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## An Efficient Synthesis of *cis*-3-Hydroxy-4-phenyl- $\beta$ -Lactams : Precursor for Taxol Side Chain

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**Abstract:** Chiral ketene precursors derived from naturally occurring (+)-3-carene have been used for the synthesis of  $\beta$ -lactams *via* the Staudinger reaction. The major diastereomer **5a** was separated by crystallization and converted in very good yield into (3*R*, 4*S*)-3-hydroxy-4-phenyl- $\beta$ -lactam, an advanced intermediate towards the taxol side chain. Copyright © 1996 Elsevier Science Ltd

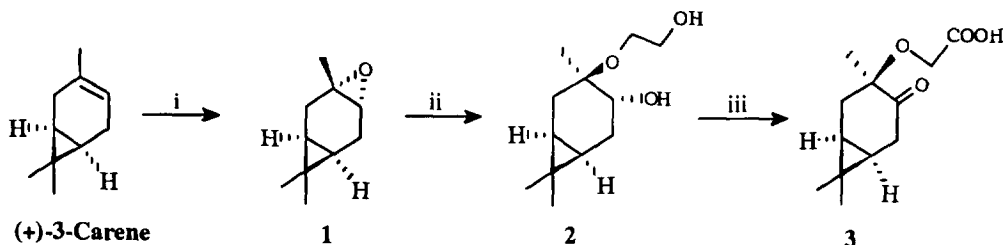
Taxol, a unique complex diterpene, is considered to be the most exciting drug of the decade in cancer chemotherapy,<sup>1</sup> in particular, for the treatment of lung, breast and ovarian cancer.<sup>2</sup> Unfortunately, this wonder drug is a plant derived product (obtained from the bark of *Taxus brevifolia*) available in very small quantities. Large scale sacrifice of yew trees in order to produce this drug is not an acceptable solution to the problem of making the drug available in sufficient quantity.<sup>3</sup> This has led to the search for semi-synthetic routes to taxol using other plant-derived products isolable in useful quantities. For instance, 10-deacetylbaaccatin III is available in the needles of *Taxus baccata*<sup>4</sup> (regenerable sources) in sufficient quantities and can be linked with (2*R*, 3*S*)-*N*-benzoyl-3-phenylisoserine<sup>5</sup> to produce taxol.

A study of the natural and semisynthetic congeners of taxol has revealed that both an intact taxane ring and an ester linkage for C-13 side chain are required for cytotoxicity.<sup>6</sup> It was also proved by a study of the structure-activity relationship (SRA) of analogues that the presence of a hydroxyl group at C2' atom of the phenylisoserine unit is crucial as it participates in the intermolecular hydrogen bonding at the receptor site.<sup>7</sup> It has been shown that a suitably protected 3-hydroxy- $\beta$ -lactam can serve as a synthetic equivalent for the phenylisoserine.<sup>8</sup> A direct coupling of 7-(triethylsilyl)baaccatin III with a protected 3-hydroxy- $\beta$ -lactam has also been reported.<sup>9</sup> We report herein an efficient synthesis of optically pure (3*R*, 4*S*)-*cis*-3-hydroxy-4-phenyl- $\beta$ -lactam starting from easily accessible, naturally abundant (+)-3-carene.

In the course of our investigation of steric factors controlling relative stereochemistry of  $\beta$ -lactams *via* the Staudinger reaction,<sup>10</sup> we were interested in studying the effect of ketenes derived from naturally occurring (+)-3-carene. We showed that sterically demanding bicyclic as well as tricyclic systems derived from (+)-3-carene<sup>11</sup> and Oppolzer sultam<sup>12</sup> play a major role in controlling the diastereoselectivity of the ketene-imine cycloaddition reaction.<sup>13</sup>

(+)-3-Carene<sup>14</sup> was converted to  $\alpha$ -epoxide **1** using ethoxy percarbonic acid by a known procedure.<sup>15</sup> The epoxide **1** was regio and stereospecifically opened with ethylene glycol using PTSA as catalyst to afford diol **2** in quantitative yield. The diol **2** was oxidized to keto acid **3** using Jones' reagent (Scheme 1).

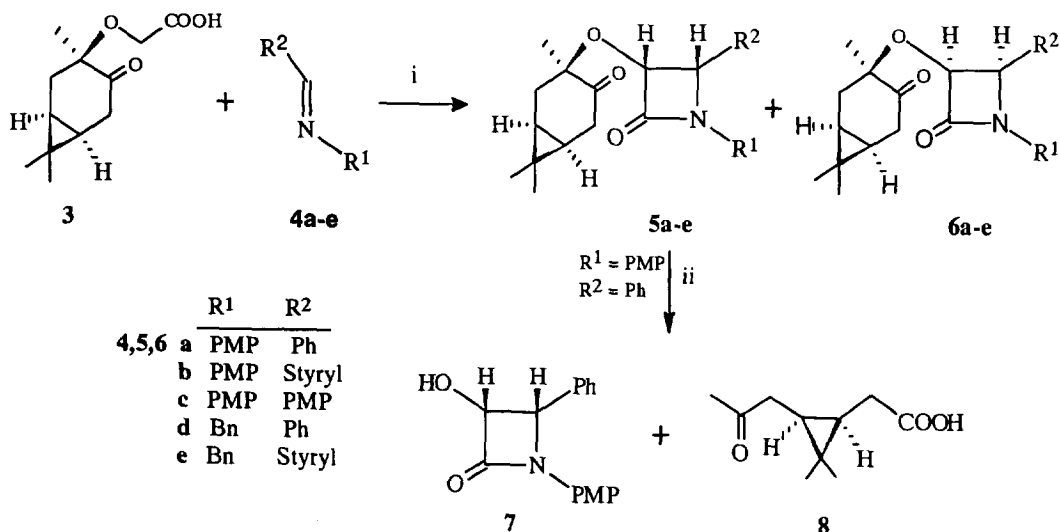
### Scheme 1



*Reagent and conditions:* i) ClCOOEt/Et<sub>3</sub>N/CH<sub>2</sub>Cl<sub>2</sub>/H<sub>2</sub>O<sub>2</sub>, 10-20 °C, 24h; ii) HOCH<sub>2</sub>CH<sub>2</sub>OH/PTSA, rt, 2 h; iii) Jones' reagent/0 °C, 4h.

The imines **4** on cycloaddition (Staudinger reaction) with keto acid **3** in the presence of phenyl dichlorophosphate and excess triethylamine gave a mixtures of only *cis*- $\beta$ -lactams **5a-e** & **6a-e** in very high yield with moderate diastereoselectivity (Scheme 2). The ratio of the two diastereomers was determined in each case from <sup>1</sup>H NMR spectral data and by HPLC analysis of the crude reaction mixture (see Table 1). Several attempts to separate these diastereomers (**5** & **6**) by column chromatography failed. However, the major isomer **5a** (57%) was obtained in optically pure form by single crystallization from benzene-pet. ether. The purity of the diastereomer **5a** was confirmed by HPLC and <sup>1</sup>H NMR spectral analysis.

### Scheme 2



*Reagent and conditions:* i) R<sup>2</sup>CH=NR<sup>1</sup> (**4a-e**)/Et<sub>3</sub>N/CH<sub>2</sub>Cl<sub>2</sub>/PhOP(O)Cl<sub>2</sub>, 0 °C, 15 h; ii) mCPBA/CH<sub>2</sub>Cl<sub>2</sub>, rt, 48 h.

Table 1 Synthesis of *cis*-β-lactams **5a-e** and **6a-e** starting from acid **3** and imines **4a-e**.

Entry No.	Product <b>5</b> & <b>6</b>	R <sub>1</sub>	R <sub>2</sub>	Yield <sup>a</sup> (%)	Ratio <sup>b</sup> of <b>5</b> & <b>6</b>
1.	<b>a</b>	PMP	Ph	74	70 : 30
2.	<b>b</b>	PMP	Styryl	69	53 : 47
3.	<b>c</b>	PMP	PMP	79	56 : 44
4.	<b>d</b>	Bn	Ph	47	61 : 39
5.	<b>e</b>	Bn	Styryl	86	54 : 46

<sup>a</sup> Isolated yields of mixture of diastereomers **5** & **6**. <sup>b</sup> The ratio of diastereomers is determined by <sup>1</sup>H NMR and HPLC analysis.

Baeyer-Villiger oxidation of the pure diastereomer **5a** using *m*-CPBA in CH<sub>2</sub>Cl<sub>2</sub> gave (*3R*, *4S*)-3-hydroxy-4-phenyl-β-lactam (**7**), an important synthon for the taxol side chain,<sup>8</sup> in 72% yield along with the keto acid **8**. The absolute configuration of the β-lactam **7** was confirmed by comparing its optical rotation with the reported values.<sup>3</sup>

The keto acid **8**, resulted from the chiral auxiliary in the same oxidation reaction, is also an intermediate for synthetic pyrethroids.<sup>16</sup>

In summary, we have devised a short and simple route for the synthesis of 3-hydroxy-4-phenyl-β-lactam **7**, a precursor for taxol side chain starting from readily available, optically pure (+)-3-carene.

### Experimental Section

<sup>1</sup>H NMR Spectra were recorded in CDCl<sub>3</sub> solution on a Bruker AC 200 spectrometer at 200 MHz and chemical shifts are reported in ppm downfield from tetramethylsilane. <sup>13</sup>C NMR spectra were recorded in CDCl<sub>3</sub> solution on a Bruker AC 200 and Bruker 300 MHz instruments and chemical shifts are reported in ppm relative to the center line of CDCl<sub>3</sub> (77.0 ppm). Infrared spectra were recorded on a Perkin-Elmer Infracord Spectrophotometer Model 599-B using sodium chloride optics. Melting points were determined on a Thermo-nik Campbell melting point apparatus and were uncorrected. The microanalysis were performed on a Carlo-Erba, CHNS-O EA 1108 Elemental analyzer. Optical rotations were recorded on a JASCO-181 digital polarimeter under standard conditions. Methylene chloride was distilled over P<sub>2</sub>O<sub>5</sub> under argon. Silica gel (SD's, 60 - 120 mesh) was used for column Chromatography.

**Preparation of diol (2).** To the solution of carene epoxide **1** (760 mg, 5 mmol) in ethylene glycol (5 mL), PTSA (20 mg) was added at 0 °C and the reaction mixture was stirred at this temperature for 4 h. After completion of the reaction (by TLC), the reaction mixture was diluted with water (40 mL) and it was extracted with EtOAc (3 x 20 mL). The combined organic extracts was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub> and concentrated in vacuo. The crude product was subsequently column chromatographed (Silica gel, 60 - 120 mesh, pet. ether/EtOAc mixture) to give diol (**2**) in 90% yield. Oil. <sup>1</sup>H NMR (90 MHz) : δ 0.9 (s, 3H, CH<sub>3</sub>); 0.95 (s, 3H, CH<sub>3</sub>); 1.0 (m, 1H, CH<sub>2</sub>); 1.2 (s, 3H, CH<sub>3</sub>); 1.4 - 2.3 (m, 5H, CH<sub>2</sub> and CH); 3.1 (bs, 2H, OH); 3.25 - 3.75 (m, 4H, 2 X CH<sub>2</sub>); IR : 3200 - 3500, 2840, 1200 cm<sup>-1</sup>.

**Preparation of keto-acid (3).** To a solution of diol **2** (535 mg, 2.5 mmol) in acetone (10 mL), Jones' reagent was added drop by drop at 0 °C until decolourization of the reagent was observed. The reaction mixture was stirred for 4 h at r.t. The green precipitate formed was filtered-off and the excess of the reagent was destroyed by adding isopropyl alcohol at 0 °C to avoid the exothermic reaction. The solution was then concentrated under vacuum and extracted with EtOAc (3 x 15 mL). The organic layer was washed with brine, dried over Na<sub>2</sub>SO<sub>4</sub>. It

was then filtered and filtrate on removal of solvent under reduced pressure gave crude product, which was crystallized from EtOAc/pet. ether to give 440 mg (77%) of keto-acid **3** as white crystals, m.p. 104 - 106 °C.  $[\alpha]_D^{27}$ : +20.7 (c 1, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR: δ 0.9 (s, 3H, CH<sub>3</sub>); 1.0 (m, 1H, CH<sub>2</sub>); 1.05 (s, 3H, CH<sub>3</sub>); 1.15 (m, 1H, CH<sub>2</sub>); 1.6 (s, 3H, CH<sub>3</sub>); 1.85 (dd, *J* = 10.0 and 15.0 Hz, 1H, CH<sub>2</sub>); 2.25 (dd, *J* = 10.0 and 15.0 Hz, 1H, CH<sub>2</sub>); 2.50 (d, *J* = 20.0 Hz, 1H, CH); 2.75 (dd, *J* = 10.0 and 20.0 Hz, 1H, CH); 4.1 (q, *J* = 10.0 Hz, 2H, CH<sub>2</sub>); 7.7 (bs, 1H, COOH). Anal. Calcd for C<sub>12</sub>H<sub>18</sub>O<sub>4</sub>: C, 63.68; H, 8.12; Found: C, 63.57; H, 8.08.

**General procedure for the preparation of β-lactams 5a-e & 6a-e.** To a stirred mixture of the acid **3** (229 mg, 1.0 mmol), imine (1.1 mmol), triethylamine (3 mmol) and dry CH<sub>2</sub>Cl<sub>2</sub> (15 mL), a solution of phenyl dichlorophosphate (210 mg, 1.0 mmol) in dry CH<sub>2</sub>Cl<sub>2</sub> (20 mL) was added drop by drop at 0 °C. The reaction mixture was allowed to warm-up to r.t. and stirred further for 15 h. It was then successively washed with water (30 mL), satd. sodium bicarbonate solution (20 mL), brine (30 mL) and dried over Na<sub>2</sub>SO<sub>4</sub>. It was then filtered and filtrate on removal of solvent under vacuum gave crude product, which was column chromatographed (Silica gel, 60 - 120, Pet. Ether/acetone) to give diastereomeric mixture of β-lactams **5a-e** and **6a-e**. The diastereomeric ratio was determined by <sup>1</sup>H NMR and HPLC analysis.

**(3R,4S,1'S,6'R) and (3S,4R,1'R,6'S) 1-(p-Anisyl)-4-phenyl-3-[3',7',7'-trimethylbicyclo(4.1.0)-hept-4'-oxo-3'-yloxy]-azetidin-2-one (5a & 6a).** M. p. 192 - 194 °C.  $[\alpha]_D^{25}$ : -23.20 (c 1, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR: δ 0.7 and 0.9 (s, 3H, CH<sub>3</sub>); 0.75 (m, 1H, CH<sub>2</sub>); 1.0 and 1.05 (s, 3H, CH<sub>3</sub>); 1.10 (m, 1H, CH<sub>2</sub>); 1.2 and 1.5 (s, 3H, CH<sub>3</sub>); 1.65 - 1.8 (m, 2H, CH<sub>2</sub>); 2.0 (m, 3H); 2.4 (dd, *J* = 10.0 and 20.0 Hz, 2H, CH<sub>2</sub>); 2.65 (dd, *J* = 10.0 and 20.0 Hz, 1H, CH); 3.75 (s, total 3H, OCH<sub>3</sub>); 5.05 (d, *J* = 5.0 Hz, 1H, CH); 5.2 (t, total 1H, CH); 5.3 (d, *J* = 5.0 Hz, 1H, CH); 6.8 (d, *J* = 10.0 Hz, total 2H, Ar.); 7.3 - 7.5 (m, total 7H, Ar.). <sup>13</sup>C NMR (300 MHz): 14.2, 14.9, 18.3, 19.6, 19.7, 21.0, 21.7, 22.7, 27.6, 32.9, 33.5, 35.6, 36.0, 55.3, 63.0, 63.2, 78.9, 79.2, 81.0, 118.7, 127.9, 128.4, 128.7, 130.9, 134.3, 156.1, 165.2, 165.3, 212.3, 212.5. IR: 2940, 1740, 1730, 1520 cm<sup>-1</sup>. Anal. Calcd for C<sub>26</sub>H<sub>29</sub>NO<sub>4</sub>: C, 74.5; H, 6.9; N, 3.4. Found: C, 75.0; H, 7.2; N, 3.1.

**(3R,4S,1'S,6'R) 1-(p-Anisyl)-4-(phenyl)-3-[3',7',7'-trimethylbicyclo(4.1.0)-hept-4'-oxo-3'-yloxy]-azetidin-2-one (5a).** Isolated from above diastereomeric mixture of **5a** and **6a** by crystallization from pet. ether - benzene in 57 % yield, m. p. 214 °C.  $[\alpha]_D^{25}$ : +44.6 (c 1, CHCl<sub>3</sub>). <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ 0.7 (s, 3H); 1.0 (s, 3H); 1.2 (d, 2H); 1.5 (s, 3H); 1.65-1.75 (m, 2H); 2.0 (dd, 1H, *J* = 5.0 and 15.0 Hz); 2.4 (dd, 1H, *J* = 7.5 and 17.5 Hz); 3.75 (s, 3H); 5.2 (d, 1H, *J* = 5.0 Hz); 5.3 (d, 1H, *J* = 5.0 Hz); 6.75 (d, 2H, *J* = 10.0 Hz); 7.3 (m, 7H); IR: 1740 cm<sup>-1</sup>; Anal. Calcd for C<sub>26</sub>H<sub>29</sub>NO<sub>4</sub>: C, 74.5, H, 6.9, N, 3.3. Found: C, 74.1, H, 6.5, N, 3.0.

**(3R,4S,1'S,6'R) and (3S,4R,1'R,6'S) 1-(p-Anisyl)-4-(styryl)-3-[3',7',7'-trimethylbicyclo(4.1.0)-hept-4'-oxo-3'-yloxy]-azetidin-2-one (5b & 6b).** M. p. 184 - 185 °C.  $[\alpha]_D^{25}$ : -3.0 (c 1, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR: δ 0.8 and 0.9 (s, 3H, CH<sub>3</sub>); 1.0 and 1.05 (s, 3H, CH<sub>3</sub>); 1.5 and 1.65 (s, 3H, CH<sub>3</sub>); 1.8 and 2.0 (m, 2H, CH<sub>2</sub>); 2.3 (m, 3H); 2.5 (m, 2H, CH and CH<sub>2</sub>); 2.75 (dd, *J* = 10 and 20 Hz, 1H, CH); 3.75 (s, total 3H, OCH<sub>3</sub>); 4.85 (m, total 1H, C4H); 4.95 and 5.15 (d, *J* = 5.0 Hz, total 1H, C3H); 6.3 (m, 2H, CH); 6.75 - 6.90 (m, *J* = 10.0 Hz, total 2H, Ar.); 7.25 - 7.40 (m, total 7H, Ar.). <sup>13</sup>C NMR: 14.7, 15.2, 18.8, 19.2, 19.9, 21.5, 21.9, 23.1, 27.8, 32.9, 33.9, 35.0, 36.2, 55.5, 61.9, 62.0, 79.7, 80.1, 114.4, 118.8, 124.9, 126.8, 128.1, 128.7, 131.5, 135.6, 136.6, 156.3, 165.2, 219.0. IR: 1740, 1730, 1520 cm<sup>-1</sup>. Anal. Calcd for C<sub>28</sub>H<sub>31</sub>NO<sub>4</sub>: C, 75.5; H, 6.9; N, 3.1. Found: C, 75.9; H, 7.3; N, 2.9.

**(3R,4S,1'S,6'R) and (3S,4R,1'R,6'S) 1,4-Di(p-anisyl)-[3',7',7'-trimethylbicyclo(4.1.0)-hept-4'-oxo-3'-yloxy]-azetidin-2-one. (5c & 6c).** M. p. 158 - 161 °C.  $[\alpha]_D^{25}$ : -17.50 (c 0.6, CH<sub>2</sub>Cl<sub>2</sub>). <sup>1</sup>H NMR: δ 0.65 (s, 3H, CH<sub>3</sub>); 0.8 (m, 1H, CH<sub>2</sub>); 0.9, 1.0 and 1.05 (s, 3H, CH<sub>3</sub>); 1.10 (m, 1H, CH<sub>2</sub>); 1.2 and 1.5 (s, 3H, CH<sub>3</sub>); 1.7 - 2.2 (m, 5H, CH<sub>2</sub> and CH); 2.4 (m, 2H, CH<sub>2</sub> and CH); 2.65 (dd, *J* = 10 and 20 Hz, 1H, CH); 3.75, 3.80 and 3.85 (s, total 3H, CH<sub>3</sub>); 5.0 (d, *J* = 5.0 Hz, 1H, CH); 5.15 (dd, *J* = 5.0 Hz, total 1H, CH); 5.25 (d, *J* = 5.0 Hz, 1H, CH); 6.7 - 6.95 (m, total 4H, Ar.); 7.2 - 7.45 (m, total 4H, Ar.). <sup>13</sup>C NMR: 14.4, 15.1, 18.5, 19.1, 19.8, 20.9, 21.2, 22.7, 27.7, 33.1,

35.8, 36.2, 55.3, 55.5, 62.9, 79.3, 79.9, 81.1, 113.5, 114.4, 118.9, 129.9, 130.2, 131.2, 156.2, 159.6, 167.6, 189.4, 212.5. IR. 2940, 1740, 1730, 1520  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{27}\text{H}_{31}\text{NO}_5$ : C, 72.2; H, 6.9; N, 3.1. Found: C, 71.9; H, 7.2; N, 3.0.

(3*R*,4*S*,1'*S*,6'*R*) and (3*S*,4*R*,1'*R*,6'*S*) 1-(Benzyl)-4-(phenyl)-3-[3',7',7'-trimethylbicyclo(4.1.0)-hept-4'-oxo-3'-yloxy]-azetidin-2-one. (5d & 6d). M. p. 172 - 174 °C.  $[\alpha]_{\text{D}}^{25}$ : -22.9 (c 1,  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H NMR}$ :  $\delta$  0.65 (s, 3H,  $\text{CH}_3$ ); 0.7 (m, 1H); 0.85, 0.95, 1.0 and 1.1 (s, 3H,  $\text{CH}_3$ ); 1.2 (m, 1H,  $\text{CH}_2$ ); 1.45 (s, 3H,  $\text{CH}_3$ ); 1.6 (dd, 1H,  $J = 5.0$  and 17.0 Hz,  $\text{CH}_2$ ); 1.85 (m, 5H,  $\text{CH}_2$ ); 2.25 (m, 2H,  $\text{CH}_2$  and CH); 2.6 (dd, 1H,  $J = 10.0$  and 20.0 Hz, CH); 3.8 and 4.8 (dd, total 2H,  $J = 15.0$  and 200 Hz, Benzylic  $\text{CH}_2$ ); 4.55 (d, total 1H,  $J = 5.0$  Hz, CH); 5.0 and 5.15 (d, 1H,  $J = 5.0$  Hz, CH); 7.1 - 7.45 (m, total 10H, Ar.).  $^{13}\text{C NMR}$ : 14.2, 14.9, 18.3, 19.0, 19.6, 20.9, 21.7, 22.7, 27.6, 32.9, 33.5, 35.6, 36.1, 55.3, 63.1, 63.2, 79.2, 79.5, 81.1, 114.3, 118.7, 118.9, 127.8, 127.9, 128.4, 128.8, 130.9, 134.4, 156.1, 165.4, 212.4, 212.6. IR. 1740, 1730, 1520.  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{26}\text{H}_{29}\text{NO}_5$ : C, 77.4; H, 7.2; N, 3.4. Found: C, 77.9; H, 7.3; N, 3.1.

(3*R*,4*S*,1'*S*,6'*R*) and (3*S*,4*R*,1'*R*,6'*S*) 1-(Benzyl)-4-(styryl)-3-[3',7',7'-trimethylbicyclo(4.1.0)-hept-4'-oxo-3'-yloxy]-azetidin-2-one. (5e & 6e). M. p. 82 - 84 °C.  $[\alpha]_{\text{D}}^{25}$ : -15.7 (c 1,  $\text{CH}_2\text{Cl}_2$ ).  $^1\text{H NMR}$ :  $\delta$  0.8 (s, 3H,  $\text{CH}_3$ ); 0.85 (m, 1H,  $\text{CH}_2$ ); 0.9, 1.0, 1.05 (s, 3H,  $\text{CH}_3$ ); 1.25 (m, 1H,  $\text{CH}_2$ ); 1.5 and 1.6 (s, 3H,  $\text{CH}_3$ ); 1.95 (m, 1H); 2.25 (m, 5H,  $\text{CH}_2$  and CH); 2.6 (m, 2H); 4.0 and 4.7 (dd,  $J = 15$  and 125 Hz, total 2H, benzylic  $\text{CH}_2$ ); 4.25 (m, total 1H, CH); 4.85 and 5.05 (d,  $J = 5.0$  Hz, 1H, CH); 6.2 (m, 1H, styryl-CH); 6.55 (dd,  $J = 5.0$  and 15.0 Hz, 1H, styryl-CH); 7.1 - 7.55 (m, total 10H, Ar.).  $^{13}\text{C NMR}$ : 14.7, 15.1, 18.8, 19.2, 19.9, 21.3, 22.0, 22.9, 27.8, 33.1, 33.6, 36.0, 36.2, 44.2, 61.3, 61.5, 79.9, 80.1, 80.4, 124.9, 126.7, 127.7, 128.0, 128.2, 128.6, 128.7, 128.8, 129.0, 135.7, 135.8, 136.6, 167.9, 212.7. IR. 2920, 1750, 1730.  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{28}\text{H}_{31}\text{NO}_5$ : C, 78.3; H, 7.2; N, 3.2. Found: C, 78.7; H, 7.4; N, 2.9.

**Preparation of (3*R*, 4*S*)-3-hydroxy-4-phenyl- $\beta$ -lactam (7).** To a solution of  $\beta$ -lactam 5a (221 mg, 0.5 mmol) in  $\text{CH}_2\text{Cl}_2$  (10 mL), solid *m*-chloroperbenzoic acid (172 mg, 1 mmol) was added and the reaction mixture was stirred at room temperature for 48 h. The reaction mixture was diluted with  $\text{CH}_2\text{Cl}_2$  (15 mL) and washed successively with water (15 mL), satd.  $\text{NaHCO}_3$  (2 X 15 mL), water (15 mL) and finally with brine (15 mL). The  $\text{CH}_2\text{Cl}_2$  solution was dried over anhyd  $\text{Na}_2\text{SO}_4$  and filtered. The filtrate on removal of solvent by distillation under reduced pressure gave the crude product, which on purification by crystallization offered 96.4 mg (72%) of pure (3*R*, 4*S*)-3-hydroxy-4-phenyl- $\beta$ -lactam (7). m.p: 198-201 °C.  $[\alpha]_{\text{D}}^{25}$ : +176 (c 1,  $\text{CHCl}_3$ ) [Lit.<sup>3</sup> for antipode  $[\alpha]_{\text{D}}^{25}$ : -179 (c 1,  $\text{CHCl}_3$ )].  $^1\text{H NMR}$ :  $\delta$  2.0 - 2.3 (bs, 1H, OH); 3.8 (s, 3H,  $\text{CH}_3$ ); 5.2 (d,  $J = 5.0$  Hz, 1H, C4H); 5.3 (d,  $J = 5.0$  Hz, 1H, C3H); 6.85 (d,  $J = 10.0$  Hz, 2H, Ar.); 7.22 - 7.55 (m, 7H, Ar.).  $^{13}\text{C NMR}$ : 55.0, 61.9, 76.1, 114.0, 118.4, 127.1, 128.4, 128.6, 156.1, 166.1. IR. 3200 - 3500, 2840, 1740,  $\text{cm}^{-1}$ . Anal. Calcd for  $\text{C}_{16}\text{H}_{15}\text{NO}_3$ : C, 71.4; H, 5.6; N, 5.2. Found: C, 71.9; H, 5.9; N, 4.9.

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