

## FACIAL SELECTIVITY IN NUCLEOPHILIC EPOXIDATION OF 3-ARYL-2- PHOSPHONOACRYLATES INDUCED BY THE (-)-8-PHENYLMENTHYL MOIETY AS A CHIRAL AUXILIARY

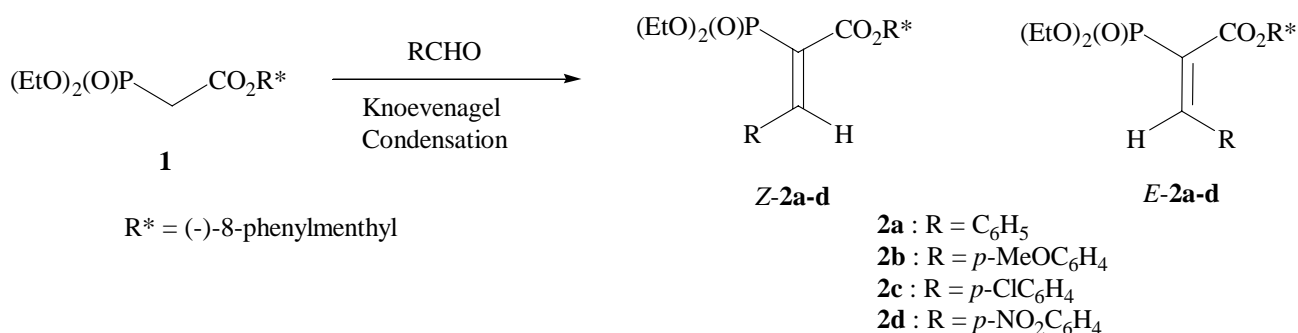
Shahnaz Begum, Md. Moshfiqur Rahman, Ryukichi Takagi, and Katsuo Ohkata\*

Department of Chemistry, Graduate School of Science, Hiroshima University,  
1-3-1 Kagamiyama, Higashi-Hiroshima, 739-8526, Japan

**Abstract** – Stereoselectivity was investigated in the epoxidation of (-)-8-phenylmenthyl *E*-3-aryl-2-phosphonoacrylates (**2a-d**) with hydrogen peroxide and potassium carbonate to give the corresponding epoxides (**3a-d**). The reaction of the *E*-isomers gave the corresponding *trans*-epoxy derivatives with the moderately higher diastereoselectivity as the major diastereomers as compared with that of the *cis* isomers.

### INTRODUCTION

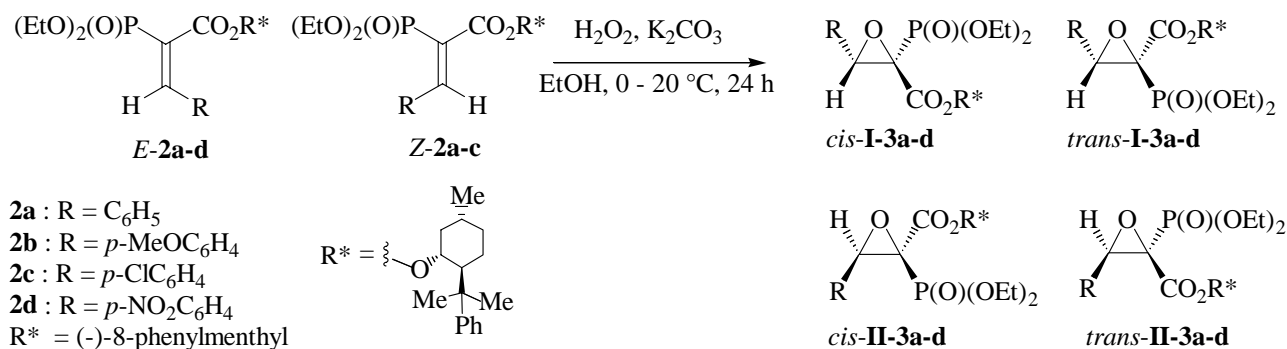
Many phosphonate derivatives have been applied in the field of agricultural chemistry, owing to the common nature of their biological activity.<sup>1</sup> Epoxides and phosphonates are widely used as a functional group of compounds and have very versatile synthetic approaches in organic chemistry.<sup>2,3</sup> Recently, we have investigated the asymmetric induction in the formation of three-membered ring compounds by means of the (-)-8-phenylmenthyl moiety as a chiral auxiliary in some of our most recent<sup>4a</sup> and previous work.<sup>4</sup> In the cyclopropanation of *E*-3-aryl-2-phosphonoacrylates (**2a-d**) with sulfonium ylide using the chiral auxiliary, considerably high diastereoselectivity (86% de) for the *trans* product was observed. The high diastereoselectivity was understandable in terms of the face-to-face interaction between the acrylate moiety and the phenyl ring of the chiral auxiliary in the *s-cis* conformer.<sup>4a</sup> In this paper, we discuss the stereoselectivity in the epoxidation of *E*- and *Z*-3-aryl-2-phosphonoacrylates containing the (-)-8-phenylmenthyl moiety as a chiral auxiliary. *E*- and *Z*-3-aryl-2-phosphonoacrylates (**2a-d**) were prepared from (-)-8-phenylmenthyl diethylphosphonoacetate (**1**) and the corresponding aryl aldehydes with high geometric selectivity by two separate methods which both utilize the titanium-mediated Knoevenagel condensation (Scheme 1).<sup>4a,5</sup>



**Scheme 1**

## RESULTS AND DISCUSSION

In order to inquire the reactivity-selectivity features in the formation of small-ring compounds (**3a-d**),<sup>4a</sup> epoxidation of **2a-d** with hydrogen peroxide and potassium carbonate<sup>6</sup> was carried out. The reactions afforded the four diastereomers of **3a-d**, which were separated by HPLC, respectively. The relative configuration of the diastereomers was assigned by the coupling constant (<sup>2</sup>J<sub>HP</sub>) between the C3-H of the epoxy group and phosphorus in the <sup>1</sup>H NMR spectra.<sup>7</sup> Of the two *cis*- and *trans*-isomers, the one with a lower field proton signal for the epoxide hydrogen in their NMR spectrum, was arbitrarily designed **I** and the other **II**. Judging from the stereochemical assignments in the cyclopropanation of **2a-d** by sulfonium ylide,<sup>4a</sup> the assignments of each configuration of the epoxides (**3a-d**) are assumed as depicted in Scheme 2.



**Scheme 2**

Table 1 shows the results of the epoxidation reaction of **2a-d** with hydrogen peroxide and potassium carbonate. The epoxidation reaction of *E*-**2a-d** at 0-20 °C preferentially afforded the *trans* isomers (*trans/cis* = 3.4-5.5, Entries 1-4), while the reaction of *Z*-**2a-c** gave a 1 : 1 mixture of the *cis*- and *trans*-products (**3a-c**) (Entries 5-7). The diastereoselective ratio in the epoxidation of *E*-**2a-d** was fair to moderate (1.8-2.8 dr) for the *trans*-**2a-d** but was very low (0.8-1.3 dr) for the *cis*-**3a-d**. The diastereoselective ratio of the epoxidation of *Z*-**2a-c** was moderate (2.2-2.8 dr) for the *cis*-**3a-c** and the ratio for the *trans*-**3a-c** was 1.6-2.5 dr. The whole mechanistic scheme for the two reactions can be outlined as shown in Scheme 3. In the epoxidation using H<sub>2</sub>O<sub>2</sub>/K<sub>2</sub>CO<sub>3</sub>, the reaction with rotation of the *E*-2-phosphonoacrylates (*E*-**2a-d**) preferentially gives rise to intermediates (**A**) via *Re* face attack (front

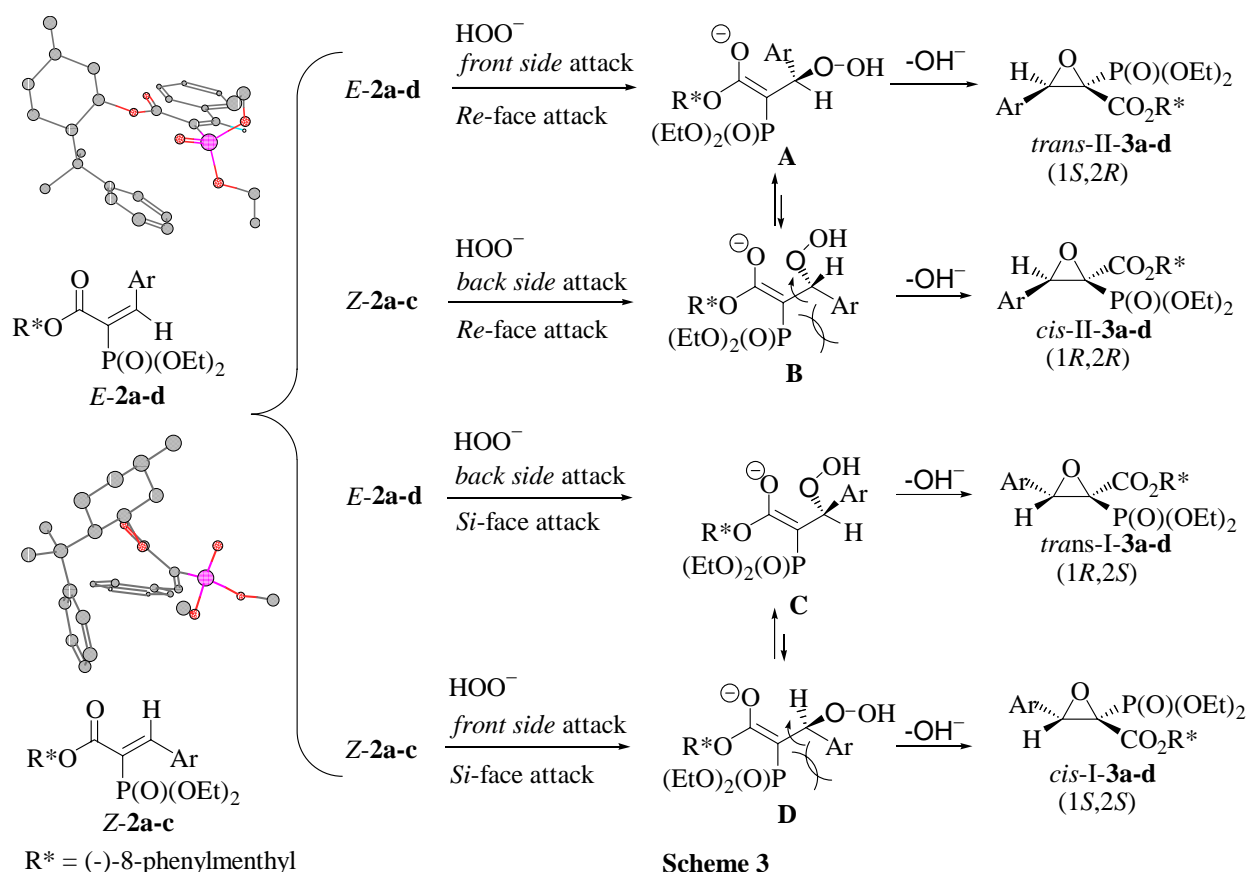
**Table 1.** The epoxidation of **2a-d** with basic hydrogen peroxide<sup>a</sup>

Entry	Subst.	Product	Yield (%)	Product ratio <sup>b</sup>				<i>trans/cis</i> <sup>c</sup>	Stereoselectivity <sup>d,e</sup>		
				<i>cis-I</i>	<i>cis-II</i>	<i>trans-I</i>	<i>trans-II</i>		<i>II/I</i> <sup>d</sup>	<i>cis</i>	<i>trans</i>
1	<i>E-2a</i> <sup>f</sup>	<b>3a</b>	81	1.0	: 1.2	: 2.0	: 5.4	3.4	2.2	1.2	2.7
2	<i>E-2b</i> <sup>f</sup>	<b>3b</b>	87	1.0	: 1.3	: 3.3	: 9.3	5.5	2.5	1.3	2.8
3	<i>E-2c</i>	<b>3c</b>	79	1.0	: 1.0	: 2.5	: 5.0	3.8	1.7	1.0	2.0
4	<i>E-2d</i>	<b>3d</b>	71	1.0	: 0.75	: 2.5	: 4.5	4.0	1.5	0.8	1.8
5	<i>Z-2a</i>	<b>3a</b>	80	1.0	: 2.5	: 0.91	: 2.3	0.9	0.4	2.5	2.5
6	<i>Z-2b</i>	<b>3b</b>	82	1.0	: 2.8	: 1.3	: 2.1	0.9	0.45	2.8	1.6
7	<i>Z-2c</i>	<b>3c</b>	85	1.0	: 2.2	: 0.77	: 1.5	0.7	0.48	2.2	1.9

<sup>a</sup> Reagents: H<sub>2</sub>O<sub>2</sub> (excess), K<sub>2</sub>CO<sub>3</sub> (10-12 eq), 95% EtOH (solvent). <sup>b</sup> The ratios of the products were determined by the integral values of <sup>1</sup>H NMR. <sup>c</sup> *cis-trans* selective ratio (*trans/cis*): (*trans-I* + *trans-II*) / (*cis-I* + *cis-II*). <sup>d</sup> facial selective ratio of attack from front side and back side in *s-cis* conformer: (*trans-II* + *cis-II*) / (*trans-I* + *cis-I*) for the *E*-series (*E-I*); (*trans-I* + *cis-I*) / (*trans-II* + *cis-II*) for the *Z*-series (*Z-I*). <sup>e</sup> diastereoselective ratio (dr): *cis-II* / *cis-I* for the *cis* product, *trans-II* / *trans-I* for the *trans* product. <sup>f</sup> contained 10% *Z*-isomer.

side attack). Ring closure directly from this conformation gives rise to products *trans-II-3a-d*. Upon C–C single bond (the original acrylic alkene double bond) rotation in intermediates (**A**) and subsequent ring closure at intermediate (**B**), *cis-II-3a-d* are formed. The fact that the ratio between *trans-II* and *cis-II* was only 1.5-2.5 indicates that the ring closing process is rather slow and allows ample time for conformational change to occur.

The facial selectivity in regards with facial attack to the acrylate moiety of *ca.* 1.5-2.5 ((*trans-II+cis-II*):(*trans-I+cis-I*)) probably reflects the reactivity of the two conformers (*s-cis* and



*s-trans*) or the front side and back side attack in the favorable *s-cis* conformer of *E-2a-d*. The fact that the ratios of *trans-II/cis-II* and *trans-I/cis-I* differ between the series of *E-2a-d* and *Z-2a-d* indicates that the elimination of hydroxide anion occurred before the equilibrium of intermediates is not complete. The facial selectivity (the ratio of **II/I**) in the *E*-series was decreased from 2.5 to 1.5 by electron-withdrawing group at the benzene ring. Calculations at the AM1 level on *E-2a* gave rise to two stable conformations that correspond to the *s-cis* and *s-trans* conformers. Between these two, the *s-cis* conformer was found to be more favorable than the *s-trans* one by 3.1 kcal mol<sup>-1</sup>.<sup>4a</sup> In the structural optimization of *Z-2a*, calculations showed a stable conformer in which the dihedral angle of the acrylate moiety is twisted to approximately 90°, in order to avoid unfavorable allylic interactions between the carbonyl oxygen and the 2-substituents. According to the conformational features of *E*- and *Z-2a*, the difference of facial selectivity in the epoxidation reactions could be understandable partially in terms of  $\pi$ - $\pi$  interaction between the phenyl ring of the chiral auxiliary and the acrylate moiety (Scheme 3).<sup>8</sup>

## EXPERIMENTAL

All reactions were carried out under N<sub>2</sub>. THF and Et<sub>2</sub>O were distilled after refluxing over Na/benzophenone prior to use. CH<sub>2</sub>Cl<sub>2</sub>, CCl<sub>4</sub> and DMSO were distilled over CaH<sub>2</sub> before use. NaH was used after washing with dry hexane. Silica gel 60F<sub>254</sub> was used for preparative thin layer chromatography. NMR spectra were recorded on a JEOL GSX-270 or a JEOL JNM-LA500 instrument. <sup>1</sup>H NMR spectra were observed in CDCl<sub>3</sub> solutions with TMS as the internal reference. <sup>13</sup>C NMR spectra were observed in CDCl<sub>3</sub> solutions with TMS as the internal reference. <sup>31</sup>P NMR spectra were observed in CDCl<sub>3</sub> solutions with 85% H<sub>3</sub>PO<sub>4</sub> as the external reference. MS spectra were recorded on a JEOL SX-102A instrument. FAB spectra were measured by using glycerol as the matrix, EI data were obtained by using 70 eV electrons.

### **(*E*)-(-)-8-Phenylmenthyl 2-(diethylphosphono)-3-phenylacrylate (*E-2a*)<sup>4a</sup>**

Titanium (IV) tetrachloride (0.06 mL, 0.55 mmol) in CCl<sub>4</sub> (1.0 mL) was added dropwise to THF (2.0 mL) at 0 °C. The yellow titanium-THF complex was produced. To this solution was added benzaldehyde (0.03 mL, 0.30 mmol) and (-)-8-phenylmenthyl diethylphosphonoacetate (**1**)<sup>9</sup> (101 mg, 0.25 mmol) in THF (2.0 mL) at 0 °C. After 10 min, *N*-methylmorpholine (0.27 mL, 2.46 mmol) was added to the solution and the reaction mixture was stirred for 3 h at 0 °C. The resulting mixture was diluted with Et<sub>2</sub>O (10 mL) and quenched with 1.0 M aqueous HCl (15 mL). The organic layer was extracted with Et<sub>2</sub>O (3 x 20 mL). The combined organic layers were washed with H<sub>2</sub>O (2 x 20 mL), brine (2 x 20 mL), dried over anhydrous MgSO<sub>4</sub>, and concentrated under reduced pressure. The residue was purified by preparative TLC (CHCl<sub>3</sub> : petroleum ether = 10 : 1, 4 times) to produce *E*- and *Z-2a*

[108 mg, 87%, *E* / *Z* = 96 / 4 (determined by <sup>1</sup>H NMR of crude product)] as a viscous colorless oil, respectively; [ $\alpha$ ]<sub>D</sub><sup>25</sup> +3.1° (*c* 0.89, CHCl<sub>3</sub>);  $\delta_{\text{H}}$  (500 MHz, CDCl<sub>3</sub>) 0.66-1.54 (6H, m), 0.86 (3H, d, *J*=6.4 Hz, CH<sub>3</sub>), 1.15 (3H, s, CH<sub>3</sub>), 1.17 (3H, s, CH<sub>3</sub>), 1.37 (6H, td, *J*=7.1, 8.9 Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 1.76-1.83 (1H, m), 2.08-2.14 (1H, m), 3.94-4.26 (4H, m, -OCH<sub>2</sub>CH<sub>3</sub>), 4.89 (1H, td, *J*=3.9, 10.7 Hz, -OCH), 7.05-7.21 (5H, m), 7.32-7.42 (3H, m), 7.47-7.51 (2H, m), 7.64 (1H, d, *J*=24.7 Hz, C <sub>$\beta$</sub> H);  $\delta_{\text{C}}$  (125 MHz, CDCl<sub>3</sub>) 16.2 (d, <sup>3</sup>*J*<sub>CP</sub>=2.9 Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 16.3 (d, <sup>3</sup>*J*<sub>CP</sub>=2.9 Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 21.7, 23.9, 27.3, 29.0, 31.3, 34.4, 40.0, 40.7, 50.6, 62.5 (d, <sup>2</sup>*J*<sub>CP</sub>=4.8 Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 62.5 (d, <sup>2</sup>*J*<sub>CP</sub>=4.8 Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 77.5 (-OCH), 125.1, 125.2 (d, <sup>1</sup>*J*<sub>CP</sub>=178.5 Hz, C <sub>$\alpha$</sub> ), 125.5 (x2), 127.9 (x2), 128.4 (x2), 129.5 (x2), 130.2, 134.0 (d, <sup>3</sup>*J*<sub>CP</sub>=21.1 Hz, C(*ipso*)), 148.4 (d, <sup>2</sup>*J*<sub>CP</sub>=6.7 Hz, C <sub>$\beta$</sub> ), 150.6, 165.6 (d, <sup>2</sup>*J*<sub>CP</sub>=12.5 Hz);  $\delta_{\text{P}}$  (202 MHz, CDCl<sub>3</sub>) 16.5.

#### **(*Z*)-(-)-8-Phenylmenthyl 2-(diethylphosphono)-3-phenylacrylate (*Z*-2a)<sup>4a</sup>**

To a solution of (-)-8-phenylmenthyl diethylphosphonoacetate (**1**)<sup>9</sup> (100 mg, 0.25 mmol) in THF (4.0 mL) at -78 °C were added chlorotitanium triisopropoxide (0.12 mL, 0.50 mmol) and benzaldehyde (0.03 mL, 0.30 mmol), and then the mixture was treated with Et<sub>3</sub>N (0.34 mL, 2.44 mmol) at -78 °C. The amine hydrochloride precipitated from in the solution. The solution containing precipitates of the amine hydrochloride was allowed to warm slowly to rt over a period of 10 h. The resulting mixture was diluted with Et<sub>2</sub>O (10 mL) and quenched with 1.0 M aqueous HCl (15 mL). The organic layer was extracted with Et<sub>2</sub>O (3 x 20 mL). The combined organic layers were washed with H<sub>2</sub>O (2 x 20 mL) and brine (2 x 20 mL), and then dried over anhydrous MgSO<sub>4</sub>. Removal of solvent left a residue, which was purified by preparative TLC (CHCl<sub>3</sub> : petroleum ether = 10 : 1, 4 times) to produce of *E*- and *Z*-**2a** [72 mg, 94%, *E* / *Z* = 6 / 94 (determined by <sup>1</sup>H NMR of crude product)] as a viscous colorless oil, respectively;  $\delta_{\text{H}}$  (500 MHz, CDCl<sub>3</sub>) 0.84-1.20 (3H, m), 0.89 (3H, d, *J*=6.7 Hz, -OCHCH<sub>3</sub>), 1.08 (6H, dt, *J*=7.0, 11.9 Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 1.23 (3H, s, CH<sub>3</sub>), 1.35 (3H, s, CH<sub>3</sub>), 1.46-1.56 (1H, m), 1.64-1.71 (1H, m), 1.73-1.80 (1H, m), 1.93-2.00 (1 H, m), 2.11-2.20 (1H, m), 3.88-4.07 (4H, m, -OCH<sub>2</sub>CH<sub>3</sub>), 5.01 (1H, td, *J*=4.3, 10.7 Hz, -OCH), 6.89-6.94 (1H, m), 7.16-7.32 (5H, m), 7.33-7.37 (3H, m), 7.42-7.47 (2H, m);  $\delta_{\text{C}}$  (125 MHz, CDCl<sub>3</sub>) 15.9 (d, <sup>3</sup>*J*<sub>CP</sub>=4.7 Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 16.0 (d, <sup>3</sup>*J*<sub>CP</sub>=4.7 Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 21.7, 24.7, 26.6, 28.3, 31.3, 34.5, 39.6, 41.6, 50.4, 62.3 (d, <sup>2</sup>*J*<sub>CP</sub>=5.8 Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 62.4 (d, <sup>2</sup>*J*<sub>CP</sub>=5.8 Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 75.7 (-OCH), 124.7 (d, <sup>1</sup>*J*<sub>CP</sub>=209.0 Hz, C <sub>$\alpha$</sub> ), 125.1, 125.4 (x2), 127.6 (x2), 128.0 (x2), 129.7, 130.0 (x2), 134.3 (d, <sup>3</sup>*J*<sub>CP</sub>=6.7 Hz, C(*ipso*)), 151.4, 153.2 (d, <sup>2</sup>*J*<sub>CP</sub>=3.8 Hz, C <sub>$\beta$</sub> ), 164.9 (d, <sup>2</sup>*J*<sub>CP</sub>=16.3 Hz);  $\delta_{\text{P}}$  (202 MHz, CDCl<sub>3</sub>) 12.1.

#### **General procedure for preparation of epoxide from the acrylates**

To a stirred solution of 3-phenyl-2-phosphonoacrylates (**2**) (52.6 mg, 0.168 mmol) and 30% aq. H<sub>2</sub>O<sub>2</sub> (0.5 mL) in 95% ethanol (5 mL), K<sub>2</sub>CO<sub>3</sub> (1.0 g, 7.23 mmol) was added at 0°C. The resulting mixture was stirred at 15-20 °C for 24 h. TLC examination showed a single UV active spot of the epoxidation product. The reaction mixture was quenched with H<sub>2</sub>O to dissolve the excess of K<sub>2</sub>CO<sub>3</sub> and then extracted with

CH<sub>2</sub>Cl<sub>2</sub> (3 x 15 mL). The combined organic layers were washed with sat.-aqueous solution of sodium thiosulfate pentahydrate to remove the excess H<sub>2</sub>O<sub>2</sub> and then dried over anhydrous MgSO<sub>4</sub>. Evaporation of the solvent gave a pale yellow oily crude product, which was then purified by preparative TLC (hexane : EtOAc, 3: 1) and obtained 81% of the product. The following compounds were prepared and separated by using the same procedure.

*trans*-**I-3a**: colorless oil,  $[\alpha]_D^{25}$  -23.4° (c 0.31, CHCl<sub>3</sub>),  $\delta_H$  (500 MHz, CDCl<sub>3</sub>): 0.22-0.31 (1H, q,  $J$ =12.4 Hz), 0.45-0.60 (1H, m), 0.57 (3H, d,  $J$ =6.6 Hz, CH<sub>3</sub>), 0.66-0.85 (2H, m), 1.05-1.35 (3H, m), 1.24 (3H, s, CH<sub>3</sub>), 1.37 (3H, s, CH<sub>3</sub>), 1.42 (3H, t,  $J$ =7.1 Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 1.44 (3H, t,  $J$ =7.1 Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 1.66-1.73 (1H, m), 4.27-4.35 (4H, m, -OCH<sub>2</sub>CH<sub>3</sub>), 4.56 (1H, d,  $J$ =4.6 Hz, C3-H), 4.72 (1H, td,  $J$ =4.6, 10.5 Hz, -OCH), 7.13-7.42 (10H, m, Ar-H);  $\delta_C$  (125 MHz, CDCl<sub>3</sub>): 16.4 (d,  $^3J_{cp}$ =4.8 Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 16.5 (d,  $^3J_{cp}$ =4.8 Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 21.4, 22.4, 27.4, 31.0, 31.5, 34.0, 40.5, 40.6, 50.2, 60.6 (d,  $^2J_{cp}$ =1.9 Hz, C3), 61.0 (d,  $^1J_{cp}$ =188.1 Hz, C2), 63.7 (d,  $^2J_{cp}$ =5.8 Hz, OCH<sub>2</sub>CH<sub>3</sub>), 63.9 (d,  $^2J_{cp}$ =5.8 Hz, OCH<sub>2</sub>CH<sub>3</sub>), 77.9 (OCH), 125.4, 125.9 (x2), 126.7 (x2), 127.9 (x2), 128.3 (x2), 129.0, 131.8, 149.8 (*ipso*), 163.6 (d,  $^2J_{cp}$ =20.2 Hz);  $\delta_p$  (202 MHz): 14.1; HRMS m/z (FAB) 515.2562 (M+H, C<sub>29</sub>H<sub>40</sub>O<sub>6</sub>P requires m/z 515.2563).

*trans*-**II-3a**: colorless oil,  $\delta_H$  (500 MHz, CDCl<sub>3</sub>): 0.57-0.76 (3H, m), 0.73 (3H, d,  $J$ =6.4 Hz, CH<sub>3</sub>), 0.88 (3H, s, CH<sub>3</sub>), 1.08 (3H, s, CH<sub>3</sub>), 1.06-1.11 (1H, m), 1.22-1.30 (1H, m), 1.36-1.41 (1H, m), 1.42 (3H, t,  $J$ =7.1 Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 1.45 (3H, t,  $J$ =7.1 Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 1.52-1.58 (1H, m), 1.71-1.78 (1H, m), 4.29-4.39 (4H, m, -OCH<sub>2</sub>CH<sub>3</sub>), 4.55 (1H, d,  $J$ =4.6 Hz, C3-H), 4.67 (1H, td,  $J$ =4.4 Hz, 10.8, -OCH), 7.11-7.42 (10H, m, Ar-H);  $\delta_C$  (125 MHz, CDCl<sub>3</sub>): 16.4 (d,  $^3J_{cp}$ =5.8 Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 16.4 (d,  $^3J_{cp}$ =5.8 Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 21.5, 22.1, 27.3, 30.8, 31.1, 34.2, 40.1, 40.8, 50.4, 60.5 (d,  $^1J_{cp}$ =192.9 Hz, C2), 61.1 (d,  $^2J_{cp}$ =1.9 Hz, C3), 64.4 (d,  $^2J_{cp}$ =6.7 Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 64.5 (d,  $^2J_{cp}$ =6.7 Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 77.8 (OCH), 125.3, 125.7 (x2), 127.0 (x2), 127.9 (x2), 128.3 (x2), 129.1, 132.0, 150.0 (*ipso*), 163.4 (d,  $^2J_{cp}$ =21.1 Hz);  $\delta_p$  (202 MHz): 15.7; HRMS m/z (FAB) 515.2574 (M+H, C<sub>29</sub>H<sub>40</sub>O<sub>6</sub>P requires m/z 515.2563).

*cis*-**I-3a**: colorless oil,  $\delta_H$  (500 MHz, CDCl<sub>3</sub>): 0.72-0.82 (1H, m), 0.87 (3H, d,  $J$ =6.0 Hz, CH<sub>3</sub>), 0.90-1.05 (1H, m), 1.10-1.50 (1H, m), 1.16 (3H, t,  $J$ =5.7 Hz, OCH<sub>2</sub>CH<sub>3</sub>), 1.18 (3H, t,  $J$ =5.7 Hz, OCH<sub>2</sub>CH<sub>3</sub>), 1.31-1.33 (1H, m), 1.35 (3H, s, CH<sub>3</sub>), 1.4-1.55 (2H, m), 1.47 (3H, s, CH<sub>3</sub>), 1.97-2.08 (2H, m), 3.73-3.82 (1H, m, OCH<sub>2</sub>CH<sub>3</sub>), 3.85-4.30 (3H, m, OCH<sub>2</sub>CH<sub>3</sub>), 4.20 (1H, d,  $J$ =3.4 Hz, C3-H), 5.05 (1H, td,  $J$ =4.5, 10.5 Hz, OCH), 7.16-7.20 (1H, m), 7.29-7.37 (7H, m), 7.41-7.44 (2H, m, Ar-H);  $\delta_C$  (125 MHz, CDCl<sub>3</sub>): 16.2 (d,  $^3J_{cp}$ =5.7 Hz, OCH<sub>2</sub>CH<sub>3</sub>), 16.2 (d,  $^3J_{cp}$ =4.8 Hz, OCH<sub>2</sub>CH<sub>3</sub>), 21.7, 23.8, 27.2, 30.5, 31.4, 34.3, 40.5, 41.4, 50.5, 58.5 (d,  $^1J_{cp}$ =206.0 Hz, C2), 61.9 (d,  $^2J_{cp}$ =1.9 Hz, C3), 62.8 (d,  $^2J_{cp}$ =5.7 Hz, OCH<sub>2</sub>CH<sub>3</sub>), 63.3 (d,  $^2J_{cp}$ =5.7 Hz, OCH<sub>2</sub>CH<sub>3</sub>), 77.4 (OCH), 125.5, 125.8 (x2), 127.1 (x2), 127.9 (x2), 128.1 (x2), 128.7, 132.1, 150.0 (*ipso*), 166.0 (d,  $^2J_{cp}$ =21.1 Hz);  $\delta_p$  (202 MHz): 13.4; HRMS m/z (FAB) 515.2546 (M+H, C<sub>29</sub>H<sub>40</sub>O<sub>6</sub>P requires m/z 515.2563).

*cis*-**II-3a**: colorless oil,  $\delta_{\text{H}}$  (500 MHz,  $\text{CDCl}_3$ ): 0.80-0.90 (1H, m), 0.89 (3H, d,  $J=6.4$  Hz,  $\text{CH}_3$ ), 0.95-1.16 (2H, m), 1.12 (3H, t,  $J=7.1$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 1.14 (3H, t,  $J=7.1$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 1.25 (3H, s,  $\text{CH}_3$ ), 1.38 (3H, s,  $\text{CH}_3$ ), 1.40-1.65 (3H, m), 1.97-2.03 (1H, m), 2.10-2.17 (1H, m), 3.63 (1H, d,  $J=3.7$  Hz, C3-H), 3.74-3.84 (1H, m,  $\text{OCH}_2\text{CH}_3$ ), 3.86-4.06 (3H, m,  $\text{OCH}_2\text{CH}_3$ ), 5.04 (1H, td,  $J=4.4, 10.6$  Hz, OCH), 7.02-7.07 (1H, m, Ar-H), 7.24-7.40 (9H, m, Ar-H);  $\delta_{\text{C}}$  (125 MHz,  $\text{CDCl}_3$ ): 16.1 (d,  $^3J_{\text{cp}}=3.9$  Hz,  $-\text{OCH}_2\text{CH}_3$ ), 16.2 (d,  $^3J_{\text{cp}}=3.9$  Hz,  $-\text{OCH}_2\text{CH}_3$ ), 21.7, 26.4, 27.1, 27.4, 31.4, 34.3, 40.0, 41.5, 49.5, 58.4 (d,  $^1J_{\text{cp}}=206.3$  Hz, C2), 61.4 (d,  $^2J_{\text{cp}}=1.9$  Hz, C3), 62.8 (d,  $^2J_{\text{cp}}=5.8$  Hz,  $-\text{OCH}_2\text{CH}_3$ ), 63.4 (d,  $^2J_{\text{cp}}=6.7$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 77.6 (OCH), 125.5, 125.6 (x2), 127.0 (x2), 127.8 (x2), 128.2 (x2), 128.5, 132.3, 150.7 (*ipso*), 166.4 (d,  $^2J_{\text{cp}}=23.0$  Hz);  $\delta_{\text{p}}$  (202 MHz): 13.4; HRMS  $m/z$  (FAB) 515.2570 (M+H,  $\text{C}_{29}\text{H}_{40}\text{O}_6\text{P}$  requires  $m/z$  515.2563).

*trans*-**I-3b**: colorless oil,  $[\alpha]_{\text{D}}^{25} -26.7^\circ$  (*c* 0.21,  $\text{CHCl}_3$ ),  $\delta_{\text{H}}$  (500 MHz,  $\text{CDCl}_3$ ): 0.18-0.27 (1H, q,  $J=12.4$  Hz), 0.45-0.55 (1H, m), 0.51 (3H, d,  $J=6.6$  Hz,  $\text{CH}_3$ ), 0.60-0.85 (2H, m), 1.00-1.28 (3H, m), 1.18 (3H, s,  $\text{CH}_3$ ), 1.30-1.45 (1H, m), 1.34 (3H, t,  $J=7.1$  Hz,  $-\text{OCH}_2\text{CH}_3$ ), 1.37 (3H, t,  $J=7.1$  Hz,  $-\text{OCH}_2\text{CH}_3$ ), 1.60-1.68 (1H, m), 3.70 (3H, s,  $\text{OCH}_3$ ), 4.18-4.27 (4H, m,  $-\text{OCH}_2\text{CH}_3$ ), 4.44 (1H, d,  $J=4.4$  Hz, C3-H), 4.67 (1H, td,  $J=4.4, 10.5$  Hz, OCH), 6.80 (2H, d,  $J=8.8$  Hz, Ar-H), 7.06-7.11 (1H, m, Ar-H), 7.15-7.22 (4H, m, Ar-H), 7.25 (2H, d,  $J=8.8$  Hz, Ar-H);  $\delta_{\text{C}}$  (125 MHz,  $\text{CDCl}_3$ ): 16.4 (d,  $^3J_{\text{cp}}=5.7$  Hz,  $-\text{OCH}_2\text{CH}_3$ ), 16.5 (d,  $^3J_{\text{cp}}=5.7$  Hz,  $-\text{OCH}_2\text{CH}_3$ ), 21.4, 22.5, 27.4, 30.9, 31.5, 34.0, 40.5, 40.8, 50.1, 55.15, 60.5 (d,  $^2J_{\text{cp}}=1.9$  Hz, C3), 61.0 (d,  $^1J_{\text{cp}}=189.1$  Hz, C2), 63.6 (d,  $^2J_{\text{cp}}=6.7$  Hz,  $-\text{OCH}_2\text{CH}_3$ ), 63.9 (d,  $^2J_{\text{cp}}=5.8$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 77.8 (OCH), 113.7 (x2), 123.6, 125.4, 125.9 (x2), 127.9 (x2), 128.0 (x2), 149.6 (*ipso*), 160.2, 163.5 (d,  $^3J_{\text{cp}}=21.1$  Hz);  $\delta_{\text{p}}$  (202 MHz): 14.2; HRMS  $m/z$  (FAB) 545.2681 (M+H,  $\text{C}_{30}\text{H}_{42}\text{O}_7\text{P}$  requires  $m/z$  545.2668).

*trans*-**II-3b**: colorless oil,  $[\alpha]_{\text{D}}^{25} +1.96^\circ$  (*c* 0.51,  $\text{CHCl}_3$ ),  $\delta_{\text{H}}$  (500 MHz,  $\text{CDCl}_3$ ): 0.58-0.80 (3H, m), 0.75 (3H, d,  $J=6.4$  Hz,  $\text{CH}_3$ ), 0.91 (3H, s,  $\text{CH}_3$ ), 1.02 (3H, s,  $\text{CH}_3$ ), 1.05-1.50 (3H, m), 1.42 (3H, t,  $J=7.2$  Hz,  $-\text{OCH}_2\text{CH}_3$ ), 1.44 (3H, t,  $J=7.2$  Hz,  $-\text{OCH}_2\text{CH}_3$ ), 1.61 (1H, m), 1.72-1.79 (1H, m), 3.77 (3H, s,  $\text{OCH}_3$ ), 4.26-4.36 (4H, m,  $-\text{OCH}_2\text{CH}_3$ ), 4.49 (1H, d,  $J=4.3$  Hz, C3-H), 4.69 (1H, td,  $J=4.3, 11.0$  Hz, OCH), 6.85 (2H, d,  $J=8.5$  Hz, Ar-H), 7.10-7.33 (5H, m), 7.35 (2H, d,  $J=8.8$  Hz, Ar-H);  $\delta_{\text{C}}$  (125 MHz,  $\text{CDCl}_3$ ): 16.4 (d,  $^3J_{\text{cp}}=6.7$  Hz,  $-\text{OCH}_2\text{CH}_3$ ), 16.5 (d,  $^3J_{\text{cp}}=6.7$  Hz,  $-\text{OCH}_2\text{CH}_3$ ), 21.5, 21.9, 27.3, 31.0, 31.2, 34.3, 40.2, 40.9, 50.5, 55.3, 61.0 (d,  $^1J_{\text{cp}}=190.0$  Hz, C2), 61.1 (d,  $^2J_{\text{cp}}=1.0$  Hz, C3), 63.8 (d,  $^2J_{\text{cp}}=1.9$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 63.9 (d,  $^2J_{\text{cp}}=1.9$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 77.8 (OCH), 113.8 (x2), 123.6, 125.4, 125.8 (x2), 127.9 (x2), 128.4 (x2), 150.0 (*ipso*), 160.4, 163.7 (d,  $^2J_{\text{cp}}=21.1$  Hz);  $\delta_{\text{p}}$  (202 MHz): 14.9; HRMS  $m/z$  (FAB) 545.2672 (M+H,  $\text{C}_{30}\text{H}_{42}\text{O}_7\text{P}$  requires  $m/z$  545.2668).

*cis*-**I-3b**: colorless oil,  $\delta_{\text{H}}$  (500 MHz,  $\text{CDCl}_3$ ): 0.72-0.82 (1H, m), 0.89 (3H, d,  $J=6.4$  Hz,  $\text{CH}_3$ ), 0.91-1.02 (1H, m), 1.10-1.20 (1H, m), 1.19 (3H, t,  $J=7.1$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 1.21 (3H, t,  $J=7.1$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 1.28-1.33 (1H, m), 1.34 (3H, s,  $\text{CH}_3$ ), 1.40-1.55 (2H, m), 1.46 (3H, s,  $\text{CH}_3$ ), 1.96-2.08 (2H, m), 3.8 (3H,

s, OCH<sub>3</sub>), 3.80-3.41 (4H, m, OCH<sub>2</sub>CH<sub>3</sub>), 4.17 (1H, d,  $J=3.4$  Hz, C3-H), 5.04 (1H, td,  $J=4.6, 10.8$  Hz, OCH), 6.87 (2H, d,  $J=8.9$  Hz, Ar-H), 7.16-7.21 (1H, m, Ar-H) 7.24-7.33 (4H, m, Ar-H), 7.36 (2H, d,  $J=8.5$  Hz, Ar-H);  $\delta_C$  (125 MHz, CDCl<sub>3</sub>): 16.2 (d,  $^3J_{cp}=4.8$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 16.3 (d,  $^3J_{cp}=3.8$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 21.7, 22.7, 23.9, 27.3, 31.3, 31.7, 34.4, 40.6, 41.5, 50.6, 59.1 (d,  $^1J_{cp}=207.0$  Hz, C2), 61.8 (d,  $^2J_{cp}=1.9$  Hz, C3), 62.8 (d,  $^2J_{cp}=6.7$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 63.3 (d,  $^2J_{cp}=26.7$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 77.4 (OCH), 113.3 (x2), 125.6, 125.8 (x3), 128.1 (x2), 128.5 (x2), 150.0 (*ipso*), 159.9, 166.0 (d,  $^2J_{cp}=20.1$  Hz);  $\delta_p$  (202 MHz): 13.4; HRMS  $m/z$  (FAB) 545.2664 (M+H, C<sub>30</sub>H<sub>42</sub>O<sub>7</sub>P requires  $m/z$  545.2668).

*cis*-**II-3b**: colorless oil,  $\delta_H$  (500 MHz, CDCl<sub>3</sub>): 0.60-0.85 (1H, m), 0.81 (3H, d,  $J=6.6$  Hz, CH<sub>3</sub>), 0.91-1.10 (2H, m), 1.08 (3H, t,  $J=7.1$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 1.10 (3H, t,  $J=7.1$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 1.17 (3H, s, CH<sub>3</sub>), 1.30 (3H, s, CH<sub>3</sub>), 1.32-1.55 (3H, m), 1.85-1.97 (1H, m), 2.01-2.09 (1H, m), 3.53 (1H, d,  $J=3.7$  Hz, C3-H), 3.74 (3H, s, OCH<sub>3</sub>), 3.75-3.97 (4H, m, OCH<sub>2</sub>CH<sub>3</sub>), 4.95 (1H, td,  $J=4.6, 10.8$  Hz, OCH), 6.80 (2H, d,  $J=8.7$  Hz, Ar-H), 6.97-7.01 (1H, m), 7.17 (6H, m, Ar-H);  $\delta_C$  (125 MHz, CDCl<sub>3</sub>): 16.2 (d,  $^3J_{cp}=3.8$  Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 16.2 (d,  $^3J_{cp}=3.8$  Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 21.7, 26.3, 27.1, 27.7, 31.4, 34.4, 40.2, 41.6, 49.6, 55.3, 59.4 (d,  $^1J_{cp}=205.4$  Hz, C2), 61.3 (d,  $^2J_{cp}=1.9$  Hz, C3), 62.8 (d,  $^2J_{cp}=6.7$  Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 63.4 (d,  $^2J_{cp}=5.8$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 77.3 (OCH), 113.3 (x2), 125.5, 125.6 (x3), 128.2 (x2), 128.5 (x2), 150.8 (*ipso*), 159.8, 166.5 (d,  $^2J_{cp}=23.0$  Hz);  $\delta_p$  (202 MHz): 13.7; HRMS  $m/z$  (FAB) 545.2668 (M+H, C<sub>30</sub>H<sub>42</sub>O<sub>7</sub>P requires  $m/z$  545.2668).

*trans*-**I-3c**: colorless oil,  $[\alpha]_D^{25} -73.1^\circ$  (*c* 0.27, CHCl<sub>3</sub>),  $\delta_H$  (500 MHz, CDCl<sub>3</sub>): 0.25-0.34 (1H, q,  $J=12.1$  Hz), 0.48-0.68 (1H, m), 0.63 (3H, d,  $J=6.6$  Hz, CH<sub>3</sub>), 0.69-0.81 (2H, m), 1.07-1.16 (1H, m), 1.23-1.27 (1H, m), 1.24 (3H, s, CH<sub>3</sub>), 1.30-1.36 (1H, m), 1.35 (3H, s, CH<sub>3</sub>), 1.42 (3H, t,  $J=7.1$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 1.44 (3H, t,  $J=7.1$  Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 1.66-1.75 (1H, m), 4.27-4.35 (4H, m, OCH<sub>2</sub>CH<sub>3</sub>), 4.54 (1H, d,  $J=4.6$  Hz, C3-H), 4.74 (1H, td,  $J=4.6, 10.5$  Hz, -OCH), 7.13-7.18 (1H, m, Ar-H), 7.22-7.3 (4H, m, Ar-H), 7.31-7.37 (4H, m, Ar-H);  $\delta_C$  (125 MHz, CDCl<sub>3</sub>): 16.3 (d,  $^3J_{cp}=2.9$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 16.4 (d,  $^3J_{cp}=2.9$  Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 21.4, 22.5, 27.4, 31.0, 31.5, 33.9, 40.4, 40.8, 50.0, 60.0 (d,  $^2J_{cp}=1.0$  Hz, C3), 60.7 (d,  $^1J_{cp}=190.0$  Hz, C2), 64.1 (d,  $^2J_{cp}=5.8$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 64.5 (d,  $^2J_{cp}=5.8$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 78.3 (OCH), 125.5, 125.9 (x2), 128.0 (x2), 128.2 (x2), 128.6 (x2), 130.2, 135.0, 149.6 (*ipso*), 163.2 (d,  $^2J_{cp}=19.2$  Hz);  $\delta_p$  (202 MHz): 14.3; HRMS  $m/z$  (FAB) 549.2161 (M+H, C<sub>29</sub>H<sub>39</sub>O<sub>6</sub>ClP requires  $m/z$  549.2174).

*trans*-**II-3c**: colorless oil,  $[\alpha]_D^{25} +2.77^\circ$  (*c* 0.61, CHCl<sub>3</sub>),  $\delta_H$  (500 MHz, CDCl<sub>3</sub>): 0.58-0.68 (2H, m), 0.69-0.79 (1H, m), 0.75 (3H, d,  $J=6.4$  Hz, CH<sub>3</sub>), 0.92 (3H, s, CH<sub>3</sub>), 1.10 (3H, s, CH<sub>3</sub>), 1.08-1.43 (3H, m), 1.42 (3H, t,  $J=7.1$  Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 1.44 (3H, t,  $J=7.1$  Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 1.50-1.57 (1H, m), 1.71-1.78 (1H, m), 4.26-4.37 (4H, m, -OCH<sub>2</sub>CH<sub>3</sub>), 4.51 (1H, d,  $J=4.8$  Hz, C3-H), 4.75 (1H, td,  $J=4.4, 10.8$  Hz, -OCH), 7.12-7.17 (3H, m, Ar-H), 7.23-7.28 (2H, m, Ar-H), 7.29-7.37 (4H, m, Ar-H);  $\delta_C$  (125 MHz, CDCl<sub>3</sub>): 16.4 (d,  $^3J_{cp}=6.7$  Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 16.4 (d,  $^3J_{cp}=6.7$  Hz, -OCH<sub>2</sub>CH<sub>3</sub>), 21.5, 22.3, 27.3, 30.8, 31.2, 34.2, 40.1, 40.9, 50.5, 60.48 (d,  $^2J_{cp}=1.9$  Hz, C3), 60.5 (d,  $^1J_{cp}=192.9$  Hz, C2), 64.3 (d,  $^2J_{cp}=2.9$  Hz, -OCH<sub>2</sub>CH<sub>3</sub>),



64.4 (d,  $^2J_{\text{cp}}=2.9$  Hz,  $-\text{OCH}_2\text{CH}_3$ ), 78.1 (OCH), 125.4, 125.7 (x2), 128.0 (x2), 128.5 (x4), 130.0, 135.2, 149.9 (*ipso*), 163.3 (d,  $^2J_{\text{cp}}=21.1$  Hz);  $\delta_{\text{p}}$  (202 MHz): 14.9; HRMS m/z (FAB) 549.2172 (M+H,  $\text{C}_{29}\text{H}_{39}\text{O}_6\text{CIP}$  requires m/z 549.2174).

*cis*-**I-3c**: colorless oil,  $[\alpha]_{\text{D}}^{25} -14.0^\circ$  (*c* 0.33,  $\text{CHCl}_3$ ),  $\delta_{\text{H}}$  (500 MHz,  $\text{CDCl}_3$ ): 0.74-0.84 (1H, m), 0.86 (3H, d,  $J=6.6$  Hz,  $\text{CH}_3$ ), 0.94-1.04 (1H, m), 1.04-1.15 (1H, m), 1.17 (3H, t,  $J=7.1$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 1.23 (3H, t,  $J=7.1$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 1.33 (3H, s,  $\text{CH}_3$ ), 1.35-1.56 (3H, m), 1.42 (3H, s,  $\text{CH}_3$ ), 1.99-2.06 (2H, m), 3.78-3.88 (1H, m,  $\text{OCH}_2\text{CH}_3$ ), 3.90-4.09 (3H, m,  $\text{OCH}_2\text{CH}_3$ ), 4.15 (1H, d,  $J=3.4$  Hz, C3-H), 5.02-5.09 (1H, td,  $J=4.6, 10.6$  Hz, OCH), 7.15-7.2 (1H, m), 7.28-7.37 (8H, m);  $\delta_{\text{C}}$  (125 MHz,  $\text{CDCl}_3$ ): 16.1 (d,  $^3J_{\text{cp}}=6.7$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 16.2 (d,  $^3J_{\text{cp}}=6.7$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 21.7, 24.2, 27.2, 29.9, 31.4, 34.2, 40.4, 41.4, 50.3, 59.0 (d,  $^1J_{\text{cp}}=206.2$  Hz, C2) 61.3 (d,  $^2J_{\text{cp}}=1.9$  Hz, C3), 63.4 (d,  $^2J_{\text{cp}}=6.7$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 63.9 (d,  $^2J_{\text{cp}}=6.7$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 77.7 (OCH), 125.5, 125.5 (x2), 128.1 (x2), 128.3 (x2), 128.5 (x2), 130.4, 134.8, 150.1 (*ipso*), 165.7 (d,  $^3J_{\text{cp}}=21.1$  Hz);  $\delta_{\text{p}}$  (202 MHz): 13.9; HRMS m/z (FAB) 549.2167 (M+H,  $\text{C}_{29}\text{H}_{39}\text{O}_6\text{CIP}$  requires m/z 549.2174).

*cis*-**II-3c**: colorless oil,  $[\alpha]_{\text{D}}^{25} +24.1^\circ$  (*c* 0.51,  $\text{CHCl}_3$ ),  $\delta_{\text{H}}$  (500 MHz,  $\text{CDCl}_3$ ): 0.80-0.92 (1H, m), 0.90 (3H, d,  $J=6.6$  Hz,  $\text{CH}_3$ ), 1.05-1.25 (2H, m), 1.12 (3H, t,  $J=7.3$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 1.16 (3H, t,  $J=7.1$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 1.20 (3H, s,  $\text{CH}_3$ ), 1.35 (3H, s,  $\text{CH}_3$ ), 1.40-1.70 (3H, m), 1.90-1.99 (1H, m), 2.13-2.21 (1H, m), 3.34 (1H, d,  $J=3.4$  Hz, C3-H), 3.78-4.10 (4H, m,  $\text{OCH}_2\text{CH}_3$ ), 5.04 (1H, td,  $J=4.4, 10.5$  Hz, OCH), 6.96-7.02 (1H, m), 7.22-7.38 (8H, m);  $\delta_{\text{C}}$  (125 MHz,  $\text{CDCl}_3$ ): 16.1 (d,  $^3J_{\text{cp}}=6.7$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 16.2 (d,  $^3J_{\text{cp}}=6.7$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 21.7, 26.1, 26.8, 27.6, 31.4, 34.3, 40.0, 41.5, 49.2, 58.5 (d,  $^1J_{\text{cp}}=206.3$  Hz, C2), 60.8 (d,  $^2J_{\text{cp}}=1.9$ , C3), 63.4 (d,  $^2J_{\text{cp}}=6.7$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 64.1 (d,  $^2J_{\text{cp}}=6.7$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 77.8 (OCH), 125.5 (x3), 128.1 (x2), 128.2 (x2), 128.5 (x2), 130.7, 134.4, 150.1 (*ipso*), 166.0 (d,  $^3J_{\text{cp}}=21.1$  Hz);  $\delta_{\text{p}}$  (202 MHz): 14.1; HRMS m/z (FAB) 549.2164 (M+H,  $\text{C}_{29}\text{H}_{39}\text{O}_6\text{CIP}$  requires m/z 549.2174).

*trans*-**I-3d**: colorless oil,  $[\alpha]_{\text{D}}^{25} -43.6^\circ$  (*c* 0.37,  $\text{CHCl}_3$ ),  $\delta_{\text{H}}$  (500 MHz,  $\text{CDCl}_3$ ): 0.27 (1H, q,  $J=11.0$  Hz), 0.47-0.56 (1H, m), 0.53 (3H, d,  $J=6.4$  Hz,  $\text{CH}_3$ ), 0.68-0.78 (1H, m), 0.80-0.90 (1H, m), 1.05-1.17 (2H, m), 1.23 (3H, s,  $\text{CH}_3$ ), 1.30-1.36 (1H, m), 1.36 (3H, s,  $\text{CH}_3$ ), 1.44 (3H, t,  $J=7.0$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 1.46 (3H, t,  $J=7.0$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 1.60-1.75 (1H, m), 4.28-4.36 (4H, m,  $\text{OCH}_2\text{CH}_3$ ), 4.64 (1H, d,  $J=5.0$  Hz, C3-H), 4.7 (1H, td,  $J=4.6, 10.5$  Hz, OCH), 7.14-7.30 (5H, m, Ar-H), 7.60 (2H, d,  $J=8.7$  Hz, Ar-H), 8.23 (2H, d,  $J=8.7$  Hz, Ar-H);  $\delta_{\text{C}}$  (125 MHz,  $\text{CDCl}_3$ ): 16.5 (d,  $^3J_{\text{cp}}=6.7$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 16.5 (d,  $^3J_{\text{cp}}=6.7$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 21.3, 22.6, 27.3, 31.0, 31.4, 33.9, 40.5, 40.9, 50.1, 59.9 (d,  $^2J_{\text{cp}}=1.0$  Hz, C3), 61.1 (d,  $^1J_{\text{cp}}=191.0$  Hz, C2), 64.6 (d,  $^2J_{\text{cp}}=6.7$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 64.63 (d,  $^2J_{\text{cp}}=5.8$  Hz,  $\text{OCH}_2\text{CH}_3$ ), 78.5 (OCH), 123.6 (x2), 125.6, 125.9 (x2), 128.0 (x2), 128.1(x2), 139.1, 148.4, 149.6 (*ipso*), 162.9 (d,  $^2J_{\text{cp}}=19.2$  Hz);  $\delta_{\text{p}}$  (202 MHz): 13.3; HRMS m/z (FAB) 560.2415 (M+H,  $\text{C}_{29}\text{H}_{39}\text{O}_8\text{NP}$  requires m/z 560.2413).

*trans*-**II-3d**: colorless oil,  $[\alpha]_{\text{D}}^{25} +5.15^\circ$  (*c* 0.45,  $\text{CHCl}_3$ ),  $\delta_{\text{H}}$  (500 MHz,  $\text{CDCl}_3$ ): 0.55-0.80 (3H, m), 0.70 (3H, d,  $J=6.4$  Hz,  $\text{CH}_3$ ), 0.89 (3H, s,  $\text{CH}_3$ ), 1.10 (3H, s,  $\text{CH}_3$ ), 1.09-1.17 (1H, m), 1.20-1.32 (1H, m),

1.42-1.46 (2H, m), 1.44 (3H, t,  $J=7.1$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 1.45 (3H, t,  $J=7.1$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 1.72-1.75 (1H, m), 4.29-4.39 (4H, m, OCH<sub>2</sub>CH<sub>3</sub>), 4.61 (1H, d,  $J=4.8$  Hz, C3-H), 4.67 (1H, td,  $J=4.4, 10.8$  Hz, OCH), 7.10-7.20 (3H, m), 7.22-7.28 (2H, m), 7.60 (2H, d,  $J=8.2$  Hz, Ar-H), 8.20 (2H, d,  $J=8.9$  Hz, Ar-H);  $\delta_C$  (125 MHz, CDCl<sub>3</sub>): 16.5 (d,  $^3J_{cp}=5.8$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 16.6 (d,  $^3J_{cp}=5.8$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 21.5, 22.6, 27.3, 30.7, 31.2, 34.1, 40.2, 41.1, 50.5, 60.1 (d,  $^2J_{cp}=1.9$  Hz, C3), 60.5 (d,  $^1J_{cp}=194.8$  Hz, C2), 64.6 (d,  $^2J_{cp}=6.7$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 64.7 (d,  $^2J_{cp}=6.7$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 78.4 (OCH), 123.4 (x2), 125.5, 125.7 (x2), 128.0 (x2), 128.3 (x2), 138.7, 148.5, 149.8 (*ipso*), 163.0 (d,  $^2J_{cp}=21.1$  Hz);  $\delta_p$  (202 MHz): 14.1; HRMS m/z (FAB) 560.2404 (M+H, C<sub>29</sub>H<sub>39</sub>O<sub>8</sub>NP requires m/z 560.2413).

*cis-I-3d*: colorless oil,  $[\alpha]_D^{25} -11.6^\circ$  (*c* 0.11, CHCl<sub>3</sub>),  $\delta_H$  (500 MHz, CDCl<sub>3</sub>): 0.75-0.92 (2H, m), 0.88 (3H, d,  $J=6.4$  Hz, CH<sub>3</sub>), 0.95-1.17 (1H, m), 1.20 (3H, t,  $J=7.1$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 1.22 (3H, t,  $J=7.1$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 1.33 (3H, s, CH<sub>3</sub>), 1.4-1.56 (3H, m), 1.41 (3H, s, CH<sub>3</sub>), 1.99-2.06 (2H, m), 3.92-4.08 (4H, m, OCH<sub>2</sub>CH<sub>3</sub>), 4.18 (1H, d,  $J=3.4$  Hz, C3-H), 5.00 (1H, td,  $J=5.2, 11.3$  Hz, OCH), 7.16-7.21 (1H, m, Ar-H), 7.31-7.34 (4H, m, Ar-H), 7.59 (2H, d,  $J=8.5$  Hz, Ar-H), 8.22 (2H, d,  $J=8.5$  Hz, Ar-H);  $\delta_C$  (125 MHz, CDCl<sub>3</sub>): 16.3 (d,  $^3J_{cp}=6.7$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 16.4 (d,  $^3J_{cp}=6.7$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 21.8, 24.8, 27.2, 29.4, 31.4, 34.3, 40.4, 41.5, 50.5, 59.1 (d,  $^1J_{cp}=207.3$  Hz, C2), 60.8 (d,  $^2J_{cp}=1.9$  Hz, C3), 63.4 (d,  $^2J_{cp}=6.7$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 63.8 (d,  $^2J_{cp}=6.7$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 77.4 (OCH), 123.2 (x2), 125.7, 125.8 (x2), 128.2 (x2), 128.3 (x2), 130.4, 139.2, 150.2 (*ipso*), 165.7 (d,  $^2J_{cp}=21.1$  Hz);  $\delta_p$  (202 MHz): 13.9; HRMS m/z (FAB) 560.2402 (M+H, C<sub>29</sub>H<sub>39</sub>O<sub>8</sub>NP requires m/z 560.2413).

*cis-II-3d*: colorless oil,  $[\alpha]_D^{25} +14.7^\circ$  (*c* 0.19, CHCl<sub>3</sub>),  $\delta_H$  (500 MHz, CDCl<sub>3</sub>): 0.80-0.95 (1H, m), 0.93 (3H, d,  $J=6.4$  Hz, CH<sub>3</sub>), 1.08-1.23 (2H, m), 1.14 (3H, t,  $J=7.1$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 1.16 (3H, t,  $J=7.1$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 1.30 (3H, s, CH<sub>3</sub>), 1.40 (3H, s, CH<sub>3</sub>), 1.45-1.70 (3H, m), 1.92 (1H, m), 2.18-2.24 (1H, m), 3.23 (1H, d,  $J=3.4$  Hz, C3-H), 3.90-4.10 (4H, m, OCH<sub>2</sub>CH<sub>3</sub>), 5.05 (1H, td,  $J=4.4, 10.8$  Hz, OCH), 6.94-6.98 (1H, m, Ar-H), 7.20-7.36 (6H, m, Ar-H), 7.5-7.53 (2H, d,  $J=8.5$  Hz, Ar-H);  $\delta_C$  (125 MHz, CDCl<sub>3</sub>): 16.14 (d,  $^3J_{cp}=5.8$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 16.2 (d,  $^3J_{cp}=5.8$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 21.7, 25.5, 26.8, 28.3, 31.4, 34.3, 39.8, 41.5, 49.1, 58.6 (d,  $^1J_{cp}=206.3$  Hz, C2), 60.2 (d,  $^2J_{cp}=1.9$  Hz, C3), 63.4 (d,  $^2J_{cp}=6.7$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 64.1 (d,  $^2J_{cp}=6.7$  Hz, OCH<sub>2</sub>CH<sub>3</sub>), 77.9 (OCH), 123.0 (x2), 125.4, 125.5 (x2), 128.2 (x2), 128.2 (x2), 139.4, 147.9, 151.2 (*ipso*), 165.6 (d,  $^2J_{cp}=23.0$  Hz);  $\delta_p$  (202 MHz): 14.1; HRMS m/z (FAB) 560.2417 (M+H, C<sub>29</sub>H<sub>39</sub>O<sub>8</sub>NP requires m/z 560.2413).

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NMR measurements were carried out on JEOL GSX-270 and LA-500 instruments, and HRMS measurements on a JEOL SX-102A spectrometer at the Instrument center for Chemical Analysis, Hiroshima University.

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