Application of *erythro*-2-Amino-1,2-diphenylethanol as a Highly Efficient Chiral Auxiliary. Highly Stereoselective Staudinger-Type β-Lactam Synthesis Using a 2-Chloro-1-methylpyridinium Salt as the Dehydrating Agent

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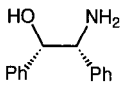
Abstract: The Staudinger-type reaction of carboxylic acids with imines, using a 2-chloro-1-methylpyridinium salt as the dehydrating reagent, proceeded smoothly under mild conditions to afford the desired β-lactams in high yields with excellent *cis*-selectivity. This reaction was successfully applied to the asymmetric synthesis of β-lactams using a chiral glycine derivative as the acid component, which was prepared from an artificial chiral auxiliary, (1*S*,2*R*)-2-amino-1,2-diphenylethanol. The corresponding β-lactams were obtained in high yields with excellent stereoselectivity.

Key words: Staudinger-type reaction, [2+2] cycloaddition, β-lactams, 2-chloro-1-methylpyridinium salt, (1*S*,2*R*)-2-amino-1,2-diphenylethanol

Asymmetric synthesis is one of the most extensively investigated categories in organic chemistry. A number of chiral auxiliaries have been developed and these have enabled us to prepare target compounds having absolute desired configuration with high stereoselectivity. Most of these chiral auxiliaries are derived from naturally occurring compounds; usually a chiral natural compound is properly chosen and converted to a suitable structure for asymmetric induction. However, the availability of both enantiomers is not always guaranteed. On the other hand, an artificial chiral auxiliary is expected to be more valuable from the following respects: 1) it can be designed without structural limitation; 2) if the corresponding racemate can be resolved easily, both enantiomers of the auxiliary can be available and equally be used in asymmetric syntheses.



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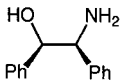

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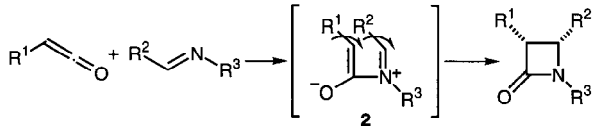
In the course of our studies concerning optical resolution, we have successfully resolved several kinds of amines and amino alcohols, and applied them as artificial chiral auxiliaries.[1, 2] Among them, *erythro*-2-amino-1,2-diphenylethanol **(1)** was found to be easily resolved,[3] and successful applications of **1** to asymmetric reactions have been reported by ourselves[2] and others.[4] This amino alcohol **1** is an excellent auxiliary from the following viewpoints: 1) both enantiomers of **1** can be obtained equally; 2) two phenyl groups offer large bulkiness, which enable discrimination of diastereo- or enantiotopic face; 3) the derivatives of **1** usually have high crystallizability. In order to apply this quite beneficial amino alcohol to the asymmetric synthesis of valuable targets such as biologically active compounds, we focused on the asymmetric synthesis of β-lactams. In this paper we report highly diastereoselective Staudinger reaction using **1**-derived oxazolidinone as a chiral auxiliary.[5]

The β-lactam structure is a fundamental skeleton, which can be found in penicillins, cephalosporins, and related antibiotics. Among various methods for the construction of β-lactams, the Staudinger reaction, which is a [2+2] cycloaddition between ketenes and imines (Scheme 1), is one of the most effective methods, since it usually allows their *cis*-selective formation.[6] Its asymmetric versions have been already reported by several groups[7, 8] and applied to the synthesis of biologically active β-lactams.



Scheme 1

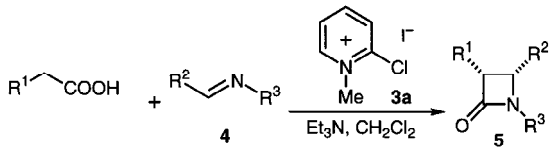
Generally, acid chlorides are used as precursors of ketenes in the Staudinger reaction.[6] However, acid chlorides are sometimes difficult to isolate and handle because of their instability, especially when they have a complicated structure. Therefore, various methods to generate ketenes directly from carboxylic acids by utilizing a dehydrating reagent[9] or others[10] have been developed for the Staudinger reaction.

Among various dehydrating reagents, we called our attention to the 2-chloro-1-methylpyridinium salts **3**, which were originally developed by Mukaiyama, one of the authors, and co-workers in the synthesis of esters or amides from carboxylic acids.[11] This reagent has been applied to the generation of ketenes from carboxylic acids,[12] and applications to the Staudinger reaction have been already reported by Amin et al.[13] and Georg et al.[14] However, because of relatively low yield and/or low stereoselectivity, there is room for improvement in their reaction conditions. In order to develop asymmetric Staudinger β-lactam synthesis using **3**, we first thoroughly reinvestigated the reaction conditions.

First, the reaction of phenoxyacetic acid with *N*-benzylbenzaldimine was carried out in the presence of 1.1 equivalents of 2-chloro-1-methylpyridinium iodide **(3a)** and 2.2 equivalents of triethylamine in CH_2Cl_2 at 0 °C for 10 hours then at room temperature for 14 hours. The

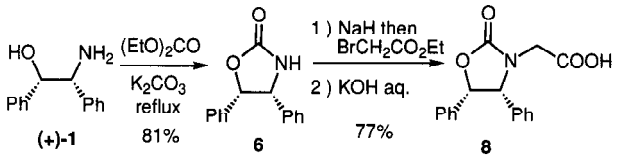
reaction proceeded smoothly, and the desired β-lactam was obtained in high yield with complete *cis*-selectivity (Table 1, entry 1). This procedure has an advantage that the generation of a ketene prior to the addition of an imine is unnecessary in contrast to the previously reported procedures;[13, 14] all the reactants could be mixed at the same time.

On the basis of this successful result, the reaction of phenoxyacetic acid or *N*-phthaloylglycine with various imines was performed under similar mild conditions to those mentioned above (Scheme 2). The results are summarized in Table 1. When the reactions of phenoxyacetic acid with imines, derived from *p*-anisidine, were carried out, the corresponding β-lactams were obtained in good to high yields with excellent *cis*-selectivity (entries 2–6). Most of the products (except for that of entry 6) were *cis*-isomers, and the *trans*-isomers were not detected at all. The formation of the *trans*-isomer in entry 6 would be mainly due to the stereochemical heterogeneity of the starting imine (*E*/*Z* 94:6). Furthermore, *N*-phthaloylglycine, as well as phenoxyacetic acid, reacted readily with imines in the presence of **3a** and triethylamine to give the corresponding β-lactams in high yields with complete *cis*-selectivity (entries 7 and 8). This *cis*-selectivity for the reactions of *N*-phthaloylglycine is in contrast to the *trans*-selectivity previously reported,[13, 14] which was observed when the corresponding acid chloride was employed or formed in situ.[14] This contrast indicates that in the present Staudinger reaction the ketenes are formed not from the acid chlorides but directly from the carboxylic acids. Thus, we found that the Staudinger reaction of imines with carboxylic acids using pyridinium salt **3a** as a dehydrating agent proceeded smoothly under mild conditions to give the corresponding β-lactams in high yields with excellent *cis*-selectivity; this reaction system is quite practical, since the starting carboxylic acids can be easily handled and stored.



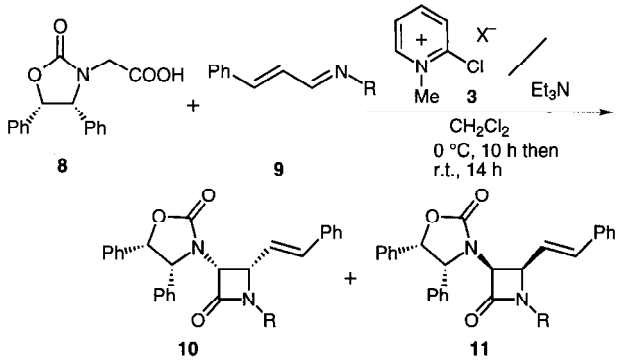
Scheme 2

On the basis of these results, we next tried to develop an asymmetric version of this reaction. The chiral glycine derivative **8**, which has a (+)-**1**-derived oxazolidinone moiety as a chiral auxiliary, was synthesized as shown in Scheme 3. Oxazolidinone **6** was easily obtained from (+)-**1** by refluxing in diethyl carbonate in the presence of a catalytic amount of potassium carbonate. Sodium salt of **6** was then alkylated with ethyl bromoacetate to give glycine ethyl ester derivative **7**. Finally, hydrolysis of **7** afforded the desired homochiral carboxylic acid **8** in good overall yield.



Scheme 3

Next, the asymmetric Staudinger reaction of optically active carboxylic acid **8** was carried out with several kinds of cinnamaldimines **9** using 2-chloro-1-methylpyridinium salts **3** (Scheme 4). The results are summarized in Table 2.[15] When the reaction of *N*-benzylimine **9a** was performed using pyridinium salt **3a** as a dehydrating reagent, the β-lactam consisting of a (3*R*,4*S*)-azetidinone ring was obtained as a single diastereomer. However, the chemical yield was unsatisfactory, probably due to side reactions arising from the nucleophilicity of iodide ion of **3a**; the bulky substituent in **3a** suppressed the ring closure step of



Scheme 4

Table 1. Synthesis of β-Lactams Using 2-Chloro-1-methylpyridinium Iodide (**3a**)

Entry	R^1	R^2	R^3	Product	Yield (%)	Ratio *cis*/*trans*	Conditions[a]
1	PhO	Ph	$PhCH_2$	**5a**	87	>99:1	A
2	PhO	Ph	*p*-$MeOC_6H_4$	**5b**	88	>99:1	B
3		*p*-$MeOC_6H_4$		**5c**	85	>99:1	B
4		*p*-ClC_6H_4		**5d**	95	>99:1	B
5		PhCH=CH		**5e**	quant.	>99:1	A
6		PhC≡C[b]		**5f**	92	91:9	B
7	PhthN	Ph	$PhCH_2$	**5g**	89	>99:1	A
8	PhthN	PhCH=CH	*p*-$MeOC_6H_4$	**5h**	89	>99:1	B

[a] Reaction conditions: A: 0°C, 10 h then r.t., 14 h; B: r.t., 7 h.
[b] This imine was used as an *E*/*Z* mixture in a ratio of 94:6.

Table 2. Asymmetric β-Lactam Synthesis Using Cinnamaldimine **9** Under Various Conditions

Entry	R	X	Product[a]	Yield (%)	Ratio **10**/**11**
1	$PhCH_2$	I	**10a** + **11a**	41[b]	>99:1
2		TsO	**10a** + **11a**	54	>99:1
3	Ph_2CH	I	**10b** + **11b**	85	81:19
4		TsO	**10b** + **11b**	99	84:16
5	*p*-$MeOC_6H_4$	TsO	**10c** + **11c**	97	94:6

[a] trans-Isomers were not detected at all.
[b] Reaction conditions: 0 °C, 8 h then r.t., 22 h.

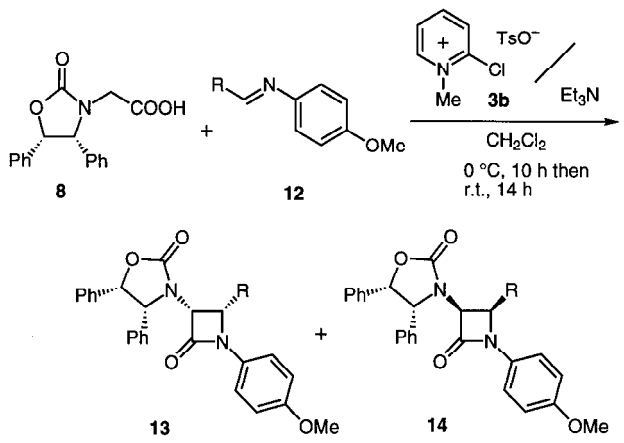
Table 3. Asymmetric β-Lactam Synthesis Using 2-Chloro-1-methylpyridinium *p*-Toluenesulfonate (**3b**)

Entry	R	Product	Yield (%)[a]	Ratio **13**/**14**
1	*p*-$MeOC_6H_4$	**13a** + **14a**	91	>99:1
2	Ph	**13b** + **14b**	94	>99:1
3	*p*-ClC_6H_4	**13c** + **14c**	quant.	>99:1
4	PhCH=CH	**13d** + **14d**	97	94:6
5	PhC≡C[b]	**13e** + **14e**	90	91:9

[a] The *trans*-isomers were not detected at all.
[b] This imine was used as an *E*/*Z* mixture in a ratio of 94:6.

a zwitterionic intermediate like **2** in Scheme 1, and the nucleophilic attack of the iodide ion to the iminium moiety of the intermediate would cause side reactions. On the basis of this consideration, the reaction using 2-chloro-1-methylpyridinium *p*-toluenesulfonate **(3b)**, of which the counter anion has weak nucleophilicity, was performed (entry 2). Although **3b** gave a better result than **3a**, high yield was not achieved. Therefore, we next exam-ined the effect of the *N*-substituent of the imine component; *N*-benzhydrylimine **9b** was used with an expectation that the nucleophilic attack of iodide ion of **3a** to the iminium moiety of the zwitterionic intermediate would be suppressed by steric hindrance (entries 3 and 4). In these cases, yields were much improved as expected, but diastereoselectivities were diminished. Then *N*-*p*-methoxyphenylimine **9c** was employed in order to stabilize the zwitterionic intermediate (entry 5). In this case, the reaction proceeded smoothly, and the desired *cis*-β-lactam was obtained in nearly quantitative yield with excellent diastereoselectivity. Thus, from the viewpoints of yield and diastereoselectivity it was concluded that the combined use of an imine having *N*-*p*-methoxyphenyl moiety and the tosylate **3b** was the best for the present asymmetric Staudinger reaction.

Finally, under the optimized conditions, the asymmetric Staudinger reaction of optically active carboxylic acid **8** with various imines **12**, derived from *p*-anisidine, was carried out using **3b** in CH_2Cl_2 (Scheme 5). The results are summarized in Table 3.[15] As can be seen from Table 3, β-lactams **13** were obtained in nearly quantitative yields with high diastereoselectivity. Particularly, aromatic aldimines gave diastereomerically pure isomers, and the other stereoisomers were not detected at all (entries 1–3). In addition, each product of optically active β-lactams in Table 3 had excellent crystallizability, and diastereomerically pure isomer could be obtained very easily from a crude reaction mixture by a single recrystallization process.



Scheme 5

The preferable formation of **13** with a high degree of diastereoselectivity as shown in Table 3 can be explained as follows: the origin of diastereoselectivity for the asymmetric Staudinger reaction of ketenes with imines was thoroughly examined using AM1 calculations by Cossío and co-workers;[16] the diastereoselectivity was controlled by the difference in thermodynamic stability between two conformations in the transition states for the ring closure step of the zwitterionic intermediate **2**. In that report, they calculated the diastereoselectivity of the reaction of a chiral ketene, derived from 5-phenyloxazolidinone, with *N*-vinylformaldimine and concluded that this selectivity arose from the electrostatic repulsion between the lone pair of the carbonyl oxygen and the phenyl group of the oxazolidinone in the transition state leading to the minor isomer. This explanation is also applicable to the present asymmetric Staudinger reaction using an auxiliary derived from **1**. In addition, since the ketene derived from **1** has a bulkier auxiliary part compared with that derived from 5-phenyloxazolidinone, it can be assumed that the difference in thermodynamic stability between two conformations in the transition states would be larger than that in the case of 5-phenyloxazolidinone.

In summary, the Staudinger reaction of achiral carboxylic acids with various imines **4** proceeded smoothly under mild conditions by using **3a** to give β-lactams in high yields with excellent *cis*-selectivity. Upon applying this reaction system, a highly efficient asymmetric Staudinger reaction was accomplished, when a (+)-**1**-derived oxazolidinone was used as a chiral auxiliary. Since both enantiomers of **1** are available, proper use of the enantiomers gave β-lactams with desired absolute configuration. The present asymmetric Staudinger reaction would be quite useful for the synthesis of the precursors of various antibiotics, since the chiral auxiliary and the *N*-protected group in the products could be removed by simple chemical transformations.[17]

^{1}H NMR spectra were recorded in $CDCl_3$ solutions on a JEOL JNM-EX 270 at 270 MHz or a JEOL JNM-PMX60$_{SI}$ at 60 MHz, and chemical shifts are reported in ppm downfield from TMS. IR spectra were recorded on a Jasco IR 810 using KBr disks. Mps were determined on a Mitamura Riken Kogyo MEL-TEMP in open capillary tubes and are uncorrected. Elemental analyses were performed by a Perkin Elemeter PE 2400. Optical rotations were recorded on a Jasco DIP-360. CH_2Cl_2 was distilled over P_2O_5 and then over CaH_2, and stored over molecular sieves. Merck Kieselgel 60 was used for column chromatography. Wako Wakogel B-5F was used for TLC (0.75 mm) on a glass plate (20 × 20 cm).

Imines; General Procedure:
To a stirred solution of an aldehyde (20 mmol) in anhyd CH_2Cl_2 (30 mL) at 0°C were successively added an amine (20 mmol) and a large excess of $MgSO_4$. The resulting mixture was stirred for 10 h at r.t.. The filtered solution was evaporated to give the crude imine, which was recrystallized from anhyd hexane/CH_2Cl_2 to give the pure imine.

(4*R*,5*S*)-4,5-Diphenyloxazolidin-2-one (6):
A mixture of (+)-(1*S*,2*R*)-2-amino-1,2-diphenylethanol [(+)-**1**][3] (4.28 g, 20.0 mmol), K_2CO_3 (0.28 g, 2.03 mmol), and diethyl carbonate (20 mL, 166 mmol) was heated under reflux for 8 h. The resulting mixture was washed with water (10 mL) and extracted with CH_2Cl_2 (300 mL), and then the extract was dried ($MgSO_4$). After removal of the volatiles under vacuum, the residue was recrystallized from toluene (45 mL) to give 3.93 g (81%) of **6** as a white solid; mp 237–239°C (lit.[18] mp 232.5–233.5°C).
^{1}H NMR ($CDCl_3$): δ = 5.3 (d, *J* = 8 Hz, 1H, PhC*H*N), 5.8 (br s, 1H, N*H*), 6.1 (d, *J* = 8 Hz, 1H, PhC*H*O), 6.9–7.5 (m, 10H, arom).
IR (KBr): ν = 3275, 1745, 1709, 1238, 717 cm^{-1}.
Anal. Calcd for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.85. Found: C, 75.30; H, 5.47; N, 5.88.

Ethyl [(4*R*,5*S*)-2-Oxo-4,5-diphenyloxazolidin-3-yl]acetate (7):
NaH (0.66 g, 60% mineral oil dispersion, 20.8 mmol) was placed in a two necked flask under argon and washed with anhyd hexane (3 × 5 mL). After addition of DMF (10 mL) to NaH, a solution of **6** (4.96 g, 20.7 mmol) in DMF (30 mL) was added to the suspension, and the mixture was stirred for 2 h at r.t.. Then, ethyl bromoacetate (2.74 mL, 24.9 mmol) was added dropwise in a period of 30 min, and the mixture was stirred for 30 min. The reaction was quenched with water (10 mL), and water (100 mL) was added to the mixture. Then, the solution was extracted with CH_2Cl_2 (3 × 50 mL). The combined extracts were washed with sat. aq NaCl (50 mL) and dried ($MgSO_4$). After removal of the solvent under vacuum, the product was isolated by silica gel column chromatography (hexane/EtOAc 4:1) to give 6.10 g (89%) of **7** as a white solid; mp 88°C; $[\alpha]_D$ –104.2 (*c* = 1.00, $CHCl_3$).
^{1}H NMR ($CDCl_3$): δ = 1.3 (t, *J* = 8 Hz, 3H, C*H*$_3$CH$_2$), 3.5 (d, *J* = 18 Hz, 1H, NC*H*$_2$COO), 4.2 (q, *J* = 8 Hz, 2H, CH$_3$C*H*$_2$), 4.6 (d, *J* = 18 Hz, 1H, NC*H*$_2$COO), 5.0 (d, *J* = 9 Hz, 1H, PhC*H*N), 6.0 (d, *J* = 9 Hz, 1H, PhC*H*O), 6.8–7.3 (m, 10H, arom).
IR (KBr): ν = 1763, 1738, 1417, 1215, 1022, 708 cm^{-1}.
Anal. Calcd for $C_{19}H_{19}NO_4$: C, 70.14; H, 5.89; N, 4.30. Found: C, 70.05; H, 5.97; N, 4.28.

[(4*R*,5*S*)-2-Oxo-4,5-diphenyloxazolidin-3-yl]acetic Acid (8):
A THF (20 mL) solution of **7** was added to a solution of KOH (2.99 g, 53.3 mmol) in aq MeOH/THF (35 mL, H_2O/MeOH/THF, 3:3:8), and the mixture was stirred for 1 h at r.t.. Then, 1 M aq HCl (100 mL) was added to the mixture. The organic layer was extracted with Et_2O (3 × 100 mL), and the combined extracts were washed with sat. aq NaCl (50 mL) and dried ($MgSO_4$). After removal of the solvent under vacuum, the residue was recrystallized from toluene (45 mL) to give 4.56 g (87%) of **8** as a white solid; mp 168°C; $[\alpha]_D$ –123.3 (*c* = 1.01, $CHCl_3$).
^{1}H NMR ($CDCl_3$): δ = 3.6 (d, *J* = 18 Hz, 1H, NC*H*$_2$COO), 4.6 (d, *J* = 18 Hz, 1H, NC*H*$_2$COO), 5.5 (d, *J* = 8 Hz, 1H, PhC*H*N), 6.0 (d, *J* = 8 Hz, 1H, PhC*H*O), 7.1–7.4 (m, 10H, arom), 10.6 (s, 1H, CO$_2$*H*).
IR (KBr): ν = 1750, 1704, 1441, 1223 cm^{-1}.

Table 4. Yields, Properties, and Spectroscopic Data of β-Lactams **5**

Product[a]	Yield (%)	mp (°C)	IR (KBr) ν (cm^{-1})	^{1}H NMR ($CDCl_3$/TMS) δ, *J* (Hz)
5a	87	114–115	1750, 1502, 1238, 760, 703	3.9 (d, *J* = 14, 1H, NC*H*$_2$Ph), 4.8 (d, *J* = 4, 1H, PhC*H*), 4.9 (d, *J* = 14, 1H, NC*H*$_2$Ph), 5.4 (d, *J* = 4, 1H, PhOC*H*), 6.6–7.5 (m, 15H, arom)
5b	88	202–203	1750, 1518, 1498, 1245	3.8 (s, 3H, O*Me*), 5.4 (d, *J* = 5, 1H, PhC*H*), 5.6 (d, *J* = 5, 1H, PhOC*H*), 6.7–7.8 (m, 14H, arom)
5c	85	177–178	1742, 1518, 1242	3.8 (s, 6H, 2O*Me*), 5.4 (d, *J* = 5, 1H, *p*-MeOC$_6$H$_4$C*H*), 5.6 (d, *J* = 5, 1H, PhOC*H*), 6.6–7.6 (m, 13H, arom)
5d	95	184–186	1742, 1518, 1498, 1235	3.8 (s, 3H, O*Me*), 5.4 (d, *J* = 5, 1H, *p*-ClC$_6$H$_4$C*H*), 5.6 (d, *J* = 5, 1H, PhOC*H*), 6.8–7.6 (m, 13H, arom)
5e	quant.	181–182	1738, 1518, 1252, 1120, 755	3.8 (s, 3H, O*Me*), 5.0 (dd, *J* = 5, 8, 1H, PhCH=CHC*H*), 5.5 (d, *J* = 5, 1H, PhOC*H*), 6.4 (dd, *J* = 8, 16, 1H, PhCH=C*H*CH), 6.9 (d, *J* = 16, 1H, PhC*H*=CHCH), 6.9–7.8 (m, 14H, arom)
5f[b]	92	147–148	1745, 1515, 1240, 758	3.8 (s, 3H, O*Me*), 5.2 (d, *J* = 5, 1H, PhC≡CC*H*), 5.5 (d, *J* = 5, 1H, PhOC*H*), 6.8–8.1 (m, 14H, arom)
5g	89	185–196	1782, 1765, 1725, 1395, 728, 705	4.2 (d, *J* = 16, 1H, NC*H*$_2$Ph), 5.0 (d, *J* = 5, 1H, PhthNC*H*), 5.1 (d, *J* = 16, 1H, NC*H*$_2$Ph), 5.5 (d, *J* = 5, 1H, PhOC*H*), 7.1–8.1 (m, 14H, arom)
5h	89	192–195	1750, 1723, 1515, 1388, 1250, 835	3.8 (s, 3H, O*Me*), 5.1 (dd, *J* = 5, 8, 1H, PhCH=CHC*H*), 5.7 (d, *J* = 5, 1H, PhthN), 6.3 (dd, *J* = 8, 16 Hz, 1H, PhCH=C*H*CH), 6.6–8.1 (m, 14H, arom + PhC*H*=CHCH)

[a] All new compounds gave satisfactory microanalyses: C ± 0.31, H ± 0.30, N ± 0.30.
[b] Data for the *cis*-isomer.

Table 5. Yields, Properties, and Spectroscopic Data of Optically Active β-Lactams **10**, **13**

Product[a]	Yield (%)	mp (°C)	$[\alpha]_D$ (*c*, $CHCl_3$)	IR (KBr) ν (cm^{-1})	^1H NMR ($CDCl_3$/TMS) δ, *J* (Hz)
10a	54	240–242	–81.9 (0.11)	1758, 1748, 1460, 1435, 1403, 700	4.17 (d, *J* = 14.5, 1H, NC*H*$_2$Ph), 4.25 (dd, *J* = 5.0, 8.9, 1H, PhCH=CHC*H*), 4.48 (d, *J* = 4.9, 1H, NC*H*), 4.66 (d, *J* = 15.2, 1H, NC*H*$_2$Ph), 5.06 (d, *J* = 8.3, 1H, PhC*H*N), 5.82 (d, *J* = 8.6, 1H, PhC*H*O), 6.21 (dd, *J* = 8.9, 15.8, 1H, PhCH=C*H*CH), 6.57 (d, *J* = 15.8, 1H, PhC*H*=CHCH), 6.98–7.60 (m, 20H, arom)
10b[b]	99	224–225	16.9 (0.12)	1760, 1745, 1458, 1382, 700	4.24 (dd, *J* = 5.3, 8.9, 1H, PhCH=CHC*H*), 4.48 (d, *J* = 4.9, 1H, NC*H*), 5.08 (d, *J* = 8.6, 1H, PhC*H*N), 5.82 (d, *J* = 8.3, 1H, PhC*H*O), 6.05 (s, 1H, NC*H*Ph$_2$), 6.25 (dd, *J* = 8.9, 15.8, 1H, PhCH=C*H*CH), 6.38 (d, *J* = 16.2, 1H, PhC*H*=CHCH), 6.89–7.34 (m, 25H, arom)
13a	91	274–276	–58.4 (0.11)	1768, 1518, 1250	3.75 (s, 3H, O*Me*), 3.83 (s, 3H, O*Me*), 4.62 (d, *J* = 5.3, 1H, NC*H*), 4.71 (d, *J* = 8.6, 1H, PhC*H*N), 5.16 (d, *J* = 5.3, 1H, *p*-MeOC$_6$H$_4$C*H*), 5.31 (d, *J* = 8.6, 1H, PhC*H*O), 6.78–7.36 (m, 20H, arom)
13b	94	261–263	–41.5 (0.12)	1755, 1517, 1250, 703	3.75 (s, 3H, O*Me*), 4.65 (d, *J* = 5.3, 1H, NC*H*), 4.70 (d, *J* = 8.6, 1H, PhC*H*N), 5.21 (d, *J* = 5.3, 1H, PhC*H*), 5.21 (d, *J* = 7.9, 1H, PhC*H*O), 6.78–7.51 (m, 19H, arom)
13c	quant.	295–299	–23.8 (0.09)	1768, 1517, 1253	3.75 (s, 3H, O*Me*), 4.77 (d, *J* = 5.3, 1H, NC*H*), 4.84 (d, *J* = 8.6, 1H, PhC*H*N), 5.20 (d, *J* = 5.3, 1H, *p*-ClC$_6$H$_4$C*H*), 5.45 (d, *J* = 8.3, 1H, PhC*H*O), 6.78–7.36 (m, 18H, arom)
13d[b]	97	270–275	–79.2 (0.11)	1745, 1510, 1245	3.75 (s, 3H, O*Me*), 4.64 (d, *J* = 5.3, 1H, PhCH=CHC*H*), 4.84 (dd, *J* = 5.3, 8.9, 1H, NC*H*), 5.14 (d, *J* = 8.3, 1H, PhC*H*N), 5.85 (d, *J* = 8.3, 1H, PhC*H*O), 6.41 (dd, *J* = 8.9, 16.2, 1H, PhCH=C*H*CH), 6.81–7.45 (m, 20H, arom + PhC*H*=CHCH)
13e[b]	90	257–261	–90.4 (0.11)	1765, 1758, 1519, 1418, 1395, 1250, 760, 699	3.77 (s, 3H, O*Me*), 4.56 (d, *J* = 5.0, 1H, NC*H*), 4.95 (d, *J* = 4.9, 1H, PhC≡CC*H*), 5.31 (d, *J* = 8.9, 1H, PhC*H*N), 5.86 (d, *J* = 8.6, 1H, PhC*H*O), 6.86–7.57 (m, 19H, arom)

[a] All new compounds gave satisfactory microanalyses: C ± 0.31, H ± 0.30, N ± 0.30.
[b] Data for the major diastereomer.

Anal. Calcd for $C_{17}H_{15}NO_4$: C, 68.68; H, 5.09; N, 4.71. Found: C, 68.66; H, 5.15; N, 4.75.

β-Lactams 5a; Typical Procedure:
To an anhyd CH_2Cl_2 (5 mL) solution of phenoxyacetic acid (298.8 mg, 1.91 mmol) and 2-chloro-1-methylpyridinium iodide **3a** (515.2 mg, 2.02 mmol) were successively added Et_3N (0.64 mL, 4.59 mmol) and an imine (2.29 mmol) under argon, and the mixture was stirred under the conditions listed in Table 1. Then, water (5 mL) was added to the mixture in order to quench the reaction. The organic layer was extracted with CH_2Cl_2 (3 × 30 mL), and the combined extracts were washed with sat. aq NaCl (30 mL) and dried ($MgSO_4$). After removal of the solvent under vacuum, the product was isolated by silica gel column chromatography (CH_2Cl_2/hexane 1:1) to give **5** as a white solid (for analytical and spectral data, see Table 4).

Optically Active β-Lactams 10a–c; 11a–c, 13a–e; 14a–e; General Procedure:
To an anhyd CH_2Cl_2 (5 mL) solution of chiral glycine derivative **8** (0.30 mmol) and 2-chloro-1-methylpyridinium *p*-toluenesulfonate **(3b)**[19] (0.36 mmol) were successively added Et_3N (0.72 mmol) and (*N*-*p*-methoxyphenyl)imine **12** (0.33 mmol) at 0 °C under argon, and the solution was stirred for 10 h. The mixture was allowed to warm up to r.t. and further stirred for 14 h. Then, water (5 mL) was added to the mixture. The organic layer was extracted with CH_2Cl_2 (3 × 30 mL), and the combined extracts were washed with sat. aq NaCl (30 mL) and dried ($MgSO_4$). After removal of the solvent under vacuum, the product was isolated by silica gel column chromatography (CH_2Cl_2/hexane 1:1) to give a mixture of **13** and **14** as a white solid (Table 5).

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