A Facile and Highly Diastereoselective Aziridination of Chiral Camphor *N*-Enoylpyrazolidinones with *N*-Aminophthalimide

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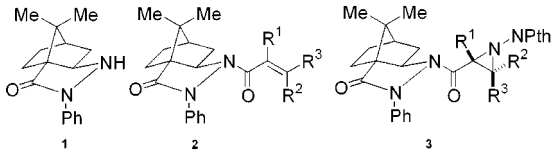
Reaction of various chiral camphor *N*-enoylpyrazolidinones **2a**−**g** with *N*-aminophthalimide in the presence of lead tetraacetate in CH_2Cl_2 proceed smoothly afford the corresponding *N*-phthalimidoaziridines (**3a**−**e**, **4f**−**g**) with excellent material yields (86−95%) at room temperature in 5 min. High levels of diastereoselectivities (up to >95:5 dr) were obtained. The solvent effect was investigated, and the auxiliary can be easily recovered in high yields under mild reaction conditions.

The synthesis of aziridine derivatives has received much attention in recent years, for they are versatile building blocks for the synthesis of a wide range of nitrogen-containing substances.[1] Many biologically active substances such as amino acids, β-lactam antibiotics, and alkaloids were derived from aziridines. The regiospecific reductive cleavage of aziridine-2-carboxylates providing α- or β-amino acids has been reported with excellent yield.[2] The use of metal-mediated chiral aziridines for asymmetric transformations has been reported.[3] It is not surprising that many efforts have been devoted to an efficient construction of the constrained three-membered ring system.[3,4] Diastereoselective addition of a nitrogen source to chiral α,β-unsaturated carboxylic acid derivatives is a conventional approach and has not yet been fully explored.[5] In continuation of our work on the stoichiometric reagent controller strategy in asymmetric synthesis, we were intrigued by the potential of the synthetic utility toward the preparation of aziridines from α,β-unsaturated carbonyl substrates **2a**−**g** derived from camphor pyrazolidinone **1**. Herein, we disclose high diastereofacial selectivities (up to >95:5 dr) of *N*-phthalimidoaziridine **3a**−**e**, **4f**−**g** can be obtained by treatment of the corresponding chiral *N*-enoylpyrazolidinones **2a**−**g** with *N*-aminophthalimide in the presence of lead tetraacetate.



1 2 3 4 5

a	R^1=H	R^2=H	R^3=H
b	R^1=H	R^2=H	R^3=Me
c	R^1=H	R^2=H	R^3=Et
d	R^1=H	R^2=H	R^3=Ph
e	R^1=H	R^2=Me	R^3=Me
f	R^1=Me	R^2=H	R^3=H
g	R^1=Me	R^2=H	R^3=Me
h	R^1=H	R^2=H	R^3=COOEt

Results and Discussion

A novel camphor pyrazolidinone auxiliary **1** has been developed in this laboratory and has proved to be

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synthetically useful for asymmetric reactions in several reaction types to achieve high stereoselection.[6] *N*-Enoylpyrazolidinones **2a**−**g** can be easily prepared from **1** with high chemical yields following standard acylation procedures. Vederas et al. have reported the oxidation of *N*-aminophthalimide with lead tetraacetate in the presence of *N*-enoylbornane[10,2]sultams resulting in stereospecific syn addition to afford the corresponding *N*-phthalimidoaziridines with 33−95% de.[5g] The analogous process was carried out with **2a** in CH_2Cl_2 for 5 min to give aziridine **3a** as the major product (entry 1). The structure of **3a** was initially assigned by ^{1}H and ^{13}C NMR and HRMS analyses, and the absolute stereochemistry was confirmed by single-crystal X-ray analysis.

Under the optimum conditions, treatment of **2b** with *N*-aminophthalimide in CH_2Cl_2 in the presence of lead tetraacetate provided 90% chemical yield with a ratio of >95:5 in favor the formation of **3b** (entry 2). The relative configuration of the aziridine moiety was initially assigned by ^{1}H NMR analysis ($^3J_{trans}$ = 5.0 Hz),[7] and the absolute stereochemistry was again confirmed by X-ray analysis of a single crystal. The use of *N*-2-pentenoyl pyrazolidinone (**2c**) gave a very high diastereoselectivity (entry 3). The electron-rich *N*-cinnamoylpyrazolidinone (**2d**) was investigated, and the desired products were isolated with low stereoselectivity (entry 4). The use of β,β-dimethyl substituent (**2e**) affords aziridine **3e** with high stereoselectivity (entry 5). The stereoselectivity drops significantly if an α-substituent is present. Thus, the use of *N*-methacryloyl pyrazolidinone (**2f**) to give moderate stereoselectivity (**3f**/**4f** = 20:80) (entry 6). Interestingly, the selectivity rebounds with the presence of an additional β-substituent (entry 7). The major isomeric product was assigned to be **4g**. The absolute stereochemistry assignments of **4f** and **4g** are based on the conformational analysis of **2f** and **2g** in the solid state, but studies are in progress to confirm these assignments.

The solvent effect was studied to improve the diastereoselectivity of **2d** and **2f**. A wide variety of solvents (THF, CH_3CN, toluene, DMSO, $PhCF_3$) were screened without success. To our surprise, high stereoselectivity (**3d**/**4d** = 95:5) was obtained when **2d** was treated with *N*-aminophthalimide in $CHCl_3$ (entry 8). However, for **2f** the selectivity was still moderate under the same reaction conditions (entry 9).

An interesting N-interconversion phenomena was observed for **3a**.[8] The kinetically formed *trans*-**3a** inverts at the aziridine nitrogen atom to the thermodynamically preferred *cis*-**3a**. Thus, the isolated pure (flash column chromatography, E. Merck silica gel 60, R_f = 0.2, hexane/ethyl acetate = 2:1) *trans*-**3a** slowly converts into its N-invertomer (R_f = 0.5, hexane/ethyl acetate = 2:1) and reached an equilibrium to give an 1:1 ratio of *trans*-**3a** and *cis*-**3a** after 18 h at room temperature. Several attempts to crystallize both isomers for absolute stereochemistry assignment failed. Finally, the single-crystal structure of *trans*-**3a** and co-crystal structures of *trans*-**3a** and *cis*-**3a** were obtained separately, which allowed for X-ray crystallographic analyses.[9] The inversion barrier at the aziridine nitrogen atom, as can be expected, is larger with the presence of α- and/or β-substituents and has a retarding effect on the rate of N-interconversion in the aziridine adducts.[10] Thus, the major aziridine **3b** (the phthalimido group and the C=O is cis-disposed) gives only detectable amounts of the corresponding isomer (TLC and ^{1}H NMR analyses) at room temperature over 18 h under the same operation conditions. To complete one cycle of the chiral auxiliary the initial adduct was subject to deacylation conditions.[11] Exposure of **3a** in MeOH to DMAP at 40 °C provided the desired 2-carboxyl aziridine derivatives **5a** without incident (82%). The auxiliary **1** was recovered in 94% yield.

The stereochemical outcome of the present study can be rationalized as reported previously.[6b,12] Preference for the planar s-cis conformation in *N*-enoylpyrazolidinones **2a**−**e** has been attributed to the presence of significant steric interactions in the s-trans between the Cα substituent and the camphor nucleus (Figure 1). The X-ray

Table 1. Aziridination of a Variety of *N*-Enoylpyrazolidinones (2a−g) with *N*-Aminophthalimide in the Presence of Lead Tetraacetate[a]

entry	substrate	solvent	*t* (min)	% yield[b] (**3** + **4**)	dr[c] (**3**:**4**)
1	**2a**	CH_2Cl_2	5	94	>95:5
2	**2b**	CH_2Cl_2	5	90	>95:5
3	**2c**	CH_2Cl_2	5	95	>95:5
4	**2d**	CH_2Cl_2	5	86	61:39
5	**2e**	CH_2Cl_2	5	92	>95:5
6	**2f**	CH_2Cl_2	5	88	20:80
7	**2g**	CH_2Cl_2	5	90	<5:95
8	**2d**	$CHCl_3$	5	91	95:5
9	**2f**	$CHCl_3$	5	89	20:80

[a] All reactions were carried out at room temperature. [b] Isolated yield. [c] Ratio determined by 200 MHz ^{1}H NMR and/or HPLC analyses with Japan Spectroscopic Co., LTD Finepak SIL NH2 column (4.6 × 250 mm, 10 μm); flow rate: 1.0 mL/min, *n*-hexane/2-propanol, 70/30 (v/v).

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(9) For the X-ray ORTEP drawings of *trans*-**3a** and *cis*-**3a**, see the Supporting Information.

(10) The reaction of monoethyl fumaroyl *N*-enoylpyrazolidinone **2h** (R^1 = R^2 = H R^3 = COOEt) with *N*-aminophthalimide affords the corresponding aziridines with 93% yield. However, the ^{1}H NMR spectrum as well as TLC analyses indicates a mixture of 1:1 N-invertomers were present. In addition to the steric repulsion (camphor nucleus and the phthalimido group), the dipole moment interaction between the ester functionality and the phthalimido group may play an important role for the rapid interconversion.

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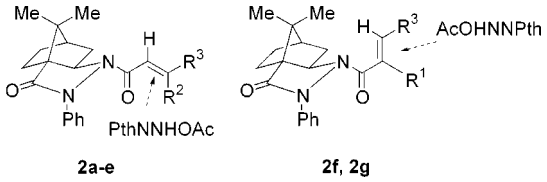

Figure 1. Proposed mechanism of the diastereoselective aziridination.

crystal structures of **2a**,**c**−**e** reveal this conformation in the solid state. On the other hand, for α-substituted *N*-methacryloylpyrazolidinone **2f** and *N*-tigloylpyrazolidinone **2g** the s-trans conformation predominates (X-ray crystallographic analyses) with the *β*-olefinic hydrogen toward the C3 (camphor numbering) orientation in these two structures. For **2a**−**e**, the syn attack of an *N*-acetoxyaminophthalimide intermediate is from the Cα *re* face while from the *si* face for **2f** and **2g** to afford the observed diastereoselectivity. The difference in stereoselectivity between **2f** and **2g** may be due to conformational changes induced by the presence of an additional *β*-methyl group in a congested area.

In summary, an efficient method has been developed for the synthesis of high to excellent stereoselectivity of *N*-phthalimidoaziridine adducts. Our procedure represents a simple and effective alternative to enantiopure 2-carboxylaziridine derivatives. This extends the synthetic application to the versatile and general utility of chiral auxiliary **1**. Further investigations on the enantioselective version of aziridination are currently undergoing.

Experimental Section

General Methods. All reactions were carried out in flame- or oven-dried glassware under a positive pressure of nitrogen. Air- and moisture-sensitive compounds were introduced by the use of a cannula through a rubber septum. Most reagents were commercially available and of synthetic grade. Tetrahydrofuran was distilled from sodium/benzophenone ketyl. Dichloromethane and toluene were dried over CaH_2 and distilled before use. Analytical thin-layer chromatography was performed with E. Merck silica gel 60F glass plates and flash column chromatography by the use of E. Merck silica gel 60 (230−400 mesh). HRMS values were measured by Finingan Mat TSQ-46C GC/MS/MS/DS spectrometer. Elemental analyses were performed by a Perkin-Elmer 2400 or 2400II Elemental Analyzer. ^{1}H and ^{13}C NMR spectra were recorded routinely in $CDCl_3$ on a Varian Gemini 2000 spectrometer.

General Procedure for the Preparation of *N*-Enoyl Pyrazolidinones 2a−g. Method A. To a solution of **1** (4.00 g, 15.55 mmol) in CH_2Cl_2 was added Et_3N (3.2 mL, 23.33 mmol) at 0 °C under N_2 atmosphere. This was followed by the addition of acryloyl chloride (1.54 mL, 18.66 mmol) dropwise, and the mixture was stirred for 30 min. The mixture was quenched with H_2O (15 mL) and extracted with CH_2Cl_2 (50 mL × 2). The layers were separated, and the organic layer was washed with brine and dried over Na_2SO_4. The solvent was removed in vacuo, and the product was crystallized from hexane/ethyl acetate (6:1) to give 4.66 g (96%) of **2a** as a colorless crystal: ^{1}H NMR ($CDCl_3$, 200 MHz) *δ* 7.39−7.29 (m, 4H), 7.18−7.12 (m, 1H), 6.38 (dd, 1H, *J* = 16.8, 2.6 Hz), 6.25 (dd, 1H, *J* = 16.8, 9.4 Hz), 5.68 (dd, 1H, *J* = 9.4, 2.6 Hz), 4.15 (dd, 1H, *J* = 7.8, 5.0 Hz), 2.75−2.65 (m, 1H), 2.36−2.24 (m, 1H), 2.16−2.06 (m, 1H), 2.03−1.95 (m, 2H), 1.48−1.26 (m, 2H), 1.14 (s, 3H), 1.11 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) *δ* 170.60, 164.57, 138.78, 129.77, 128.54, 127.57, 125.63, 121.14, 66.73, 59.10, 53.18, 46.46, 38.66, 28.24, 26.72, 20.15, 20.01; HRMS *m*/*z* 310.1682 (calcd for $C_{19}H_{22}N_2O_2$ 310.1681).

2b: ^{1}H NMR ($CDCl_3$, 200 MHz) *δ* 7.33−7.26 (m, 4H), 7.30−7.10 (m, 1H), 7.08 (qd, 1H, *J* = 15.2, 6.8 Hz), 5.95 (dd, 1H, *J* = 15.2, 1.8 Hz), 4.09 (dd, 1H, *J* = 7.8, 4.8 Hz), 2.70 (ddd, 1H, *J* = 9.8, 6.6, 3.4 Hz), 2.36−1.92 (m, 4H), 1.84 (dd, 3H, *J* = 6.8, 1.6 Hz), 1.52−1.25 (m, 2H), 1.13 (s, 3H), 1.10 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) *δ* 170.54, 165.68, 144.09, 138.95, 128.46, 128.42, 125.41, 122.03, 120.98, 66.49, 59.11, 53.37, 46.37, 38.99, 28.22, 26.77, 20.14, 20.09, 18.22; HRMS *m*/*z* 324.1838 (calcd for $C_{20}H_{24}N_2O_2$ 324.1838). Anal. Calcd for $C_{20}H_{24}N_2O_2$: C, 74.04; H, 7.26; N, 8.64. Found: C, 74.09; H, 7.30; N, 8.64.

2d: ^{1}H NMR ($CDCl_3$, 200 MHz) *δ* 7.66 (d, 1H, *J* = 15.6 Hz), 7.47−7.35 (m, 9H), 7.17−7.04 (m, 1H), 6.55 (d, 1H, *J* = 15.6 Hz), 4.20 (dd, 1H, 8.0, 4.8 Hz), 2.82 (ddd, 1H, *J* = 6.8, 5.6, 3.2 Hz), 2.35−2.26 (m, 2H), 2.08−2.04 (m, 2H), 1.55−1.48 (m, 2H), 1.18 (s, 3H), 1.14 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) *δ* 170.64, 165.50, 143.85, 139.01, 134.61, 130.32, 128.93, 128.63, 128.02, 125.64, 121.21, 117.49, 66.93, 59.17, 53.32, 46.53, 38.81, 28.31, 26.80, 20.20, 20.14; HRMS *m*/*z* 386.1976 (calcd for $C_{25}H_{26}N_2O_2$ 386.1994).

2e: ^{1}H NMR ($CDCl_3$, 200 MHz) *δ* 7.39−7.29 (m, 4H), 7.18−7.10 (m, 1H), 5.73 (s, 1H), 4.02−3.95 (dd, 1H, *J* = 8.0, 4.8 Hz), 2.77−2.68 (m, 2H), 2.33−2.23 (m, 1H), 2.14−1.99 (m, 3H), 2.07 (s, 3H), 1.85 (s, 3H), 1.52−1.36 (m, 1H), 1.13 (s, 3H), 1.10 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) *δ* 170.49, 167.55, 156.21, 139.19, 128.42, 125.19, 120.77, 116.10, 66.46, 59.13, 53.64, 46.26, 39.10, 28.21, 27.62, 26.81, 20.48, 20.12; HRMS *m*/*z* 338.1996 (calcd for $C_{21}H_{26}N_2O_2$ 338.1994). Anal. Calcd for $C_{21}H_{26}N_2O_2$: C, 74.52; H, 7.74; N, 8.28. Found: C, 74.20; H, 7.61; N, 8.10.

2f: ^{1}H NMR ($CDCl_3$, 200 MHz) *δ* 7.39−7.30 (m, 4H), 7.20−7.11 (m, 1H), 5.55 (qd, 1H, *J* = 1.6, 0.4 Hz), 5.52 (qd, 1H, *J* = 1.6, 0.8 Hz), 4.25 (dd, 1H, *J* = 8.0, 5.2 Hz), 2.29 (m, 2H), 2.01−1.92 (m, 3 H), 1.93 (dd, 3H, *J* = 0.8, 0.4 Hz), 1.41 (m, 2H), 1.14 (s, 6H); ^{13}C NMR ($CDCl_3$, 50 MHz) *δ* 169.77, 167.89, 140.31, 138.00, 128.61, 125.70, 121.02, 120.95, 69.47, 59.35, 51.78, 46.91, 39.43, 28.65, 26.47, 20.54, 19.84, 18.55; HRMS *m*/*z* 324.1842 (calcd for $C_{20}H_{24}N_2O_2$ 324.1838). Anal. Calcd for $C_{20}H_{24}N_2O_2$: C, 74.04; H, 7.46. Found: C, 73.71; H, 7.28.

Method B. A solution of thionyl chloride (7.3 mL, 100 mmol) and *trans*-2,3-dimethylacrylic acid (5.0 g, 50.0 mmol) was heated to 60 °C for 2 h. The excess thionyl chloride was removed in vacuo and the residue dried under a high vacuum pump line for 10 min. To this was then added CH_2Cl_2 (156 mL), and a solution of camphor pyrazolidinone **1** (1.5 g, 5.8 mmol) in CH_2Cl_2 was added dropwise at 25 °C under N_2 atmosphere. This was followed by the addition of Et_3N (7.5 mL, 55 mmol). The reaction was quenched with H_2O (15 mL) and extracted with CH_2Cl_2 (1 × 50 mL). The organic layer was washed (brine), dried (Na_2SO_4), filtered, and concentrated in vacuo. The crude product was purified by flash column chromatography, using hexane/ethyl acetate (4:1) as eluent to give 1.82 g (92%) of **2g** as a white solid: ^{1}H NMR ($CDCl_3$, 200 MHz) *δ* 7.36−7.27 (m, 4H), 7.19−7.10 (m, 1H), 6.25 (q, 1H, *J* = 6.2 Hz), 4.24−4.17 (dd, 1H, *J* = 7.8, 5.0 Hz), 2.38−2.23 (m, 2H), 2.06−1.87 (m, 3H), 1.81 (d, 3H, *J* = 6.2 Hz), 1.59 (s, 3H), 1.50−1.26 (m, 2H), 1.14 (s, 6H); ^{13}C NMR ($CDCl_3$, 50 MHz) *δ* 169.67, 169.61, 138.13, 132.91, 132.48, 128.59, 125.54, 120.86, 69.58, 59.34, 51.77, 46.88, 38.95, 28.69, 26.51, 20.53, 19.91, 13.93, 12.67; HRMS *m*/*z* 338.1992 (calcd for $C_{21}H_{26}N_2O_2$ 338.1994). Anal. Calcd for $C_{21}H_{26}N_2O_2$: C, 74.52; H, 7.74; N, 8.28. Found: C, 74.45; H, 7.79; N, 8.18.

2c: ^{1}H NMR ($CDCl_3$, 200 MHz) *δ* 7.33 (m, 4H), 7.20−7.16 (m, 1H), 7.05 (td, 1H, *J* = 15.2, 6.4 Hz), 5.92 (dd, 1H, *J* = 15.2, 1.8 Hz), 4.06 (dd, 1H, *J* = 8.2, 4.8 Hz), 2.71 (ddd, 1H, *J* = 8.2, 7.8, 3.4 Hz), 2.22 (m, 6H), 1.55−1.48 (m, 2H), 1.14 (s, 3H), 1.11 (s, 3H), 0.98 (t, 3H, *J* = 7.4 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) *δ* 170.57, 165.95, 150.16, 139.01, 128.54, 128.49, 125.43, 121.09, 119.66, 66.61, 59.10, 53.36, 46.39, 38.95, 28.25, 26.78, 25.40, 20.17, 20.11, 11.96; HRMS *m*/*z* 338.1991 (calcd for $C_{21}H_{26}N_2O_2$ 338.1994).

2h: ^{1}H NMR ($CDCl_3$, 200 MHz) *δ* 7.40−7.14 (m, 5H), 7.05 (d, 1H, *J* = 15.4 Hz), 6.79 (d, 1H, *J* = 15.4 Hz), 4.23 (dd, 1H, *J* = 8.0, 4.0 Hz), 4.23 (t, 2H, *J* = 7.2 Hz), 2.68−2.56 (m, 1H), 2.38−1.98 (m, 4H), 1.54−1.35 (m, 2H), 1.28 (t, 3H, *J* = 7.2 Hz), 1.14 (s, 3H), 1.13 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) *δ*

170.37, 165.12, 161.45, 138.20, 132.89, 132.32, 128.63, 126.05, 121.50, 67.06, 61.24, 59.19, 53.00, 46.63, 38.58, 28.25, 26.61, 20.15, 19.97, 13.96; HRMS *m/z* 382.1913 (calcd for $C_{22}H_{26}N_2O_4$ 382.1893). Anal. Calcd for $C_{22}H_{26}N_2O_4$: C, 69.09; H, 6.85. Found: C, 68.89; H, 6.64

General Procedure for the Preparation of Aziridines 3a−e and 4f−g. To a solution of **2c** (0.20 g, 0.59 mmol) and *N*-aminophthalimide (0.16 g, 0.89 mmol) in CH_2Cl_2 (6.0 mL) was added lead tetraacetate (0.44 g, 0.95 mmol) at room temperature under N_2 atmosphere for 5 min. The mixture was filtered and concentrated. The crude product was purified by flash column chromatography, using hexane/ethyl acetate (3:1) as eluent to give 0.28 g (95%) of **3c** as a white solid: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.69−7.56 (m, 4H), 7.37−7.23 (m, 4H), 7.12−7.03 (m, 1H), 4.90 (dd, 1H, J = 7.4, 5.0 Hz), 3.45 (td, 1H, J = 6.8, 5.0 Hz), 3.00 (d, 1H, J = 5.0 Hz), 2.74−2.64 (m, 1H), 2.40−2.29 (m, 2H), 2.15−2.03 (m, 2H), 1.86−1.68 (m, 3H), 1.58−1.47 (m, 1H), 1.16 (d, 3H, J = 7.0 Hz), 1.15 (s, 3H), 1.12 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 170.13 (x2), 164.79, 164.71, 138.27, 133.70 (×2), 129.97, 128.07 (×2), 125.10, 122.73 (×2), 120.59 (×2), 65.21, 58.90, 54.17, 49.16, 45.93, 42.92, 39.71, 27.74, 26.60, 23.94, 20.07, 19.76, 9.99; HRMS *m/z* 498.2267 (calcd for $C_{29}H_{30}N_4O_4$ 498.2267). Anal. Calcd for $C_{29}H_{30}N_4O_4$: C, 69.86; H, 6.06; N, 11.24. Found: C, 69.67; H, 6.07; N, 11.14.

trans-**3a**: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.80−7.68 (m, 4H), 7.37−7.32 (m, 4H), 7.16−7.08 (m, 1H), 4.72 (broad, 1H), 3.13 (dd, 1H, J = 7.4, 5.3 Hz), 2.85−2.65 (m, 3H), 2.40−2.26 (m, 1H), 2.19−2.01 (m, 3H), 1.68−1.40 (m, 2H), 1.25 (s, 3H), 1.14 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 170.17, 164.89 (×2), 164.68, 134.40 (×2), 133.96, 129.97 (×2), 128.68, 128.21, 125.84 (×2), 123.09 (×2), 66.56, 59.14, 53.36, 46.58, 46.03, 39.60, 36.32, 28.24, 27.84, 26.77, 20.23; HRMS *m/z* 470.1944 (calcd for $C_{27}H_{26}N_4O_4$ 470.1954). Anal. Calcd for $C_{27}H_{26}N_4O_4$: C, 68.92; H, 5.57; N, 11.91. Found: C, 68.86; H, 5.42; N, 12.05.

3b: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.67−7.55 (m, 4H), 7.37−7.25 (m, 4H), 7.13−7.02 (m, 1H), 4.92 (broad, 1H), 3.40 (qd, 1H, J = 5.6, 5.0 Hz), 2.94 (d, 1H, J = 5.0 Hz), 2.74−2.68 (m, 1H), 2.39−2.28 (m, 2H), 2.13−2.02 (m, 2H), 1.81−1.72 (m, 1H), 1.56−1.42 (m, 1H), 1.48 (d, 3H, J = 5.6), 1.14 (s, 3H), 1.11 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 170.20, 164.85, 164.76 (×2), 138.31, 133.80 (×2), 130.12, 128.18 (×2), 125.20, 122.91 (×2), 120.65 (×2), 66.12, 58.99, 54.41, 45.96, 44.40, 44.18, 39.80, 27.77, 26.70, 20.18, 19.83, 16.18; HRMS *m/z* 484.2116 (calcd for $C_{28}H_{28}N_4O_4$ 484.2111). Anal. Calcd for $C_{28}H_{28}N_4O_4$: C, 69.41; H, 5.82; N, 11.56. Found: C, 69.12; H, 5.82; N, 11.73.

3d: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.73−7.61 (m, 5H), 7.42−7.36 (m, 4H), 7.32−7.22 (m, 4H), 7.13−7.04 (m, 1H), 5.02 (dd, 1H, J = 7.8, 5.0 Hz), 4.42 (d, 1H, J = 5.0 Hz), 3.46 (d, 1H, J = 5.0 Hz), 2.75−2.67 (m, 1H), 2.44−2.33 (m, 2H), 2.16−2.05 (m, 2H), 1.87−1.76 (m, 1H), 1.62−1.51 (m, 1H), 1.15 (s, 3H), 1.13 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 170.26, 164.73 (×2), 164.07, 138.34, 134.78, 134.00 (×2), 130.27, 128.75 (×2), 128.72 (×2), 128.32 (×2), 127.22, 125.46, 123.15 (×2), 120.91 (×2), 65.36, 59.14, 54.56, 49.08, 46.17, 45.67, 40.07, 27.96, 26.84, 20.30, 19.94; HRMS *m/z* 546.2285 (calcd for $C_{33}H_{30}N_4O_4$ 546.2267). Anal. Calcd for $C_{33}H_{30}N_4O_4$: C, 72.51; H, 5.53; N, 10.25. Found: C, 71.96; H, 5.36; N, 10.19.

3e: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.73−7.59 (m, 4H), 7.40−7.14 (m, 5H), 4.46 (dd, 1H, J = 8.0, 4.8 Hz), 3.26 (s, 1H), 3.06−3.00 (m, 1H), 2.29−2.22 (m, 1H), 2.21−1.94 (m, 4H), 1.45 (s, 3H), 1.44−1.39 (m, 1H), 1.22 (s, 3H), 1.20 (s, 3H), 1.15 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 172.92 (x2), 165.20, 163.18, 139.77, 134.00 (x2), 130.25, 129.00 (x2), 126.36, 122.90 (x2), 121.39 (x2), 69.69, 58.98, 51.77, 50.78, 49.89, 47.10, 35.10, 28.56, 26.69, 20.41, 20.21, 18.82, 17.75; HRMS *m/z* 498.2291 (calcd for $C_{29}H_{30}N_4O_4$ 498.2267). Anal. Calcd for $C_{29}H_{30}N_4O_4$: C, 69.86; H, 6.06; N, 11.24. Found: C, 69.68; H, 6.21; N, 10.89.

An inseparable mixture of **3f** and **4f** (1:4) was isolated, and selected data are presented.

3f (minor): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 4.24 (dd, 1H, J = 8.0, 5.2 Hz), 1.69 (s, 3H), 1.08 (s, 3H), 1.06 (s, 3H). **4f** (major): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 4.49 (dd, 1H, J = 8.0. 5.0 Hz), 1.65 (s, 3H), 1.20 (s, 3H), 1.12 (s, 3H); HRMS *m/z* 484.2126 (calcd for $C_{28}H_{28}N_4O_4$ 484.2111).

4g: ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.61−7.51 (m, 4H), 7.26−7.09 (m, 4H), 7.01−6.93 (m, 1H), 4.24 (dd, 1H, J = 8.0, 5.0 Hz), 4.01 (q, 1H, J = 6.0 Hz), 2.61−2.52 (m, 1H), 2.30−1.97 (m, 5H), 1.68 (s, 3H), 1.52−1.37 (m, 1H), 1.30 (d, 3H, J = 6.0 Hz), 1.08 (s, 3H), 1.04 (s, 3H); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 169.84, 169.61, 165.06 (×2), 137.81, 133.55 (×2), 130.30, 128.27 (×2), 125.13, 122.70 (×2), 120.89 (×2), 68.00, 59.51, 52.60, 48.04, 46.60, 46.20, 38.80, 28.33, 26.51, 20.11, 20.07, 15.13, 12.72; HRMS *m/z* 498.2287 (calcd for $C_{29}H_{30}N_4O_4$ 498.2267). Anal. Calcd for $C_{29}H_{30}N_4O_4$: C, 69.86; H, 6.06; N, 11.24. Found: C, 69.82; H, 6.47.

Preparation of Chiral 2-Carboxylaziridines 5a. A solution of **3a** (0.10 g, 0.21 mmol) and DMAP (13 mg, 0.11 mmol) in MeOH (2 mL) was brought to 40 °C for 4 h. The mixture was filtered and concentrated. The crude product was purified by flash column chromatography, using hexane/ethyl acetate (6:1) as eluent to give 43 mg (82%) of **5a** as a white solid and the auxiliary **1** was recovered with 50 mg (94%): ^{1}H NMR ($CDCl_3$, 200 MHz) δ 7.78−7.66 (m, 4H), δ 3.81 (s, 3H), 3.21−3.14 (dd, 1H, J = 7.6, 5.8 Hz), 2.85−2.80 (dd, 1H, J = 7.6, 1.6 Hz), 2.85−2.80 (dd, 1H, J = 5.8, 1.6 Hz); ^{13}C NMR ($CDCl_3$, 50 MHz) δ 168.47, 164.45, 134.32, 129.94, 123.28, 52.65, 39.71, 36.42; HRMS *m/z* 246.0641 (calcd for $C_{12}H_{10}N_2O_4$ 246.0624). Anal. Calcd for $C_{12}H_{10}N_2O_4$: C, 58.54; H, 4.09; N, 11.38. Found: C, 58.31; H, 4.32; N, 11.12.

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Supporting Information Available: Copies of ^{1}H and ^{13}C NMR specta for compounds **2a**−**h**, **3a**−**e**,**g** and X-ray crystallographic data (tables of experimental details, bond lengths and angles and ORTEP diagrams) for structures **2a**,**c**−**g**, *trans*-**3a**, *cis*-**3a**, and **3b**,**d**,**e**. This material is available free of charge via the Internet at http://pubs.acs.org.

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