esters volatile) to give a mixture of (S)-valine methyl ester and the appropriate amino acid methyl ester 12a-f. The (S)-α-amino esters 12a, 12b, 12d, and 12e were purified by fractional distillation/removal of the more volatile (S)-valine methyl ester under high vacuum at ca. 40°C for 30 minutes. The volatile (S)-α-amino acid methyl esters 12c and 12f were purified by chromatography on silica using ethyl acetate–hexanes (3:7) as eluent and the solvent carefully removed in vacuo. The resultant amino esters were then heated in 6 M HCl under reflux for 30 minutes, and the solvents evaporated in vacuo to yield the parent α-amino acids as their HCl salts.

The enantiomeric excess of the (S)-α-amino acids was determined by chiral HPLC analysis by either method A or method B.

Method A. Benzyl chloroformate (0.15 ml) and triethylamine (0.15 ml) were added to the amino acid hydrochloride (50 mg) in dioxane (1 ml) and the mixture was stirred at room temperature for 1 hour. This crude mixture was analysed by HPLC using a Cyclobond™ I 2000 RSP (β-cyclodextrin hydroxypropyl capped bonded stationary phase) column eluting with [6–15: 94–85 CH_3CN–TEAA (1–1.5%)] with UV detection at 210 nm. The ee was determined by integration of signals and comparison of the retention times of the synthetic material and commercially available or similarly prepared racemic Cbz-α-amino acids.

Method B. The amino acid hydrochloride was analysed by HPLC using a Chirobiotic I column eluting with 33–50% water–ethanol with UV detection at 190 nm. The ee was deter-

(5S,6S)-3-Isopropyl-6-(cyclohexylmethy)lpirazin-2,5-dione 10e. Deprotection of 6e (1.46 g, 2.97 mmol) by general procedure II using CAN (9.76 g, 17.8 mmol) gave the title compound 10e (748 mg, 91%). Mp 227°C (sub.; [α]_D^22.5 = −37.8 (c 1.10, AcOH); v_max (KBr/cm^-1) 3193, 3056, 2926, 2923, 2853, 1665 (s, C=O), 1449; δ_H (500 MHz, DMSO-d_6) 0.80–1.0 (2H, m, C(CH_3)_2), 1.11–1.30 (4H, m, 2 × CH_2), 1.45–1.81 (7H, m, 3 × CH_2 and CH(CH_3)CH_2), 0.89 (3H, d, J 6.8, CH(CH_3)CH_2), 0.99 (3H, d, J 7.0, CH_3CH_2CH_3), 2.10–2.20 (1H, m, CH_3CH(CH_3)CH_2), 3.64–3.68 (1H, m, 3-H), 3.82–3.86 (1H, m, 6-H), 8.06 (1H, br s, NH), 8.20 (1H, NH). 3287 J. Chem. Soc, Perkin Trans. 1, 2001, 3281–3287.

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References


