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FORMATION OF THE 1*H*-PYRROLO[3,4-*c*]PYRIDIN-1-ONE SKELETON *VIA* INTRAMOLECULAR DIELS–ALDER REACTION OF OXAZOLES

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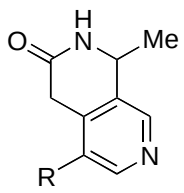
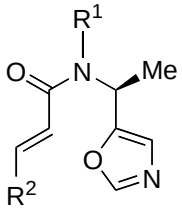
Abstract – The 1*H*-pyrrolo[3,4-*c*]pyridin-1-one derivatives (**4a**–**c**) were prepared through a route employing the intramolecular Diels–Alder reaction of the oxazole–olefins (**3a**–**c**). Conversion of the crotonamide (**3a**) into **4a** was effectively promoted by the addition of $Cu(OTf)_2$ as a catalyst.

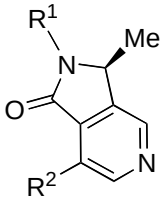
The intramolecular Diels–Alder reaction of oxazoles with olefinic dienophiles has become a useful tool to produce annulated pyridines,[1] since the first reports by two groups in 1983.[2] This procedure has been applied to the preparation of several pyridine-containing natural products, such as eupolauramine,[2a,3] normalindine,[4] suaveolines,[5] and two monoterpene alkaloids.[6] In connection with our ongoing synthetic studies on two naphthyridine alkaloids, jasminine (**1**)[7,8] and jasminidine (**2**),[7c] the formation of the 1*H*-pyrrolo[3,4-*c*]pyridin-1-one derivatives (**4a**–**c**) *via* the intramolecular Diels–Alder reaction of the oxazole–olefins (**3a**–**c**) was investigated.



1: R = CO_2Me
2: R = H



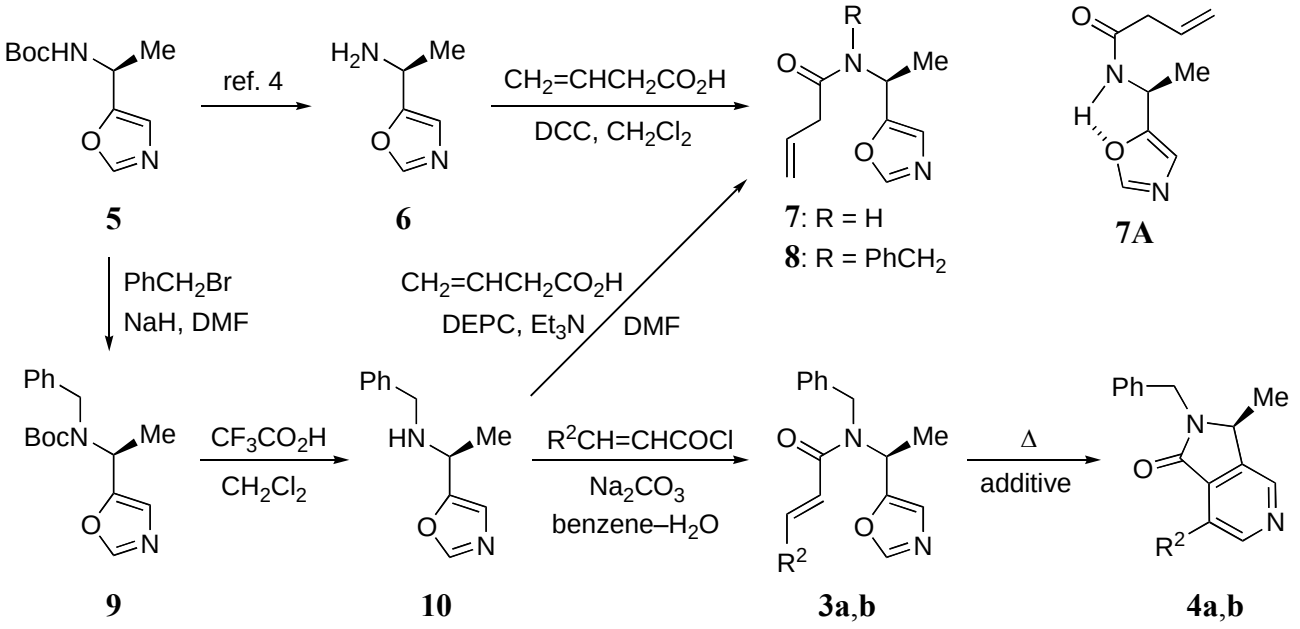
3a–c



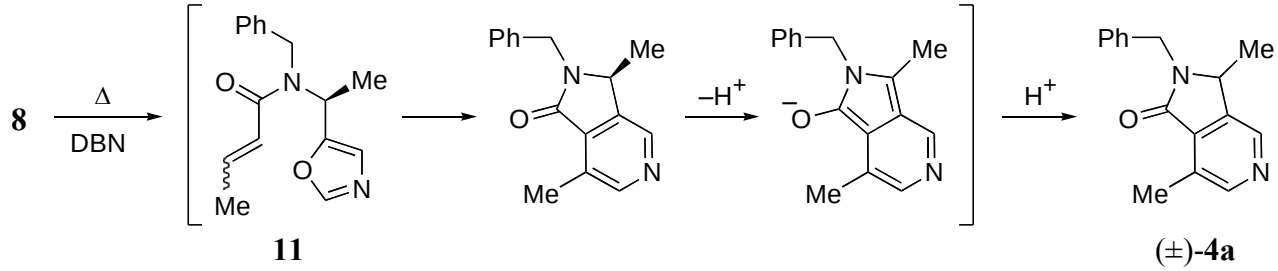
4a–c

a: $R^1 = PhCH_2$, R^2 = Me
b: $R^1 = PhCH_2$, R^2 = H
c: $R^1 = Ph_2CH$, R^2 = H

We first envisioned the 3-butenamide (**7**) as a very attractive precursor for the synthesis of **2** by exploiting the intramolecular oxazole cycloaddition. However, the initial attempt to heat **7**, derived from the oxazole amine (**6**),[4] in *o*-dichlorobenzene (*o*-DCB) at 150 °C failed to give the expected pyridine derivative, probably due to the internal hydrogen bonding of the amide NH with the oxazole oxygen as shown in **7A**, which prevents access of the dienophile to the oxazole ring.[9] Therefore, we planned to employ the *N*-benzylamide (**8**) obtained from **5**[4] through benzylation followed by deprotection of **9** and condensation of the *N*-benzylamine (**10**) with 3-butenoic acid. Treatment of **8** in *o*-DCB containing DBN (0.8 equiv)[3] at 150 °C for 8 h provided (±)-**4a** possessing the 1*H*-pyrrolo[3,4-*c*]pyridin-1-one skeleton in 62% yield, whereas the yield of the pyridine (**4a**) was quite low in the absence of DBN. The formation of (±)-**4a** under the former conditions would be considered to take place *via* the isomerization of **8** to the α,β-unsaturated isomer (**11**), as depicted in Scheme 2. These results led us to investigate the intramolecular Diels–Alder reaction of the α,β-unsaturated amides (**3a**–**c**) tethered to an oxazole ring.

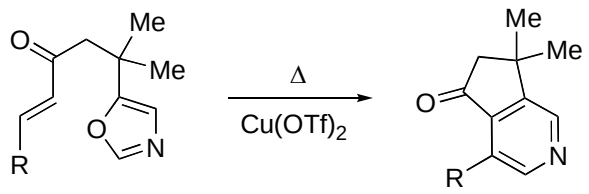


Scheme 1



Scheme 2

We initially examined the cycloaddition of the crotonamide (**3a**) derived from acylation of the amine (**10**) with crotonoyl chloride using the Schotten–Baumann conditions (Table 1). When a 0.05 M solution of **3a** in *o*-DCB was heated with DBN at 180 °C for 8 h under the conditions similar to those applied to **8**, the bicyclic pyridine (**4a**) was again obtained as a racemate in 83% yield (Entry 1). In the absence of DBN, the reaction was slow, giving **4a** in 40% yield after 24 h (Entry 2). The conversion of the oxazole–olefins (**12**) into the cyclopenta[*c*]pyridines (**13**) is known to be effectively promoted by the addition of a catalytic amount of $Cu(OTf)_2$.[10] The cycloaddition of **3a** also smoothly proceeded at 120 °C in the presence of $Cu(OTf)_2$ (10 mol %) to afford **4a** in 94% yield (Entry 3). The enantiomeric purity of the obtained **4a** was estimated to be 98% ee by a ^{1}H-NMR analysis using a chiral shift reagent. Treatment of **4a** with DBN in *o*-DCB at 180 °C for 8 h provided (±)-**4a** quantitatively, supporting the mechanism shown in Scheme 2.



12 R = CO_2Me (95%), R = H (55%) **13**

Scheme 3

Table 1. Intramolecular Diels–Alder Reactions of the Oxazole–Olefins (**3a–c**) in *o*-DCB[a)]

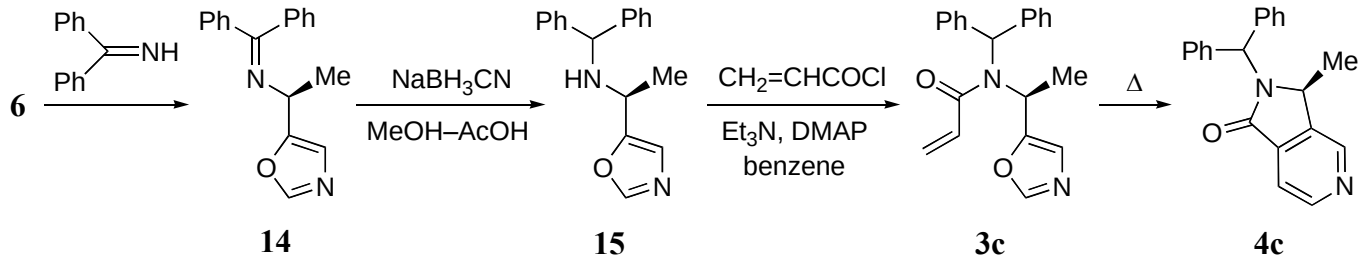
Entry	Substrate	Additive (mol %)	Temp. (°C)	Time (h)	Product	Yield (%)	% ee
1	**3a**	DBN (80)	180	8	(±)-**4a**	83	0
2	**3a**	——	180	24	**4a**	40	92
3	**3a**	$Cu(OTf)_2$ (10)	120	3	**4a**	94	98
4	**3a**	$Cu(OTf)_2$ (2)	150	0.75	**4a**	90	98
5	**3b**	DBN (80)	180	24	(±)-**4b**	56	0
6	**3b**	——	180	24	**4b**	8	70
7	**3b**	$Cu(OTf)_2$ (2)	150	5	**4b**	7	98
8	**3c**	——	180	1.5	**4c**	25	—[b)]
9	**3c**	$Cu(OTf)_2$ (10)	180	1.5	**4c**	25	—[b)]

[a)] All reactions were carried out in a 0.05 M solution.

[b)] Not determined.

The intramolecular Diels–Alder reaction of the acrylamide (**3b**) was next examined. On heating **3b**, prepared from **10** and acryloyl chloride, in *o*-DCB containing DBN at 180 °C for 24 h, the pyridine [(±)-**4b**] was obtained in 56% yield (Entry 5), whereas the yield of **4b** (70% ee) was very low without DBN (Entry 6). The desired cycloaddition of **3b** was only slightly promoted by the addition of $Cu(OTf)_2$, although **4b** obtained in low yield revealed a high enantiomeric purity (Entry 7). The differences in the reactivity between the crotonamide (**3a**) and the acrylamide (**3b**) are in general agreement with our observation that the intramolecular oxazole cycloaddition of a terminal olefin is difficult compared with that of an internal olefin possessing the ethyl group at the terminal position, probably due to the rapid decomposition of the former at elevated temperature.[11]

Sammes and co-workers have described that a bulky protecting group, such as the diphenylmethyl and trityl groups, accelerates the intramolecular Diels–Alder reaction between an olefin and a furan ring in comparison with the benzyl group.[12] The use of such steric buttresses could restrict conformational freedom and have an effect on increasing the proximity of the diene and dienophile moieties. The diphenylmethyl derivative (**3c**) was therefore prepared from the oxazole amine (**6**) through transimination with benzophenone imine,[13] followed by reduction of the imine (**14**) with sodium cyanoborohydride[14] and finally acylation of the resultant amine (**15**) with acryloyl chloride. However, the effect of the diphenylmethyl group was slight. Thus, the pyridine (**4c**) was obtained in 25% yield, regardless of the addition of $Cu(OTf)_2$, on heating **3c** at 180 °C for 1.5 h (Entries 8 and 9).



Scheme 4

In conclusion, a new access to the 1*H*-pyrrolo[3,4-*c*]pyridin-1-one skeleton has now become possible *via* the intramolecular Diels–Alder reaction of the oxazole–olefins (**3a**–**c**). The utility of the $Cu(OTf)_2$ catalyst in this reaction was exemplified by the effective conversion of the crotonamide (**3a**) into the pyridine (**4a**) accompanied by no racemization.

EXPERIMENTAL

General Notes. All melting points were determined on a Yamato MP-1 capillary melting point apparatus. Flash chromatography[15] was carried out by using Merck silica gel 60 (No. 9385). The

organic solutions obtained after extraction were dried over anhydrous $MgSO_4$ and concentrated under reduced pressure. The ratios of solvents in mixtures are shown in v/v. Spectra reported herein were recorded on a JEOL JMS-SX102A mass spectrometer, a Shimadzu FTIR-8400 IR spectrophotometer, or a JEOL JNM-GSX-500 (^{1}H 500 MHz) NMR spectrometer. Chemical shifts are reported in δ values relative to internal Me_4Si. Optical rotations were measured with a Horiba SEPA-300 polarimeter using a 1-dm sample tube.

(*S*)-*N*-[1-(5-Oxazolyl)ethyl]-3-butenamide (7). A mixture of **6**[4] (726 mg, 6.5 mmol), 3-butenoic acid (672 mg, 7.8 mmol), DCC (1.64 g, 7.9 mmol), and CH_2Cl_2 (30 mL) was stirred at rt for 70 min. The precipitate was removed by filtration, and the filtrate was washed successively with saturated aqueous $NaHCO_3$ and brine, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. Purification by flash chromatography (AcOEt) provided **7** (1.01 g, 87%) as a colorless solid, which was recrystallized from AcOEt–hexane (1 : 2) to give an analytical sample as colorless needles, mp 80–81 °C; $[\alpha]_D^{26}$ –122° (*c* 1.00, MeOH); MS *m*/*z*: 180 (M^+); IR (Nujol) ν, cm^{-1}: 3350 (NH), 1680 (amide CO); ^{1}H-NMR ($CDCl_3$) δ: 1.51 (3H, d, *J* = 6.9 Hz, Me), 3.03 (2H, ddd, *J* = 7.2, 1.2, 1.2 Hz, $COCH_2$), 5.24 (1H, ddt, *J* = 16.8, 1.2, 1.2 Hz) and 5.26 (1H, ddt, *J* = 10.2, 1.2, 1.2 Hz) (CH=C$\underline{H}_2$), 5.32 (1H, dq, *J* = 7, 6.9 Hz, C$\underline{H}$Me), 5.81 (1H, br, NH), 5.92 (1H, ddt, *J* = 16.8, 10.2, 7.2 Hz, C$\underline{H}$=CH_2), 6.93 [1H, s, C(4)-H], 7.81 [1H, s, C(2)-H]. *Anal*. Calcd for $C_9H_{12}N_2O_2$: C, 59.99; H, 6.71; N, 15.55. Found: C, 59.85; H, 6.69; N, 15.48.

(*S*)-*N*-Benzyl-[1-(5-oxazolyl)ethyl]carbamic acid *tert*-butyl ester (9). A mixture of **5**[4] (3.18 g, 15 mmol) and 60% NaH (647 mg, 16 mmol) in DMF (40 mL) was stirred at 0 °C in an atmosphere of N_2, and a solution of benzyl bromide (2.91 g, 17 mmol) in DMF (10 mL) was added dropwise over 15 min. After stirring at rt for 1.5 h, the reaction mixture was concentrated *in vacuo*. The residue was partitioned between ether and H_2O, and the ethereal extracts were washed with brine, dried, and concentrated to leave a colorless solid. Recrystallization of the solid from AcOEt–hexane (1 : 6) gave **9** (2.73 g). The mother liquor of this recrystallization was concentrated and the residual oil was purified by flash chromatography [AcOEt–hexane (1 : 3)] to furnish a second crop of **9** (1.45 g). The total yield of **9** was 4.18 g (92%). Further recrystallization from hexane afforded an analytical sample as colorless scales, mp 86.5–87.5 °C; $[\alpha]_D^{28}$ –43.0° (*c* 0.99, MeOH); MS *m*/*z*: 302 (M^+); IR (Nujol) ν, cm^{-1}: 1675 (carbamate CO); ^{1}H-NMR ($CDCl_3$) δ: 1.42 (9H, s, CMe_3), 1.45 (3H, d, *J* = 7.3 Hz, CH$\underline{Me}$), 4.2 and 4.35 (2H, br each, C$\underline{H}_2$Ph), 5.64 (1H, br, C$\underline{H}$Me), 6.88 [1H, s, C(4)-H], 7.1–7.3 (5H, m, Ph), 7.70 [1H, s, C(2)-H]. *Anal*. Calcd for $C_{17}H_{22}N_2O_3$: C, 67.53; H, 7.33; N, 9.26. Found: C, 67.55; H, 7.34; N, 9.29.

(*S*)-*N*-Benzyl-α-methyl-5-oxazolemethanamine (10). A mixture of **9** (986 mg, 3.3 mmol), trifluoroacetic acid (9 mL), and CH_2Cl_2 (9 mL) was stirred at 0 °C for 1.5 h. The reaction mixture was concentrated *in vacuo*, and the residue was dissolved in H_2O. The aqueous solution was made basic with K_2CO_3 and extracted with $CHCl_2$. The $CHCl_3$ extracts were dried and concentrated to leave **10** (635 mg, 96%) as a pale yellow oil, $[\alpha]_D^{27}$ –73.9° (*c* 1.00, MeOH); MS *m*/*z*: 202 (M^+); IR (film) ν, cm^{-1}: 3300 (NH); ^{1}H-NMR ($CDCl_3$) δ: 1.45 (3H, d, *J* = 6.8 Hz, Me), 1.85 (1H, br, NH), 3.68 and 3.76 (2H, d each, *J* = 13.2 Hz, C<u>H</u>$_2$Ph), 3.97 (1H, q, *J* = 6.8 Hz, C<u>H</u>Me), 6.93 [1H, s, C(4)-H], 7.2–7.35 (5H, m, Ph), 7.83 [1H, s, C(2)-H]; HRMS calcd for $C_{12}H_{14}N_2O$: 202.1106, found: 202.1105.

(*S*)-*N*-Benzyl-*N*-[1-(5-oxazolyl)ethyl]-3-butenamide (8). To a cooled solution of **10** (404 mg, 2.0 mmol) in DMF (6 mL) were added 3-butenoic acid (206 mg, 2.4 mmol), diethyl phosphorocyanidate (652 mg, 4.0 mmol), and Et_3N (404 mg, 4.0 mmol). After stirring at 0 °C for 30 min, the reaction mixture was partitioned between H_2O and $CHCl_3$. The $CHCl_3$ extracts were washed successively with saturated aqueous $NaHCO_3$ and brine, dried, and concentrated. Purification of the residual oil by flash chromatography [AcOEt–hexane (1 : 1)] gave **8** (414 mg, 77%) as a colorless oil, $[\alpha]_D^{21}$ –62.2° (*c* 1.01, MeOH); MS *m*/*z*: 270 (M^+); IR (film) ν, cm^{-1}: 1640 (amide CO); ^{1}H-NMR ($CDCl_3$) δ: 1.44 and 1.50 (3H, d each, *J* = 7.3 Hz, Me), 3.09 and 3.42 (2H, br d each, *J* = 6.3 Hz, $COCH_2$), 4.27, 4.63 (d each, *J* = 15.6 Hz) and 4.35, 4.51 (d each, *J* = 17.8 Hz) (2H, C<u>H</u>$_2$Ph), 5.04 (d, *J* = 17.6 Hz), 5.15 (d, *J* = 10.3 Hz), and 5.2–5.3 (m) (2H, CH=C<u>H</u>$_2$), 5.98 (1H, m, C<u>H</u>=CH_2), 6.15 (1H, q, *J* = 7.3 Hz, C<u>H</u>Me), 6.93 [1H, s, C(4)-H], 7.05–7.35 (5H, m, Ph), 7.70 [1H, s, C(2)-H]; HRMS calcd for $C_{16}H_{18}N_2O_2$: 270.1368, found: 270.1366.

(*S*)-*N*-Benzyl-*N*-[1-(5-oxazolyl)ethyl]-2-butenamide (3a). A mixture of a solution of **10** (1.37 g, 6.8 mmol) in benzene (30 mL) and a solution of Na_2CO_3 (789 mg, 7.4 mmol) in H_2O (30 mL) was stirred under ice-cooling, and a solution of crotonoyl chloride (920 mg, 8.8 mmol) in benzene (10 mL) was added dropwise over 15 min. After the mixture had been stirred for 30 min, the benzene layer was separated from the aqueous layer, which was extracted with benzene. The combined benzene solutions were washed successively with saturated aqueous $NaHCO_3$ and brine, dried, and concentrated to leave a yellow oil. Purification of the oil by flash chromatography [AcOEt–hexane (2 : 1)] provided **3a** (1.51 g, 82%) as a colorless oil, $[\alpha]_D^{24}$ –91.0° (*c* 1.02, MeOH); MS *m*/*z*: 270 (M^+); IR (film) ν, cm^{-1}: 1660 (amide CO); ^{1}H-NMR ($CDCl_3$) δ: 1.44 (3H, d, *J* = 6.8 Hz, NCH<u>Me</u>), 1.81 (3H, d, *J* = 6.3 Hz, CH=CH<u>Me</u>), 4.39 and 4.55 (2H, AB type d's, *J* = 18.1 Hz, C<u>H</u>$_2$Ph), 6.09 (1H, d, *J* = 14.7 Hz, C<u>H</u>=CHMe), 6.17 (1H, q, *J* = 6.8 Hz, NC<u>H</u>Me), 6.92 [1H, s, C(4)-H], 7.08 (1H, dq, *J* = 14.7, 6.3 Hz, CH=C<u>H</u>Me), 7.1–7.3 (5H, m, Ph),

7.68 [1H, s, C(2)-H]; HRMS calcd for $C_{16}H_{18}N_2O_2$: 270.1368, found: 270.1371.

(*S*)-*N*-Benzyl-*N*-[1-(5-oxazolyl)ethyl]-2-propenamide (3b). The Schotten–Baumann reaction of **10** (294 mg, 1.5 mmol) with acryloyl chloride (172 mg, 1.9 mmol) and work-up of the reaction mixture were carried out as described above for **3a**, giving **3b** (316 mg, 85%) as a colorless oil, $[\alpha]_D^{26}$ –87.0° (*c* 1.12, MeOH); MS *m*/*z*: 256 (M^+); IR (film) ν, cm^{-1}: 1651 (amide CO); ^{1}H-NMR ($CDCl_3$) δ: 1.47 (3H, d, *J* = 6.8 Hz, Me), 4.42 and 4.57 (2H, AB type d's, *J* = 18.1 Hz, C<u>H</u>$_2$Ph), 5.69 (1H, d, *J* = 10.0 Hz) and 6.50 (1H, d, *J* = 16.1 Hz) (CH=C<u>H</u>$_2$), 6.18 (1H, q, *J* = 6.8 Hz, C<u>H</u>Me), 6.39 (1H, dd, *J* = 16.1, 10.0 Hz, C<u>H</u>=CH$_2$), 6.95 [1H, s, C(4)-H], 7.1–7.3 (5H, m, Ph), 7.69 [1H, s, C(2)-H]; HRMS calcd for $C_{15}H_{16}N_2O_2$: 256.1211, found: 256.1210.

(*S*)-2-Benzyl-2,3-dihydro-3,7-dimethyl-1*H*-pyrrolo[3,4-*c*]pyridin-1-one (4a). Entry 3 in Table 1: A mixture of **3a** (113 mg, 0.42 mmol) and $Cu(OTf)_2$ (15.2 mg, 10 mol %) in *o*-DCB (8.4 mL) was heated at 120 °C in an atmosphere of Ar for 3 h. The reaction mixture was concentrated *in vacuo*, and the residual oil was purified by flash chromatography (AcOEt) to give **4a** (99 mg, 94%) as a yellow solid. The enantiomeric purity of this solid was shown to be 98% ee by means of ^{1}H-NMR spectroscopy using the chiral shift reagent tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]europium(III) [Eu(hfc)$_3$] in $CDCl_3$. Recrystallization from AcOEt–hexane (1 : 1) furnished an analytical sample as colorless prisms, mp 89.5–91.5 °C; $[\alpha]_D^{23}$ –123° (*c* 0.70, MeOH); IR (Nujol) ν, cm^{-1}: 1672 (lactam CO); ^{1}H-NMR ($CDCl_3$) δ: 1.47 (3H, d, *J* = 6.8 Hz, CH<u>Me</u>), 2.74 [3H, s, C(7)-Me], 4.25 and 5.30 (2H, d each, *J* = 14.9 Hz, C<u>H</u>$_2$Ph), 4.45 (1H, q, *J* = 6.8 Hz, C<u>H</u>Me), 7.25–7.35 (5H, m, Ph), 8.51 and 8.55 [1H each, s, C(4)-H and C(6)-H]. *Anal*. Calcd for $C_{16}H_{16}N_2O$: C, 76.17; H, 6.39; N, 11.10. Found: C, 76.07; H, 6.39; N, 11.10.

(*S*)-2-Benzyl-2,3-dihydro-3-methyl-1*H*-pyrrolo[3,4-*c*]pyridin-1-one (4b). Entry 7 in Table 1: A mixture of **3b** (143 mg, 0.56 mmol) and $Cu(OTf)_2$ (4.1 mg, 2 mol %) in *o*-DCB (11.2 mL) was heated at 150 °C in an atmosphere of Ar for 5 h. The reaction mixture was concentrated *in vacuo* to leave a brown oil. Purification of the oil by flash chromatography (AcOEt) afforded **4b** (9.3 mg, 7%) as a pale brown oil, $[\alpha]_D^{26}$ –102.9° (*c* 0.24, MeOH); MS *m*/*z*: 238 (M^+); IR (film) ν, cm^{-1}: 1685 (lactam CO); ^{1}H-NMR ($CDCl_3$) δ: 1.50 (3H, d, *J* = 6.8 Hz, Me), 4.27 and 5.35 (2H, d each, *J* = 15.1 Hz, C<u>H</u>$_2$Ph), 4.51 (1H, q, *J* = 6.8 Hz, C<u>H</u>Me), 7.25–7.35 (5H, m, Ph), 7.78 [1H, d, *J* = 4.9 Hz, C(7)-H], 8.76 [1H, s, C(4)-H], 8.78 [1H, d, *J* = 4.9 Hz, C(6)-H]; HRMS calcd for $C_{15}H_{14}N_2O$: 238.1106, found: 238.1103. The enantiomeric purity of this oil was estimated to be 98% ee in the same manner as described for **4a**.

(*S*)-*N*-(Diphenylmethylene)-α-methyl-5-oxazolemethanamine (14). A mixture of **6**[4] (114 mg, 1.0 mmol) and benzophenone imine (203 mg, 1.1 mmol) in CH_2Cl_2 (4 mL) was stirred at rt for 24 h. The reaction mixture was concentrated *in vacuo* to leave a yellow oil. Purification by flash chromatography [AcOEt–hexane (1 : 2)] furnished **14** (270 mg, 96%) as a yellow oil, $[\alpha]_D^{25}$ –186° (*c* 0.51, MeOH); MS *m*/*z*: 276 (M^+); IR (film) ν, cm^{-1}: 1620 (C=N); ^{1}H-NMR ($CDCl_3$) δ: 1.51 (3H, d, *J* = 6.4 Hz, Me), 4.67 (1H, q, *J* = 6.4 Hz, CHMe), 6.91 [1H, s, C(4)-H], 7.2–7.65 (10H, m, two Ph's), 7.80 [1H, s, C(2)-H]; HRMS calcd for $C_{18}H_{16}N_2O$: 276.1263, found: 276.1262.

(*S*)-*N*-(Diphenylmethyl)-α-methyl-5-oxazolemethanamine (15). A solution of **14** (780 mg, 2.8 mmol) in MeOH (15 mL) was brought to pH 6 by the addition of AcOH, and $NaCNBH_3$ (354 mg, 5.6 mmol) was added in portions. The reaction mixture was then stirred at rt for 5 h, made basic with K_2CO_3 after the addition of H_2O (20 mL), and extracted with $CHCl_3$. The $CHCl_3$ extracts were dried and concentrated. The residual oil was purified by flash chromatography [AcOEt–hexane (1 : 2)] to give **15** (611 mg, 78%) as a colorless solid. Recrystallization from hexane afforded an analytical sample as colorless fluffy needles, mp 39–41 °C; $[\alpha]_D^{24}$ –67.6° (*c* 0.49, MeOH); IR (Nujol) ν, cm^{-1}: 3280 (NH); ^{1}H-NMR ($CDCl_3$) δ: 1.45 (3H, d, *J* = 6.8 Hz, Me), 3.83 (1H, q, *J* = 6.8 Hz, CHMe), 4.75 (1H, s, $CHPh_2$), 6.84 [1H, s, C(4)-H], 7.15–7.4 (10H, m, two Ph's), 7.82 [1H, s, C(2)-H]. *Anal*. Calcd for $C_{18}H_{18}N_2O$: C, 77.67; H, 6.52; N, 10.06. Found: C, 77.68; H, 6.54; N, 10.03.

(*S*)-*N*-(Diphenylmethyl)-*N*-[1-(5-oxazolyl)ethyl]-2-propenamide (3c). A mixture of **15** (195 mg, 0.70 mmol), Et_2N (119 mg, 1.2 mmol), DMAP (9 mg), acryloyl chloride (89 mg, 0.98 mmol), and benzene (10 mL) was stirred at rt for 1.5 h. The reaction mixture was then washed successively with saturated aqueous $NaHCO_2$ and brine, dried, and concentrated. Purification of the residual oil by flash chromatography [AcOEt–hexane (1 : 1)] gave **3c** (205 mg, 88%) as a colorless oil, $[\alpha]_D^{24}$ –27.6° (*c* 0.62, MeOH); MS *m*/*z*: 332 (M^+); IR (film) ν, cm^{-1}: 1682 (amide CO); ^{1}H-NMR ($CDCl_3$) δ: 1.53 (3H, d, *J* = 7.3 Hz, Me), 5.38 (1H, br, $CHPh_2$), 6.05 (2H, br) and 6.26 (1H, d, *J* = 15.8 Hz) ($CH=CH_2$), 6.1 (1H, br, CHMe), 6.97 [1H, s, C(4)-H], 7.0–7.4 (10H, m, two Ph's), 7.67 [1H, s, C(2)-H]; HRMS calcd for $C_{21}H_{20}N_2O_2$: 332.1524, found: 332.1528.

(*S*)-2-(Diphenylmethyl)-2,3-dihydro-3-methyl-1*H*-pyrrolo[3,4-*c*]pyridin-1-one (4c). Entry 8 in Table 1: A solution of **3c** (110 mg, 0.33 mmol) in *o*-DCB (6.6 mL) was heated at 180 °C in an atmosphere of Ar for 1.5 h. The reaction mixture was concentrated *in vacuo*, and the residual oil was purified by flash chromatography [AcOEt–hexane (6 : 1)] to provide **4c** (26 mg, 25%) as a pale brown oil,

$[\alpha]_D^{24}$ +48.0° (*c* 0.13, MeOH); MS *m*/*z*: 314 (M^+); IR (film) ν, cm^{-1}: 1685 (lactam CO); ^{1}H-NMR ($CDCl_3$) δ: 1.37 (3H, d, *J* = 6.7 Hz, Me), 4.57 (1H, q, *J* = 6.7 Hz, C<u>H</u>Me), 6.69 (1H, s, C<u>H</u>Ph_2), 7.2–7.4 (10H, m, two Ph's), 7.75 [1H, d, *J* = 4.9 Hz, C(7)-H], 8.73 [1H, s, C(4)-H], 8.77 [1H, d, *J* = 4.9 Hz, C(6)-H]; HRMS calcd for $C_{21}H_{18}N_2O$: 314.1419, found: 314.1416.

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