Convenient Synthesis of Enantiomerically Enriched β-Cyclopropylalaninol Derivatives by Kinetic Resolution via (−)-Sparteine-Mediated Deprotonation

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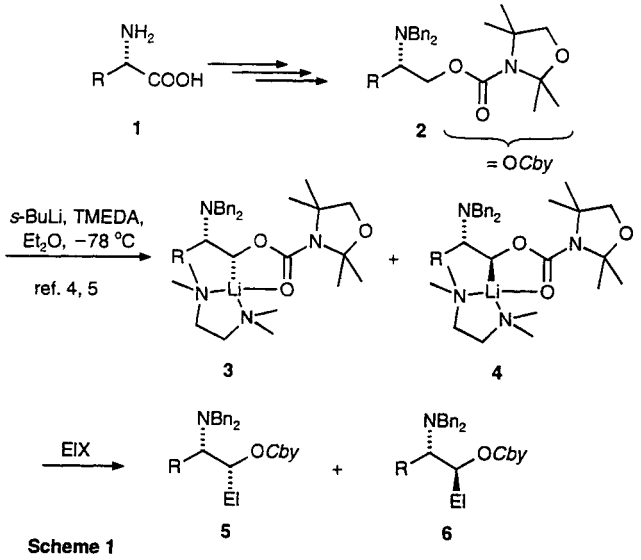
Received 11 April 1997

Dedicated to Professor Peter Welzel on the occasion of his 60th birthday

The racemic mixture of the protected β-cyclopropylalaninol derivative **11** was subjected to asymmetric deprotonation by means of *sec*-butyllithium/(−)-sparteine, resulting in a preferential abstraction of the α-*pro*-*S*-H in (*R*)-**11**; (*S*)-**11** remains untouched.

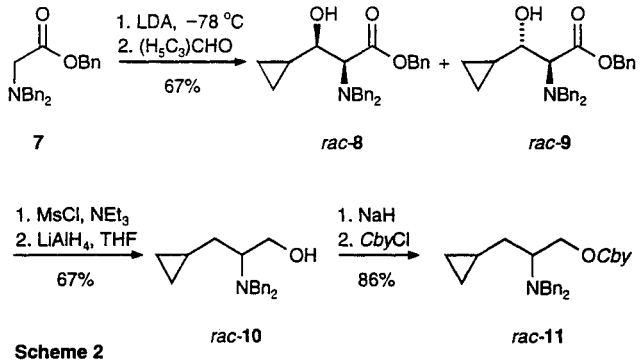
Enantio- and diastereomerically enriched β-amino alkanols play an important role in modern organic synthesis and are useful as building blocks, chiral catalysts and auxilliaries.[1] Hence this substructure is part of many pharmacologically active compounds,[2] and methods for selective preparation are a topic of current investigations.[3] Recently we published a general method for the diastereoselective synthesis of β-aminoalkyl carbamates[4] (Scheme 1). The deprotonation of (*S*)-aminoalkyl carbamates **2** (often derived from naturally occurring amino acids **1**) with *sec*-butyllithium/TMEDA (tetramethylethylenediamine) leads diastereoselectively to configurationally stable ion pairs **3** and **4**. Upon treatment of **3**/**4** with electrophiles, the substitution products **5**/**6** are obtained in high yields and with a diastereomeric ratio strongly depending on the bulkiness of the substituent R. Under the reaction conditions (Et_2O, −78 °C), kinetically controlled deprotonation of (*S*)-**2** normally leads to the abstraction of the *pro*-*R* proton, furnishing **5** as main product.



Scheme 1

Attempts to generate the diastereomers **6** from (*S*)-**2** by performing the reaction in the presence of *sec*-butyllithium/(−)-sparteine **(12)**, which shows a strong preference for the abstraction of the *pro*-*S*-proton,[5] often failed because of a marked mismatched-pair situation.[6] In contrast, the substrate-controlled *like*-preference and the reagent-induced *pro*-*S*-selectivity must match for the (*R*)-enantiomer *ent*-**2**. It is therefore presumable that the reaction of *sec*-butyllithium/(−)-sparteine with a racemic mixture of **2** can give rise to a kinetic resolution of the enantiomers, resulting in a preferred deprotonation of (*R*)-**2** and leaving (*S*)-**2** mostly unaffected.[7] This hypothesis was tested on the racemic *N*,*N*-dibenzyl-3-cyclopropylpropyl carbamate *rac*-**11**. Compound **11** was selected, since the enantio-enriched amino alcohol is not directly available from natural amino acids and, furthermore, we have an easy way for the stereochemical correlation.

The preparation of *rac*-**11** is shown in Scheme 2. *N*,*N*-Dibenzylglycine benzyl ester **(7)**[8] was converted to its enolate by means of lithium diisopropylamide (LDA), which gave, upon subsequent reaction with cyclopropane carboxaldehyde, a mixture of β-hydroxy-α-amino ester *rac*-**8** and *rac*-**9** in a total yield of 67%.[9] The relative configuration is based on NMR criteria,[9] and more importantly on the fact that the *syn*-diastereomers always have the greatest mobility on silica gel.[9] Subsequent mesylation of the hydroxy group and reductive cleavage with lithium aluminium hydride resulted in the smooth formation of β-cyclopropylalaninol *rac*-**10**. For carbamoylation, sodium alkoxide of *rac*-**10** was trapped with 2,2,4,4-tetramethyl-1,3-oxazolidine-3-carbonyl chloride[10] (*Cby*Cl) to yield the required carbamate *rac*-**11** in 86% yield.



Scheme 2

First we examined the internal induction of the existing stereogenic centre and the reactivity of the lithiated intermediates against some common electrophiles (Table 1, entries 1, 5, 7, 9) by carrying out the reaction with *sec*-

Table 1. Yields, Diastereomeric Ratios, and Enantiomeric Excesses in the Reaction of *rac*-**11** with Various Electrophiles

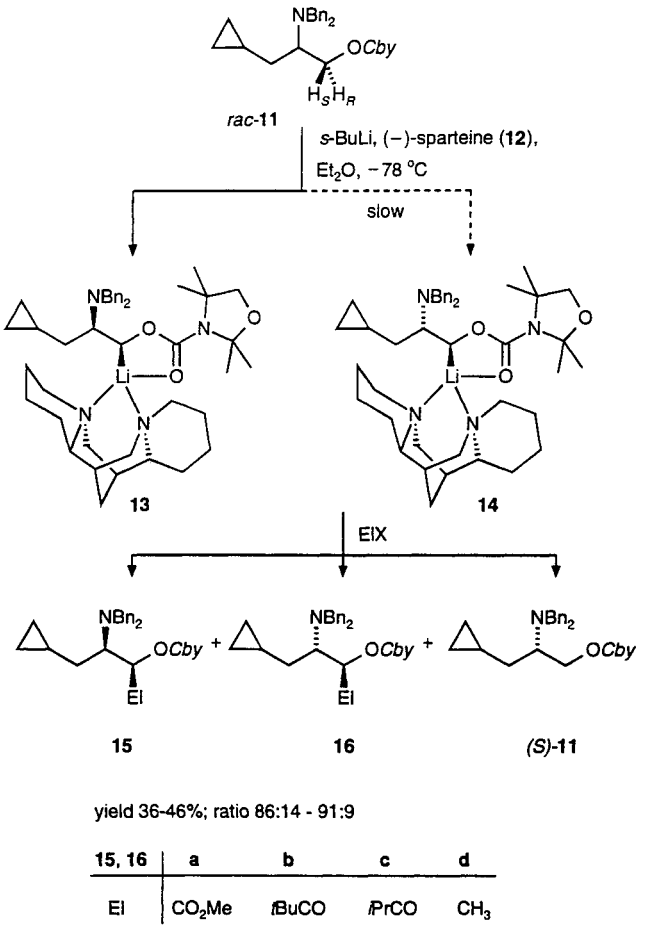
15/16	EIX	Diamine	Time (h)	Yield (%)	*dr*[a]	*ee* (**15**)[b] (%)	Yield (**11**) (%)	*ee* (**11**)[c] (%)
a	CO_2/CH_2N_2	TMEDA	3.5	89	83:17	*rac*	–	–
a	CO_2/CH_2N_2	**12**	3.5	26	91:9	> 95	67	34
a	CO_2/CH_2N_2	**12**	7	36	92:8	90	63	43
a	CO_2/CH_2N_2	**12**	10	46	86:14	> 95	42	80
b	*t*-BuCOCl	TMEDA	3.5	78	88:12	*rac*	–	–
b	*t*-BuCOCl	**12**	10	38	91:9	–	42	85[d]
c	*i*-PrCOCl	TMEDA	3.5	88	86:14	*rac*	–	–
c	*i*-PrCOCl	**12**	10	36	90:10	> 95	35	84
d	MeI	TMEDA	3.5	60	83:17	*rac*	–	–

[a] Established by ^{1}H NMR spectroscopy.
[b] Determined by ^{1}H NMR spectroscopy in the presence of $Eu(hfc)_3$.
[c] Determined after removal of *CBy* group by ^{1}H NMR spectroscopy.
[d] $[\alpha]_D^{20} = -16.9$ ($c = 1.5$, CH_2Cl_2).

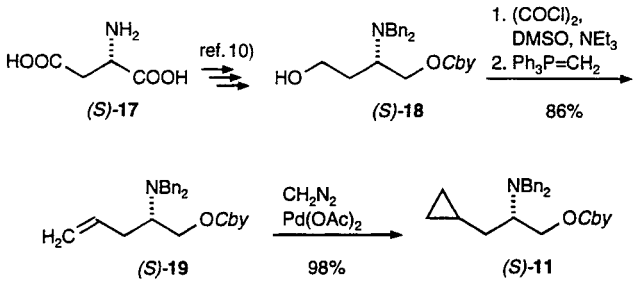
butyllithium/TMEDA. Under the reaction conditions (−78 °C, 3.5 h, Et_2O), a rapid deprotonation occurs and substitution products *rac*-**15a–d** and *rac*-**16a–d** were obtained in moderate to good yields. The diastereomeric ratio of 85:15 resembles to that observed for other aminoalkyl carbamates.[4]

The utilization of (−)-sparteine **(12)** instead of TMEDA, as well as an enhancement of reaction time up to 10 hours leads to a powerful kinetic resolution of *rac*-**11** (Scheme 3, Table 1, entry 4). The reaction of the lithiated intermediates **13** and **14** with CO_2 (followed by esterification with CH_2N_2) gave the esters **15a** and **16a** in a total yield of 46% (dr, 86:14). The enantiomeric excess of **15a** amounted to 95% ee and (*S*)-**11** was recovered consistently with a high stereoselectivity in a yield of 42% and 80% ee. Shorter reaction times of 7 hours and 3.5 hours, respectively (entries 2 and 3) resulted in lower yields of **15**/**16** and thus decreased the enantiomeric excess for recovered (*S*)-**11** (43% and 34% ee). The same procedure with other electrophiles like pivaloyl chloride or isobutyryl chloride shows similar results, indicating that the substitution step is independent of electrophile.

The (*R*)-configuration [(*S* for El = CH_3] for the new stereogenic centre of **15** is based on the well established fact that the use of the reagent *sec*-butyllithium/(−)-sparteine leads to the abstraction of *pro-S* proton and thus only the configuration of remaining (*S*)-**11** was proved by a chemical correlation (Scheme 4). The monocarbamate (*S*)-**18** [derived from (*S*)-asparaginic acid **(17)**[11]] yielded upon oxidation with oxalyl chloride/DMSO,[12] followed by Wittig methylenation,[13] the allylglycine derivative (*S*)-**19**. Cyclopropanation[14] with diazomethane/palladium(II) acetate afforded (*S*)-**11**. Its optical rotation $[\alpha]_D^{20} = -19.6$ ($c = 0.98$, CH_2Cl_2) compared with that of a sample of 85% ee prepared by kinetic resolution ($[\alpha]_D^{20} = -16.9$, $c = 1.5$, CH_2Cl_2) indicates that the configurations of (*S*)-**11** and thus **15a–d** are in agreement with our prediction mentioned above.



Scheme 3



Scheme 4

In summary we have demonstrated that action of *sec*-butyllithium/(−)-sparteine on a racemic mixture of β-cyclopropylalaninol carbamate (*rac*-**11**) leads to a powerful kinetic resolution resulting in formation of 1,2-amino alcohol derivatives of high enantiomeric excess.[15] With regard to configurations, it should be pointed out that these products could not be obtained easily from naturally occurring amino acids. Moreover, the necessary precursor is built up by a sequence of only five steps from cheap commercially available chemicals.

All experiments involving organometallic reagents were carried out under Ar in dried glasware. All solvents were purified by distillation and dried, if necessary, prior to use. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM 300 spectrometer. Optical rotations were recorded on Perkin-Elmer polarimeter 241. Products were purified by flash column chromatography on silica gel (40–63 μm).

N,N-Dibenzylglycine Benzyl Ester (7):
According to the general procedure,[8] a solution of glycine (15.0 g, 0.20 mol), K_2CO_3 (44.2 g, 0.32 mol) and NaOH (12.8 g, 0.32 mol) in H_2O/MeOH (1:1, 220 mL) was heated to reflux and subsequently benzyl bromide (119.7 g, 0.70 mol) was added dropwise. After 2 h of reflux the solution was cooled to r.t. and the residue was extracted with Et_2O (3 × 50 mL). The organic layers were dried ($MgSO_4$) and the solvents removed in vacuo. The remaining oil was recrystallized (Et_2O/EtOH, 1:1) to yield 36.1 g (52%) of **7** as colourless crystals; mp 53 °C.

IR (KBr): $\nu = 1720\ cm^{-1}$ (C=O).

^{1}H NMR ($CDCl_3$): $\delta = 3.32$ (s, 2H, NCH_2CO), 3.80 (s, 4H, NCH_2), 5.10 (s, 2H, OCH_2), 7.05–7.50 (m, 15 H_{arom}).

^{13}C NMR ($CDCl_3$): $\delta = 53.4$ (OCH_2), 57.7 (NCH_2), 65.9 (H_2CCO), 127.0, 128.2, 128.8 (CH_{arom}), 135.9 (OCH_2C_{arom}), 138.9 (NCH_2C_{arom}), 171.1 (CO_2).

$C_{23}H_{23}NO_2$	calc.	C	79.97	H	6.71	N 4.06
(345.4)	found		79.85		7.01	4.26

Benzyl *rac*-(2*R,3*S**)- and *rac*-(2*R**,3*R**) 2-Dibenzylamino-3-cyclopropyl-3-hydroxypropionate (*rac*-8 and *rac*-9):**
According to the general procedure,[9] to a solution of LDA [60.0 mmol, prepared from diisopropylamine (6.19 g) and 1.6 M BuLi (37.5 mL)] in THF (70 mL) was added at −78 °C a solution of **7** (17.62 g, 51.0 mmol) in THF (40 mL). After 1 h, cyclopropane carboxaldehyde (4.12 g, 60.0 mmol) dissolved in THF (20 mL) was added dropwise and stirring was continued for 2 h. The mixture was warmed to r.t. and poured into concd NH_4Cl solution (100 mL) and the aq layer was extracted with Et_2O (2 × 70 mL). After drying ($MgSO_4$) and removal of solvents in vacuo, the crude product was purified by column chromatography on silica gel with Et_2O/pentane as an eluent; total yield: 14.15 g (67%).

rac-**8**: colorless oil; R_f 0.46 (Et_2O/pentane, 1:2).

IR (film): $\nu = 3410$ (OH), $1715\ cm^{-1}$ (C=O).

^{1}H NMR ($CDCl_3$): $\delta = 0.0–0.3$ [m, 3H, $CH(CH_2)_2$], 0.3–0.5 [m, 1H, $CH(CH_2)_2$], 0.5–0.7 [m, 1H, $CH(CH_2)_2$], 1.6 (br s, 1H, OH), 3.25–3.50 (m, 4H, NCH, OCH, NCH_2), 3.97 (d, 2H, $J = 13.6$ Hz, NCH_2), 5.16 (d, 1H, $J = 12.2$ Hz, OCH_2), 5.25 (d, 1H, $J = 12.2$ Hz, OCH_2), 7.0–7.5 (m, 15 H_{arom}).

^{13}C NMR ($CDCl_3$): $\delta = 1.7$, 2.3 [$CH(CH_2)_2$], 13.9 [$CH(CH_2)_2$], 54.7 (NCH_2), 66.4 (OCH_2), 66.5 (COH), 70.8 (CHN), 127.4, 128.5, 128.6, 128.7, 129.1 (CH_{arom}), 135.7, 138.1 (C_{arom}), 170.3 (CO_2).

$C_{27}H_{29}NO_3$	calc.	C	78.04	H	7.04	N 3.37
(415.5)	found		77.90		7.02	3.61

rac-**9**: colorless solid; mp 106 °C; R_f 0.31 (Et_2O/pentane, 1:2).

IR (KBr): $\nu = 3440$ (OH), $1690\ cm^{-1}$ (C=O).

^{1}H NMR ($CDCl_3$): $\delta = 0.0–0.3$ [m, 3H, $CH(CH_2)_2$], 0.3–0.5 [m, 1H, $CH(CH_2)_2$], 0.8–1.0 [m, 1H, $CH(CH_2)_2$], 2.11 (br s, 1H, OH), 3.44 (d, 1H, $J = 7.2$ Hz, CHN), 3.48 (d, 2H, $J = 13.6$ Hz, NCH_2), 3.56 (dd, 1H, $J = 7.2$, 7.2 Hz, CHOH), 3.90 (d, 2H, NCH_2), 5.16 (d, 1H, $J = 12.2$ Hz, OCH_2), 5.30 (d, 1H, $J = 12.2$ Hz, OCH_2), 7.0–7.4 (m, 15 H_{arom}).

^{13}C NMR ($CDCl_3$): $\delta = 1.3$, 3.3 [$CH(CH_2)_2$], 15.1 [$CH(CH_2)_2$], 55.5 (NCH_2), 66.3 (OCH_2), 66.2 (CHOH), 73.0 (CHN), 127.1, 128.2, 128.4, 128.6, 128.8 (CH_{arom}), 135.9, 139.0 (C_{arom}), 172.1 (CO_2).

$C_{27}H_{29}NO_3$	calc.	C	78.04	H	7.04	N 3.37
(415.5)	found		77.77		7.12	3.76

***rac*-2-Dibenzylamino-3-cyclopropylpropanol (*rac*-10):**
$MeSO_2Cl$ (6.87 g, 60.0 mmol) was added at 0 °C to a solution of *rac*-**8** and *rac*-**9** (18.3 g, 44.0 mmol) and Et_3N (6.1 g, 60.0 mmol) in CH_2Cl_2 (150 mL). After 12 h of stirring at r.t., the mixture was hydrolyzed with 2 N NaOH (100 mL) and the aq phase was extracted with CH_2Cl_2 (2 × 40 mL). The organic layer was dried ($MgSO_4$) and the solvent removed in vacuo to yield a orange coloured oil which was used in the next step without purification. The oil was dissolved in THF (15 mL) and slowly added to a suspension of $LiAlH_4$ (3.80 g, 0.10 mol) in THF (150 mL) and the mixture was kept for 2 h at reflux. Workup was performed by adding H_2O (3.8 mL), 6 N NaOH (3.8 mL) and H_2O (11.4 mL), filtration of salts and removing of solvent. The crude product was purified by chromatography with Et_2O/pentane (1:4); yield: 8.76 g (67%); colourless oil.

IR (film): $\nu = 3400\ cm^{-1}$ (OH).

^{1}H NMR ($CDCl_3$): $\delta = -0.15–0.1$ [m, 2H, $CH(CH_2)_2$], 0.3–0.65 [m, 3H, $CH(CH_2)_2$], 1.06 (ddd, 1H, $^2J = 13.8$ Hz, $J = 4.3$, 9.5 Hz, CH_2CHN), 1.55 (ddd, 1H, $^2J = 13.8$ Hz, $J = 6.7$, 6.9 Hz, CH_2CHN), 2.80–2.85 (m, 1H, CH_2CHN), 3.32 (d, 2H, $^2J = 13.6$ Hz, NCH_2Ph), 3.40 (d, 1H, $^2J = 10.5$ Hz, CH_2OH), 3.57 (dd, 1H, $^2J = 10.5$ Hz, $J = 4.8$ Hz, CH_2OH), 3.74 (d, 2H, $^2J = 13.6$ Hz, NCH_2Ph), 7.0–7.4 (m, 10 H_{arom}).

^{13}C NMR ($CDCl_3$): $\delta = 4.6$, 5.6 [$CH(CH_2)_2$], 8.7 [$CH(CH_2)_2$], 30.2 (CH_2CHN), 53.2 (NCH_2Ph), 59.6 (CH_2OH), 61.0 (CH_2CHN), 128.5, 129.8, 130.4 (CH_{arom}), 139.3 (C_{arom}).

$C_{20}H_{25}NO$	calc.	C	81.30	H	8.53	N 4.74
(295.4)	found		80.91		8.72	4.58

***rac*-(2-Dibenzylamino-3-cyclopropylpropyl) 2,2,4,4-Tetramethyl-1,3-oxazolidine-3-carboxylate (*rac*-11):**
A solution of *rac*-**10** (9.45 g, 32.0 mmol) in THF (25 mL) was added to a suspension of NaH (2.40 g, 60.0 mmol, 60% in oil) in THF (80 mL). After refluxing for 1 h, 2,2,4,4-tetramethyl-1,3-oxazolidine-3-carbonyl chloride[10] (6.71 g, 35.0 mmol) was added and refluxing was continued for 12 h. Aqueous workup, extraction with Et_2O, drying ($MgSO_4$) and evaporation of the solvents gave the crude product, which was purified by column chromatography with Et_2O/pentane (1:6) as an eluent; yield: 12.4 g (86%); colourless oil.

IR (film): $\nu = 1680\ cm^{-1}$ (NC=O).

^{1}H NMR ($CDCl_3$): $\delta = -0.12$ [ddd, 1H, $^2J = 5.0$ Hz, $J = 9.1$, 9.1 H, $CH(CH_2)_2$], 0.00 [ddd, 1H, $^2J = 5.0$ Hz, $J = 9.1$, 9.1 Hz, $CH(CH_2)_2$], 0.32 [ddd, 1H, $^2J = 3.8$ Hz, $J = 9.1$, 13.1 Hz, $CH(CH_2)_2$], 0.43 [ddd, 1H, $^2J = 3.8$ Hz, $J = 9.1$, 13.1 Hz, $CH(CH_2)_2$], 0.75–0.9 [m, 1H, $CH(CH_2)_2$], 1.27, 1.29, 1.38, 1.40, 1.47, 1.54, 1.55 [each s, 12H, $C(CH_3)_3$], 1.0–1.2 (m, 1H, CH_2CHN), 1.75–1.85 (m, 1H, CH_2CHN), 2.9–3.1 (m, 1H, CHN), 3.6–3.8 (m, 4H, NCH_2Ph), 3.67 [s, 2H, $CH_2C(CH_3)_2$], 4.15–4.35 (m, 2H, CH_2OCO), 7.1–7.4 (m, 10 H_{arom}).

^{13}C NMR ($CDCl_3$): $\delta = 5.0$, 5.1 [$CH(CH_2)_2$], 8.8 [$CH(CH_2)_2$], 24.1, 24.3, 25.2, 25.3, 26.5 [$C(CH_3)_2$], 33.7 (CH_2CHN), 53.9, 54.2 (NCH_2Ph), 57.3 (CH_2CHN), 59.5, 60.6 [$C(CH_3)_2$], 63.9 (CH_2OCO), 76.0, 76.3 [$CH_2C(CH_3)_2$], 94.6, 95.9 [$C(CH_3)_2$], 126.7, 127.99, 128.7 (CH_{arom}), 140.0 (C_{arom}), 152.1, 152.8 (CH_2OCO).

$C_{28}H_{38}N_2O_3$	calc.	C	74.63	H	8.50	N 6.22
(450.6)	found		74.52		8.47	6.03

***C*-Substituted Carbamates *rac*-15a–d/*rac*-16a–d; General Procedure:**
To a solution of *rac*-**11** (451 mg, 1.0 mmol) and tetramethylethylenediamine (TMEDA, 177 mg, 1.5 mmol) in Et_2O (10 mL), cooled to −78 °C, was added dropwise a solution of *s*-BuLi (~ 1.3 N) in

Table 2. Selected Spectroscopic Data of Compounds **15a–d**

Product[a]	$[\alpha]_D^{20}$[b]	IR (film) ν (cm^{-1})	^1H NMR ($CDCl_3$/TMS)[c] δ, J (Hz)	^{13}C NMR ($CDCl_3$/TMS)[c] δ
15a	−1.2	3030, 3000, 1735, 1680	−0.31 [ddd, J = 4.9, 9.3, 9.5, 1 H, $CH(CH_2)_2$], 0.03 [ddd, J = 4.9, 9.5, 9.1, 1 H, $CH(CH_2)_2$], 0.03 [ddd, J = 4.9, 9.5, 9.1, 1 H, $CH(CH_2)_2$], 0.17 (ddd, J = 9.3, 5.0, 12.6, 1 H, 2′-H), 0.39 [ddd, J = 9.1, 5.0, 13.4, 1 H, $CH(CH_2)_2$], 0.75–0.9 [m, 1 H, $CH(CH_2)_2$], 0.95–1.1 (m, 1 H, CH_2CHN), 1.8–2.0 (m, 1 H, CH_2CHN), 3.25–3.35 (m, 1 H, CHN), 3.57 (s, 1 H, OCH_3), 5.71 [*5.52*] (d, J = 1.9 Hz, 1 H, $CHCO_2$)	4.6, 5.4 [$CH(CH_2)_2$], 8.8 [$CH(CH_2)_2$], 33.4 (CH_2CHN), 51.9 (OCH_3), 59.2 (CHN), 70.0 ($CHCO_2$), 171.0 [*170.2*] (CO_2)
15b	−62.9	3040, 3000, 1675	−0.24 [ddd, J = 4.8, 9.1, 9.1, 1 H, $CH(CH_2)_2$], 0.08 [ddd, J = 4.8, 9.1, 9.1, 1 H, $CH(CH_2)_2$], 0.25–0.40 [m, 1 H, $CH(CH_2)_2$], 0.4–0.55 [m, 1 H, $CH(CH_2)_2$], 0.8–0.9 [m, 1 H, $CH(CH_2)_2$], 0.93 [*0.86*], [s, 9 H, $C(CH_3)_3$], 1.0–1.1 (m, 1 H, CH_2CHN), 1.9–2.1 (m, 1 H, CH_2CHN), 3.2–3.3 (m, 1 H, CHN), 6.06 [*5.92*] (d, J = 0.7, 1 H, CHCOBu-*t*)	4.9, 5.8 [$CH(CH_2)_2$], 9.4 [$CH(CH_2)_2$], 26.9 [*26.4*] [$C(CH_3)_3$], 31.4 (CH_2CHN), 43.1 [$C(CH_3)_3$], 57.3 (CHN), 74.9 [*74.9*] (CHCOBu-*t*), 212.2 [*211.4*] (COBu-*t*)
15c	−60.3	3060, 3040, 3000, 1715, 1680	−0.2– −0.04 [m, 1 H, $CH(CH_2)_2$], 0.0–0.1 [m, 1 H, $CH(CH_2)_2$], 0.2–0.35 [m, 1 H, $CH(CH_2)_2$], 0.45–0.55 [m, 1 H, $CH(CH_2)_2$], 0.77, 1.08 (2 d, J = 6.5, 7.2, 6 H, $CH(CH_3)_2$], 0.9–1.0 [m, 1 H, $CH(CH_2)_2$], 1.0–1.1 (m, 1 H, CH_2CHN), 1.9–2.1 (m, 1 H, CH_2CHN), 2.3–2.5 [m, 1 H, $CH(CH_3)_2$], 3.2–3.3 (m, 1 H, CHN), 5.86 [*5.86*] (s, 1 H, CHCOPr-*i*)	4.8, 5.5 [$CH(CH_2)_2$], 9.1 [$CH(CH_2)_2$], 17.0, 19.5 [$CH(CH_3)_2$], 32.6 (CH_2CHN), 36.3 [$CH(CH_3)_2$], 57.1 (CHN), 76.4 [*78.3*] (CHCOPr-*i*), 210.8 [*209.2*] (COPr-*i*)
15d	–	3040, 3000, 1675	−0.17 [ddd, J = 5.0, 9.3, 9.5, 1 H, $CH(CH_2)_2$], 0.01 [ddd, J = 5.0, 9.3, 3.8, 1 H, $CH(CH_2)_2$], 0.30 [ddd, J = 3.8, 9.3, 13.1, 1 H, $CH(CH_2)_2$], 0.51 [ddd, J = 9.3, 13.1, 3.8, 1 H, $CH(CH_2)_2$], 0.7–0.8 [m, 1 H, $CH(CH_2)_2$], 0.9–1.1 (m, 1 H, CH_2CHN), 1.09 [*1.26*] (d, J = 6.4, 3 H, CH_3), 1.8–2.0 (m, 1 H, CH_2CHN), 2.5–2.8 (m, 1 H, CHN), 5.42 [*5.28*] (dq, J = 6.4, 3.8, 1 H, $CHCH_3$)	5.0, 6.1 [$CH(CH_2)_2$], 9.7 [$CH(CH_2)_2$], 20.4 [*17.9*] (CH_3), 32.1 (CH_2CHN), 61.5 (CHN), 69.2 [*71.5*] ($CHCH_3$)

[a] Satisfactory microanalyses obtained: C, H, N ± 0.3.
[b] c = 0.3–0.5 (CH_2Cl_2).
[c] δ-Values for diastereomers **16a–d** are italized and given in square brackets.

cyclohexane/hexane (98:2) and stirring was continued for 3.5 h at this temperature. The deep red solution was trapped with the electrophile (1.5 mmol) and slowly (14 h) warmed up to r.t. After hydrolysis with H_2O (10 mL), extraction with Et_2O (3 × 25 mL) and drying ($MgSO_4$) of organic layers, the solvent was removed under reduced pressure and the residue was purified by flash chromatography using Et_2O/pentane as an eluent (Table 2).

Kinetic Resolution of 15 and 16; General Procedure:
According to the procedure above, TMEDA was replaced (−)-sparteine (351 mg, 1.5 mmol) and the reaction time was enhanced to 10 h. Workup was accomplished in the same manner.

[(2*S*)-2-Dibenzylaminopent-4-en-1-yl] 2,2,4,4-Tetramethyl-1,3-oxazolidine-3-carboxylate [(*S*)-19]:
According to the general procedure,[12] DMSO [938 mg, 12.0 mmol, dissolved in CH_2Cl_2 (3 mL)], was added to a cooled (0 °C) solution of oxalyl chloride (761 mg, 6.0 mmol) in CH_2Cl_2 (10 mL), followed after 2 min by (*S*)-**18**[11] (2.53 g, 5.7 mmol). Stirring was continued for 15 min and the solution was treated with Et_3N (3.04 g, 30.0 mmol), warmed to r.t. and hydrolyzed with H_2O (10 mL). Extraction with CH_2Cl_2 (3 × 30 mL), drying ($MgSO_4$) and evaporation of solvent gave 2.71 g of crude aldehyde, which was used immediately in the next step without further purification. Methylenetriphenylphosphorane[13] was prepared by adding $MePh_3P^+Br^-$ (2.68 g, 7.5 mmol) to a cooled (0 °C) solution of KOBu-*t* (786 mg, 7.0 mmol) in THF (15 mL). The mixture was refluxed for 1 h, cooled (0 °C) again and the crude aldehyde (dissolved in 10 mL of THF) was added dropwise, followed by refluxing for 1 h. After hydrolysis (H_2O, 15 mL), extraction with THF (3 × 25 mL), and drying ($MgSO_4$), the solvent was removed in vacuo and the crude product purified by column chromatography using Et_2O/pentane (1:5) as an eluent; yield: 2.05 g (83%); colourless liquid; $[\alpha]_D^{20}$ = −0.95 (c = 1.1, CH_2Cl_2).

IR (film): ν = 1690 (NCO), 1640 cm^{-1} (C=C).

^1H NMR ($CDCl_3$): δ = 1.31, 1.34, 1.41, 1.44, 1.46, 1.50, 1.56, 1.58 [s, 12 H, $C(CH_3)_2$], 2.15–2.25 (m, 1 H, CH_2CHN), 2.45–2.55 (m, 1 H, CH_2CHN), 2.95–3.1 (m, 1 H, CHN), 3.65–3.75 [m, 6 H, NCH_2Ph, $OCH_2C(CH_3)_2$], 4.20 (dd, 1 H, J = 4.8, 11.5 Hz, CH_2OCO), 4.27 (dd, 1 H, J = 11.5, 6.2 Hz, CH_2OCO), 5.0–5.1 (m, 2 H, CH_2=CH), 5.79 (dddd, 1 H, J = 7.2, 7.2, 10.3, 14.3 Hz, CH_2=CH), 7.1–7.4 (m, 10 H_{arom}).

^{13}C NMR ($CDCl_3$): δ = 24.1, 25.3, 26.5 (CH_3), 32.8 (CH_2CHN), 53.8 (NCH_2Ph), 5.67 (CHN), 59.5, 60.7 [$C(CH_3)_2$], 63.4 (CH_2OCO), 76.0, 76.3 [$OCH_2C(CH_3)_2$], 94.6, 95.9 ($C(CH_3)_2$), 116.4 (H_2C=CH), 126.8, 128.2, 128.8 (CH_{arom}), 136.2 (C_{arom}), 139.7 (H_2C=CH), 152.0, 152.7 (NCO_2).

HRMS calc. 436.2726 found 436.2734

Cyclopropanation of (*S*)-19:
To a solution of (*S*)-**19** (82 mg, 0.19 mmol) and $Pd(OAc)_2$ (52 mg, 0.22 mmol) in Et_2O (4 mL) at 0 °C was added a solution of CH_2N_2 (0.28 M, 12 mL) in Et_2O. After stirring for 12 h at r.t., the precipitate was filtered off, the solvent removed in vacuo, and the residue purified by column chromatography using Et_2O/pentane (1:2) as solvent; yield: 83 mg; (98%); colourless oil; $[\alpha]_D^{20}$ = −19.6 (c = 0.98, CH_2Cl_2); 99% ee (comparison of optical rotation).

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