Tetrahedron: *Asymmetry* 19 (2008) 2678–2681

Contents lists available at ScienceDirect

Tetrahedron: *Asymmetry*

journal homepage: www.elsevier.com/locate/tetasy

Asymmetric cyclopropanation using amino acid as chiral auxiliary

Debarati Mitra, Arjun Sengupta, Kumar Biradha, Amit Basak *

Department of Chemistry, Indian Institute of Technology, Kharagpur 721 302, India

ARTICLE INFO

Article history:
Received 14 October 2008
Accepted 12 November 2008
Available online 17 January 2009

ABSTRACT

The asymmetric cyclopropanation of cinnamoyl amides derived from amino acids with CH_2N_2 in the presence of catalytic $Pd(OAc)_2$ has been studied. The reaction proceeded with moderate to excellent diastereoselection. However, the selectivity depends upon the amino acid side chain as well as the electronic nature of the cinnamoyl moiety.

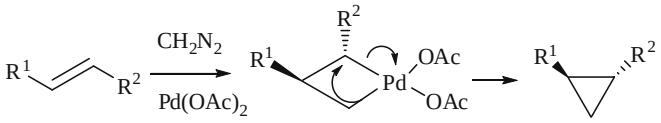
1. Introduction

Small rings have played crucial roles in imparting or controlling the biological activity of many important natural products.[1] Amongst them, cyclopropanes have played a prominent role. They are interesting due to their unusual bonding properties along with an inherent strain, many natural products are endowed with the cyclopropane moieties.[2] 2-Phenyl-1-cyclopropane carboxylates[3] are very useful intermediates in the synthesis of these chiral compounds. Compounds containing cyclopropanes have been extensively used as a probe to solve mechanistic problems.[4] These have also provided synthetic analogues with improved biological profiles. The natural and many synthetic analogues are chiral and hence asymmetric cyclopropanation[5] is an area which has drawn the attention of synthetic organic chemists for a long time. Several methods based on chiral auxiliaries as well as chiral catalysis have been reported.[6] Herein we report a simple chiral auxiliary based approach to a cyclopropane carboxamide which proceeds with a moderate to excellent degree of diastereoselectivity.

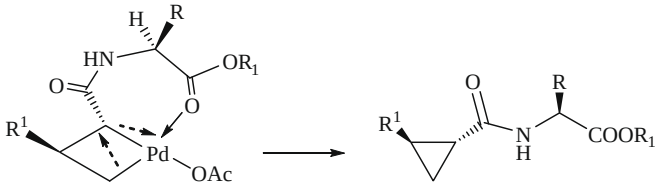
2. Results and discussion

Since the discovery of the palladium(II)-catalyzed cyclopropanation of olefins by Suda (Scheme 1),[7] various reports have appeared involving chiral palladium(II)-catalysis as well as auxiliary based approaches to induce enantioselectivity/diastereoselectivity in the reaction. The commonly accepted[8] mechanism of cyclopropanation involving Pd(II) is shown below:

The addition of the carbene is stereospecific in the sense that the geometry around the double bond is retained in the product. In order to introduce enantio/diastereoselectivity, an additional chiral ligand has to complex with the Pd(II). It occurred to us that attaching an amino acid into an α,β-unsaturated acid through an amide linkage might bring in the extra conjugation as shown below (Scheme 2), the metallo cyclobutane should then collapse to the cyclopropane predominantly via the intermediate shown in order to avoid the steric hindrance between the amino acid alkyl group and the acyl group.



Scheme 1. Possible mechanism of $Pd(OAc)_2$ catalyzed cyclopropanation.



Scheme 2. Possible stereoselective collapse of the metallocycle.

With this in mind, we proceeded to prepare the starting synthons. Thus the various cinnamic acids were coupled with the appropriate amino acid benzyl ester in the presence of EDCI[9] and diisopropyl ethylamine. The various amides were then treated with excess diazomethane in presence of $Pd(OAc)_2$ in dry ether and the solution was stirred at rt for 6–7 h. It was then evaporated and the residue was purified by chromatography over Si-gel. The two cyclopropane diastereomers were checked for ^1H NMR spectroscopy. The benzylic hydrogens showed up as separate signals in the region of $\sim\delta$ 5.1 for the two diastereomers (Fig. 1). The combined yields and the diastereomeric ratios are shown in Table 1.

The results indicated that there is considerable degree of asymmetric induction in all the cyclopropanation reactions. The extent of diastereoselectivity was found to be dependent upon the amino acid side chain and the electronic nature of the cinnamoyl moiety

* Corresponding author. Fax: +91 3222 55303.
E-mail address: absk@chem.iitkgp.emet.in (A. Basak).

0957-4166/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tetasy.2008.11.009

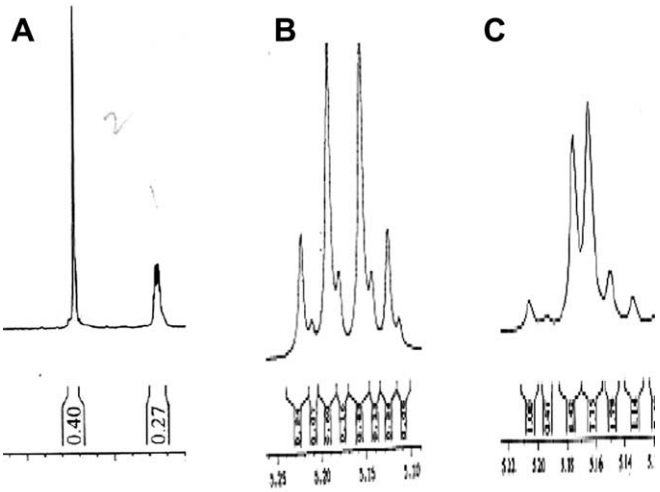


Figure 1. ^{1}H NMR of the benzylic region as used for determination of *diastereomeric excess* (A for **2d**, B for **2a**, C for **2b**).

Table 1
Results of cyclopropanation

Entry	Compounds	Combined yield (%)	Diastereomeric ratio
1	**2a** (R = $CH(CH_3)_2$)	95	4:1
2	**2b** (R = $CH_2CH(CH_3)_2$)	90	4:1
3	**2c** (R = $CH(CH_3)CH_2CH_3$)	94	6:1
4	**2d** (R = CH_2OH)	88	>19:1
5	**2e** (R = CH_3)	92	7:3
6	**4a** (R = $CH(CH_3)_2$)	90	2:1
7	**4b** (R = $CH_2CH(CH_3)_2$)	85	3:2
8	**4c** (R = $CH(CH_3)CH_2CH_3$)	82	6:1
9	**6a** (R = $CH(CH_3)_2$)	92	4:1
10	**6b** (R = $CH_2CH(CH_3)_2$)	84	4:1

(Scheme 3). The selectivity generally increased with an increase in steric bulk of the side chain. However, the highest selectivity was obtained when R = CH_2OH (serine). Greater electron donation of the phenyl moiety decreased the diastereoselectivity (entries 6–8). Electron withdrawal however did not have any effect on the degree of diastereoselectivity.

The absolute configuration of the one of the cyclopropane derivatives (R = CH_3) was confirmed by single crystal X-ray analysis (Fig. 2).[10] It was found to be (2*R*,3*R*). The stereochemistry matched with what has been predicted based on the following TS model (Fig. 3).

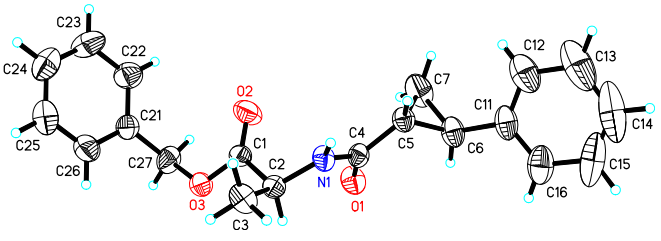


Figure 2. ORTEP structure of compound (2*R*,3*R*)-2-(2-phenyl carbonyl amino) propionic acid benzyl ester **2e**.

3. Conclusion

In conclusion, we have developed a simple asymmetric cyclopropanation using a cinnamoyl (or its derivative) amide with a protected amino acid. By varying the amino acid side chain, the extent of distereoselectivity could be increased to >90%. Future work regarding the generality of the reaction for aliphatic unsaturated acid derivatives is currently underway.

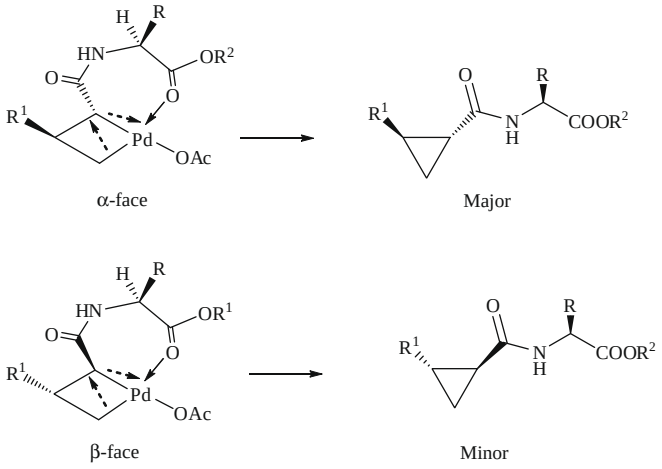


Figure 3. Explanation of the observed diastereoselectivity.

4. Experimental

4.1. Synthesis of cinnamic acid–amino acid conjugates

To cinnamic acid or its substituted analogue (dimethoxy/nitro) in CH_2Cl_2 (30 ml) at 0 °C, 1.2 equiv of HOBT and 1.2 equiv of EDC·HCl were added and was allowed to stir for 1 hr. Then, the free amine triflate (1.0 equiv) in CH_2Cl_2 (15 ml) was added followed by the addition of 5.0 equiv of DIPEA at 0 °C. The reaction was stirred for 12 h. Then it was partitioned between 2 × 45 ml of 1 (N) HCl and CH_2Cl_2 each. The CH_2Cl_2 layer was then washed with saturated solution of $NaHCO_3$, brine and then finally dried over anhydrous Na_2SO_4. The corresponding target compounds were obtained by column chromatography using suitable solvent systems depending upon the polarity of the compounds.

4.1.1. For compound 1a

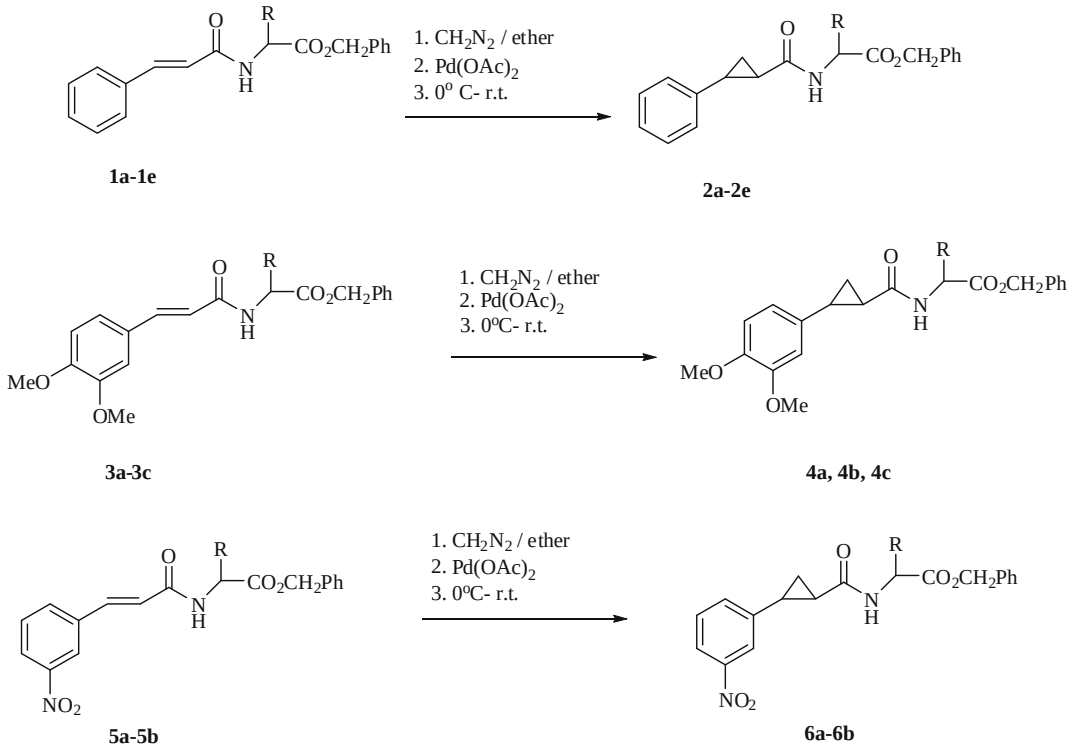
State: oily liquid; Yield: 65%; ν_{max} (KBr, cm^{-1}): 1632, 1217, 772; δ_H (400 MHz, $CDCl_3$): 7.65 (1H, d, *J* = 15.5 Hz), 7.53-7.51 (2H, m), 7.37-7.34 (8H, m), 6.47 (1H, d, *J* = 15.5 Hz), 6.12 (1H, d, *J* = 8.5 Hz), 5.20 (2H, dd, *J* = 12.0, 8.0 Hz), 4.79 (1H, dd, *J* = 5.0, 4.0 Hz), 2.28-2.23 (1H, m), 0.97 (3H, d, *J* = 7.0 Hz,), 0.91 (3H, d, *J* = 7.0 Hz); δ_C (100 MHz, $CDCl_3$): 172.0, 165.6, 141.8, 134.6, 129.7, 128.8, 128.6, 128.5, 128.4, 127.8, 120.1, 67.1, 57.0, 31.6, 18.9, 17.7; Mass (ESI) 338 (MH$^+$).

4.1.2. For compound 1b

White solid; Yield: 78%; ν_{max} (KBr, cm^{-1}): 1638, 1218, 772; δ_H (400 MHz, $CDCl_3$): 7.65 (H, d, *J* = 15.6 Hz), 7.50 (3H, d, *J* = 5.6 Hz), 7.36 (7H, m), 6.43 (H, d, *J* = 15.6 Hz), 6.00 (H, d. *J* = 8.4 Hz), 5.19 (2H, s), 4.84 (H, m), 1.73–1.68 (2H, m), 1.25 (H, m), 0.97–0.93 (6H, m); δ_C (100 MHz, $CDCl_3$): 171.6, 163.2, 141.8, 129.8, 128.8, 128.6, 128.4, 128.2, 67.1, 50.9, 41.9, 24.8, 22.8. 22.0; Mass (ESI) 352 (MH$^+$).

4.1.3. For compound 1c

White solid; Yield:75%; ν_{max} (KBr, cm^{-1}): 1637, 1350, 1212, 1189, 751; δ_H (400 MHz, $CDCl_3$): 7.64 (H, d, *J* = 15.6 Hz), 7.52–7.49 (10H, m), 6.45 (H, d, *J* = 15.6 Hz), 6.14 (H, d, *J* = 8.4 Hz), 5.20 (2H, dd, *J* = 12.0 Hz, *J* = 11.0 Hz), 4.83–4.80 (H, m), 1.98–1.96 (H, m), 1.44–1.42 (H, m), 1.25–1.18 (H, m), 0.93–0.89 (6H, m); δ_C (100 MHz, $CDCl_3$): 172.0, 165.5, 141.7, 135.2, 134.6, 129.8, 128.8, 128.6, 128.4, 128.3, 127.8, 121.0, 67.1, 56.5, 38.3, 25.1, 15.4, 11.5.



For compounds of **a** series: R = -$CH(CH_3)_2$; For compounds of **b** series R = -$CH_2CH(CH_3)_2$
For compounds of **c** series: R = -$CH(CH_3)CH_2CH_3$; For compounds of **d** series: R= –CH_2OH
For compounds of **e** series: R = -CH_3

Scheme 3. Cyclopropanation reactions.

4.1.4. For compound 1d

White solid, Yield: 82%; ν_{max} (KBr, cm^{-1}), 1654, 1638, 1219, 553; δ_H (400 MHz, $CDCl_3$): 7.67 (H, d, J = 15.6 Hz), 7.53–7.51 (2H, m), 7.38–7.34 (8H, m), 6.58 (H, d, J = 6.4 Hz), 6.49 (H, d, J = 15.6 Hz), 5.26 (2H, s), 4.05 (2H, m), 2.46 (H, t, J = 6.0 Hz); δ_C (100 MHz, $CDCl_3$): 170.3, 166.1, 142.3, 134.9, 134.4, 130.0, 128.8, 128.7, 128.6, 128.2, 127.9, 119.6, 67.6, 63.8, 55.1; Mass (ESI) 326 (MH^+).

4.1.5. For compound 1e

Oily liquid, Yield: 80%; ν_{max} (KBr, cm^{-1}), 1638, 1220, 772; δ_H (400 MHz, $CDCl_3$): 7.64 (H, d, J = 15.6 Hz), 7.52–7.47 (3H, m), 7.42–7.32 (7H, m), 6.44 (H, d, J = 15.6 Hz), 6.32 (H, d, J = 14.8 Hz), 5.21 (2H, s), 4.80 (H, t, J = 14.4 Hz), 1.49 (3H, d, J = 14.4Hz); δ_C (100 MHz, $CDCl_3$): 173.1, 165.3, 141.7, 135.3, 134.7, 129.8, 128.8, 128.7, 128.5, 128.2, 127.9, 120.1, 67.3, 48.4, 18.7; Mass (ESI) 310 (MH^+).

4.1.6. For compound 3a

Oily liquid; Yield: 82%; ν_{max} (KBr, cm^{-1}): 2345, 2079, 1639, 1262, 1141, 1025, 772, 689; δ_H 7.57 (1H, d, J = 15.5 Hz), 7.35-7.32 (5H, m), 7.06 (1H, d, J = 8.5 Hz),7.01 (1H, s), 6.83 (1H, d, J = 8.5 Hz), 6.36 (1H, d, J = 15.5 Hz), 6.25 (1H, s), 5.12 (2H, dd, J = 12.0, 9.0 Hz), 4.79 (1H, dd, J = 5.0, 4.0 Hz), 3.89 (6H, s), 2.26-2.21 (1H, m), 0.96 (3H, d, J = 7.0 Hz), 0.90 (3H, d, J = 7.0 Hz); δ_C 172.2, 166.0, 150.6, 149.0, 141.5, 135.2, 128.5, 128.4, 128.3, 127.6, 122.1, 118.0, 110.9, 109.5, 67.1, 57.1, 55.9, 55.8, 31.5, 29.6, 19.0, 17.7; Mass (ESI) 398 (MH^+).

4.1.7. For compound 3b

Oily liquid; Yield: 78%; ν_{max} (KBr, cm^{-1}): 1736, 1654, 1624, 1263, 1147, 1025, 768; δ_H (400 MHz, $CDCl_3$): 7.61 (H, d, J = 15.6 Hz), 7.36–7.32 (5H, s), 7.09–7.01 (2H, m), 6.84 (H, d, J = 16.4 Hz), 6.31 (H, d, J = 31.2 Hz), 6.07 (H, d, J = 17.2 Hz), 5.18 (2H, s), 4.90–4.79 (H, m), 3.90 (6H, s), 1.70–1.67 (3H, m), 0.97–0.91 (6H, m); δ_C (100 MHz, $CDCl_3$): 173.2, 165.8, 150.6, 149.0, 141.6, 135.3, 128.6, 128.4, 128.2, 127.6, 122.1, 117.8, 111.0, 109.5, 67.1, 55.9, 55.8, 50.9, 41.8, 29.6, 24.8, 22.8, 21.9.

4.1.8. For compound 3c

Oily mass; ν_{max} (KBr, cm^{-1}): 1736, 1541, 1263, 1025, 754; δ_H (400 MHz, $CDCl_3$): 7.70 (H, d, J = 15.2 Hz), 7.35–7.32 (5H, m), 7.08–7.02 (2H, m), 6.84 (H, d, J = 8.4 Hz), 6.34 (H, d, J = 15.6 Hz), 6.20 (H, d, J = 8.8 Hz), 5.18 (2H, dd, J = 12.0, 11.6 Hz), 4.83–4.80 (H, m), 3.90 (6H, s), 1.96 (H, m), 1.76 (H, m), 1.46–1.40 (H, m), 1.27–1.14 (H, m), 0.93–0.89 (5H, m); δ_C (100 MHz, $CDCl_3$): 172.1, 165.8, 150.6, 149.0, 141.5, 135.2, 128.6, 128.4, 128.3, 127.6, 122.1, 118.0, 110.9, 109.4, 67.0, 56.5, 55.9, 55.8, 38.3, 25.1, 15.4, 11.6.

4.1.9. For compound 5a

Oily mass; ν_{max} (KBr, cm^{-1}): 1656, 1530, 1352, 1192, 978, 771; δ_H (400 MHz, $CDCl_3$): 8.38 (H, s), 8.21 (H, m), 7.79 (H, d, J = 7.6 Hz), 7.69 (H, d, J = 15.6 Hz), 7.57 (H, t, J = 8.0 Hz), 7.38–7.34 (5H, m), 6.61 (H, d, J = 15.6 Hz), 6.24 (H, d, J = 8.8 Hz), 5.24–5.16 (2H, m), 4.80–4.77 (H, m), 2.29–2.24 (H, m), 0.97 (3H, d, J = 8.0 Hz) 0.92 (3H, d, J = 8.0Hz); δ_C (100 MHz, $CDCl_3$): 171.8, 164.7, 148.6, 139.1, 136.4, 135.1, 133.8, 129.9, 128.6, 128.5, 128.4, 124.1, 123.2, 121.8, 67.2, 57.2, 31.6, 18.9, 17.6; Mass (ESI) 383 (MH^+).

4.2. Synthesis of cyclopropane derivatives of cinnamic acid–amino acid conjugates

To the ether solution of cinnamic acid–amino acid conjugates, 0.1 mol percent of $Pd(OAc)_2$ was added followed by the addition of freshly generated CH_2N_2 in ether (~50-fold excess). The reaction

was allowed to stir for 6–7 h. It was then filtered through a silica column to get the pure product. The spectral and other physical data are mentioned for the major isomer.

4.2.1. For compound 2a

State: Oily liquid; Yield: 95%; $[\alpha]_D = -76$ (*c* 0.34, $CHCl_3$); ν_{max} (KBr, cm^{-1}): 1654, 1638, 1262, 1220, 1145, 1027, 771; δ_H 7.40–7.36 (5H, m), 7.35–7.29 (2H, m), 7.22–7.18 (H, m), 7.11–7.07 (2H, m), 6.20 (H, d, *J* = 8.4 Hz), 5.22–5.11 (2H, m), 4.69–4.65 (1H, m), 2.54–2.49 (H, m), 2.21–2.16 (H, m), 1.74–1.69 (2H, m), 1.65–1.59 (H, m), 0.95–0.86 (6H, m); δ_C 172.0, 171.9, 140.7, 135.2, 128.6, 128.5, 128.4, 128.3, 126.2, 126.0, 125.9, 67.0, 57.1, 31.5, 31.4, 29.6, 26.6, 26.5, 25.3, 25.2, 18.9, 17.7, 17.6, 16.3, 16.1; Mass (ESI) 352 (MH^+).

4.2.2. For compound 2b

Oily liquid; Yield: 90%; $[\alpha]_D = -27$ (*c* 0.34, $CHCl_3$); ν_{max} (KBr, cm^{-1}): 1639, 1220, 772, 689; δ_H: 7.38–7.36 (5H, m), 7.34–7.28 (3H, m), 7.21–7.19 (H, m), 7.10–7.06 (H, m), 6.09 (H, d, *J* = 8.0 Hz), 5.18–5.15 (2H, m), 4.73–4.70 (H, m), 2.51–2.48 (H, m), 1.69–1.54 (4H, m), 1.28–1.23 (2H, m), 0.94–0.88 (6H, m); δ_C 173.0, 171.6, 140.7, 135.3, 128.5, 128.4, 128.3, 128.2, 126.2, 126.0, 125.9, 67.0, 50.9, 41.8, 29.6, 26.5, 26.4, 25.2, 25.1, 24.8, 22.7, 21.9, 16.3, 15.9; Mass (ESI) 366 (MH^+).

4.2.3. For compound 2c

Oily liquid; Yield: 90%; ν_{max} (KBr, cm^{-1}): 1639, 1220, 1190, 1144, 1079, 1028, 772; δ_H 7.36–7.34 (4H, m), 7.30–7.34 (3H, m), 7.22–7.20 (H, m), 7.10–7.08 (2H, m) 6.15 (H, d, *J* = 8.4 Hz), 5.18 (2H, dd, *J* = 12.4, 16.4 Hz), 4.72–4.68 (H, m), 2.52–2.48 (H, m), 1.90–1.89 (H, m), 1.70–1.67 (H, m), 1.66–1.58 (H, m), 1.39–1.37 (H, m), 1.28–1.23 (H, m), 1.16–1.14 (H, m) 0.89–0.86 (6H, m); δ_C 172.0, 171.7, 140.7, 135.2, 128.5, 128.4, 128.3, 126.3, 126.0, 125.9, 77.3, 77.2, 77.0, 76.6, 67.0, 56.5, 38.2, 26.6, 26.5, 25.2, 25.1, 16.3, 15.4, 11.5; Mass (ESI) 366 (MH^+).

4.2.4. For compound 2d

White solid; Yield: 88%; $[\alpha]_D = -85$ (*c* 0.34, $CHCl_3$); ν_{max} (KBr, cm^{-1}): 1638, 1193, 698; δ_H 7.40–7.35 (4H, m), 7.28 (3H, t, *J* = 7.6 Hz), 7.20 (H, m), 7.09 (2H, d, *J* = 7.6 Hz), 6.63 (H, d, *J* = 6.8 Hz), 5.23 (2H, s), 4.75 (H, m), 3.99–3.96 (2H, m), 2.53–2.44 (1H, m), 1.75–1.72 (H, m), 1.65–1.63 (H, m), 1.31–1.26 (H, m); δ_C 172.5, 170.3, 140.3, 135.0, 128.6, 128.5, 128.4, 128.2, 126.4, 126.0, 125.9, 116.1, 67.6, 63.7, 55.1, 26.4, 25.6, 16.5; Mass (ESI) 340 (MH^+).

4.2.5. For compound 2e

White solid; Yield: 95%; $[\alpha]_D = -38$ (*c* 0.34, $CHCl_3$); ν_{max} (KBr, cm^{-1}): 3916, 3866, 3834, 2370, 2079, 1471, 1220, 766, 694; δ_H 7.38–7.31 (4H, m), 7.28–7.19 (4H, m), 7.11–7.07 (2H, m), 6.22, (H, d, *J* = 14.0 Hz), 5.18 (2H, s), 4.69 (H, t, *J* = 14.4 Hz), 2.53–2.45 (H, m), 1.68–1.66 (2H, m), 1.45–1.44 (3H, m), 1.32–1.21 (H, m); δ_C 173.0, 171.4, 140.7, 135.3, 128.6, 128.5, 128.2, 126.3, 126.1, 126.0, 116.4, 100.0, 67.2, 48.3, 26.5, 26.4, 25.3, 18.7, 16.3, 16.0.

4.2.6. For compound 4a

Oily liquid; Yield: 95%; ν_{max} (KBr, cm^{-1}): 1640, 1220, 1144, 1027, 772; δ_H 7.35 (5H, d, *J* = 5.2 Hz), 6.80–6.77 (H, m), 6.64–6.23 (2H, m), 6.13 (H, d, *J* = 8.8 Hz), 5.23–5.12 (2H, m), 4.67–4.64 (H, m), 3.91–3.86 (6H, m), 2.50–2.45 (H, m), 2.21–2.16 (H, m), 1.67–1.64 (3H, m), 0.94–0.87 (6H, m); δ_C 172.0, 171.9, 148.9, 147.6, 135.2, 133.2, 128.6, 128.4, 128.3, 117.7, 117.6, 111.2, 110.0, 109.7, 67.0, 57.2, 56.0, 55.8, 31.4, 26.4, 25.0, 24.9, 18.9, 17.7, 16.1; Mass (ESI) 412 (MH^+).

4.2.7. For compound 4b

State: Oily liquid; Yield: 90%; ν_{max} (KBr, cm^{-1}): 1638, 1253, 698; δ_H 7.40–7.34 (5H, m), 6.80 (H, m), 6.64–6.60 (2H, m), 6.04–6.01 (H, m), 5.18–5.14 (2H, m), 4.73–4.70 (H, m), 3.86 (6H, d, *J* = 5.6 Hz), 2.47–2.45 (H, m), 1.68–1.60 (4H, m), 1.43–1.28 (2H, m), 1.18–1.16 (6H, m); δ_C 172.9, 171.7, 147.6, 135.3, 133.1, 128.5, 128.4, 128.2, 117.7, 117.6, 111.2, 110.0, 109.8, 67.0, 55.9, 55.8, 51.0, 41.9, 41.8, 31.9, 29.6, 29.3, 26.3, 26.1, 24.9, 24.8, 22.7, 22.6, 16.0, 15.7, 14.1; Mass (ESI) 426 (MH^+).

4.2.8. For compound 4c

Oily liquid; Yield: 93%; ν_{max} (KBr, cm^{-1}): 1655, 1390, 1255, 1106, 772; δ_H 7.36 (5H, m), 6.80–6.78 (H, m), 6.64–6.62 (2H, m), 6.16 (H, d, *J* = 8.4 Hz), 5.23–5.12 (2H, m), 4.71–4.68 (H, m), 3.86 (6H, d, *J* = 6.0 Hz), 2.49–2.44 (H, m), 1.92–1.88 (H, m), 1.64–1.62 (H, m), 1.57–1.55 (H, m), 1.25–1.20 (2H, m), 0.89–0.86 (7H, m); δ_C 172.2, 172.1, 149.2, 147.9, 135.5, 133.5, 128.8, 128.7, 128.6, 118.0, 117.9, 111.6, 111.5, 110.3, 110.1, 67.2, 56.8, 56.2, 56.1, 38.5, 38.4, 29.9, 26.7, 26.6, 25.4, 25.2, 16.3, 16.1, 15.7, 11.8.

4.2.9. For compound 6a

Oily liquid; Yield: 95%; ν_{max} (KBr, cm^{-1}): 3963, 3834, 3764, 2370, 2080; δ_H 8.06–8.04 (H, m), 7.90–7.87 (H, m), 7.57–7.45 (2H, m), 7.40–7.35 (5H, m), 6.22 (H, d, *J* = 8.0 Hz), 5.23–5.14 (2H, m), 4.67–4.64 (2H, m), 2.65–2.60 (H, m), 2.22 (H, m), 1.83–1.78 (H, m), 1.71–1.66 (H, m), 1.34–1.31 (H, m), 0.98–0.87 (6H, m); Mass (ESI) 397 (MH^+).

4.2.10. For compound 6b

Oily liquid; Yield: 92%; ν_{max} (KBr, cm^{-1}): 3963, 3764, 2370, 2080; δ_H 8.05–8.04 (H, m), 7.90 (H, s), 7.46–7.42 (2H, m), 7.39–7.33 (5H, m), 6.11 (H, d, *J* = 8.0 Hz), 5.21–5.14 (2H, m), 4.74–4.69 (H, m), 2.65–2.60 (H, m), 1.79–1.74 (H, m), 1.71–1.62 (2H, m), 1.35–1.25 (3H, m), 0.94–0.90 (6H, m); δ_C 172.8, 170.8, 170.7, 148.4, 142.9, 136.5, 135.2, 132.9, 132.7, 129.3, 129.2, 128.6, 128.4, 128.2, 121.3, 120.3, 116.1, 67.1, 51.1, 41.8, 31.9, 31.4, 30.1, 29.6, 29.3, 26.6, 24.8, 24.5, 24.4, 22.7, 22.6, 22.0, 19.7, 16.4, 14.1; Mass (ESI) 411 (MH^+).

Acknowledgements

The author DM is grateful to CSIR, Government of India for a fellowship. DST is thanked for providing funds for 400 MHz NMR facility under the IRPHA program.

References

1. (a) *Chemistry and Biology of β-Lactam Antibiotics*; Vols. 1–3 Morin, R. B., Gorman, M., Eds.; Academic Press, 1982; (b) Nicolaou, K. C.; Dai, W. M. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1387; (c) Basak, A.; Mandal, S. M.; Bag, S. S. *Chem. Rev.* **2003**, *10*, 4077; (d) Klein, M.; Walenzyk, T.; Konig, B. *Collect. Czech. Chem. Commun.* **2004**, *69*, 945; (e) Kar, M.; Basak, A. *Chem. Rev.* **2007**, *107*, 2861; (f) Grisom, J. W.; Gunawardena, G. U.; Klingberg, D.; Huang, D. *Tetrahedron* **1996**, *52*, 6453; (g) Guanti, G.; Banfi, L. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2393; (h) Banfi, L.; Guanti, G. *Eur. J. Org. Chem.* **2002**, 3745; (i) Basak, A.; Khamrai, U. K.; Mallik, U. *Chem. Commun.* **1996**, 749; (j) Basak, A.; Mandal, S. *Tetrahedron Lett.* **2002**, *43*, 4241; (k) Basak, A.; Khamrai, U. K. *Tetrahedron Lett.* **1995**, *36*, 7913; (l) Doroshow, J. H. *J. Natl. Cancer Inst.* **1992**, *84*, 1138.
2. (a) Lebel, H.; Marcoux, J. F.; Molinaro, C.; Charette, A. B. *Chem. Rev.* **2003**, *103*, 971; (b) Li, Z. N.; Liu, G. S.; Zheng, Z.; Chen, H. *Tetrahedron* **2000**, *56*, 7187.
3. Huang, K.; Huang, Z.-Z. *Synlett* **2005**, *10*, 1621.
4. Baldwin, J. E.; Adlington, R. M.; Domayne-Hayman, B. P.; Knight, G.; Ting, H.-H. *J. Chem. Soc., Chem. Commun.* **1987**, 1661.
5. (a) Gnad, F.; Reiser, O. *Chem. Rev.* **2003**, *103*, 1603; (b) Larionov, O. V.; de Meijere, A. *Org. Lett.* **2004**, *6*, 2153.
6. Uozumi, Y.; Kyota, H.; Kishi, E.; Kitayama, K.; Hayashi, T. *Tetrahedron: Asymmetry* **1996**, *7*, 1603.
7. Soda, M. *Synthesis* **1981**, 714.
8. Denmark, S. E.; Scavenger, R. A.; Faucet, A.-M.; Edwards, J. P. *J. Org. Chem.* **1997**, *62*, 3375.
9. Jiang, W.; Wanner, J.; Lee, R. J.; Bounaud, P.-Y.; Boger, D. L. *J. Am. Chem. Soc.* **2003**, *125*, 1877.
10. The CCDC number is CCDC 706633. The absolute configuration has not been established by anomalous dispersion effects in diffraction measurements on the crystal as the molecule contains lighter atoms than Si. The enantiomer was assigned by reference to an unchanging stereogenic centre originating from the amino acid in the synthetic procedure.