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Enantioselective synthesis of 1,2-diamines via nucleophilic 1,2-addition to dibenzylamino-acetaldehyde-SAMP-hydrazone†

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Summary — Nucleophilic 1,2-addition of RM/$CeCl_3$ in THF or allyl Grignard reagent in toluene to dibenzylamino-acetaldehyde-SAMP-hydrazone **2** after reductive N–N bond cleavage leads to differently protected 1,2-diamines **4** in good yields and of high enantiomeric purity (ee = 92–99%). The absolute configuration was determined by X-ray structure analysis on the 1,2-adduct **3e**.

SAMP-hydrazone / nucleophilic 1,2-addition / asymmetric synthesis / vicinal diamine / organocerium reagent

Résumé — Synthèse énantiosélective de 1,2-diamines chirales obtenues par addition nucléophile sur la dibenzylamino-acétaldéhyde-SAMP-hydrazone. L'addition nucléophile 1,2 de RM/$CeCl_3$ dans le THF, ou du réactif de Grignard dans le toluène sur la dibenzylamino-acétaldéhyde-SAMP-hydrazone **2**, conduit, après coupure de la liaison N–N, à différentes 1,2-diamines **4** protégées, avec de bons rendements et une bonne stéréosélectivité (ee = 92–99 %). La configuration absolue a été déterminée par l'analyse radiocristallographique aux rayons X du composé **3e**.

SAMP-hydrazone / diamine vicinale / addition nucléophile 1,2 / synthèse asymétrique / réactif organocérique

The asymmetric synthesis of vicinal diamines has recently received considerable attention. Molecules with a 1,2-diamino structural unit are not only of great importance in medicinal chemistry, but there is also a growing interest in these compounds because of their use as chiral ligands and auxiliaries in asymmetric synthesis. They are frequently used for enantioselective Diels–Alder, Michael and aldol reactions, the asymmetric dihydroxylation of alkenes, the enantioselective reduction of ketones or the 1,2-addition of organometallics to aldehydes [1]. In addition, a new method for the determination of enantiomeric excesses of chiral alcohols, thiols and amines is based on the application of vicinal diamines [2]. They are also used as chiral reagents to determine the optical purity of chiral carboxylic acids by NMR-spectroscopy [3]. However, general methods for their diastereo- and enantioselective synthesis are limited [4]. Most of these methods are based on the transformation of chiral alcohols via the corresponding azides [5] or the transition-metal mediated reductive coupling of imines [6]. The latter is generally limited to the synthesis of symmetrical 1,2-diamines [7].

Some interesting new strategies developed recently in our group are the diastereoselective addition of organometallics to enantiopure hydrazones [8] (**a**), the Michael-addition of *N*-nucleophiles to nitroalkenes [9] (**b**), or the diastereoselective α-alkylation of *N*,*N*-dibenzylamino-acetaldehyde-SAMP- hydrazones [10] (**c**) (fig 1).

We wish to report here the enantioselective synthesis of unsymmetrical, differently protected 1,2-diamines, based on our SAMP/RAMP-hydrazone method [11] via the nucleophilic 1,2-addition of RM/$CeCl_3$ or Grignard reagents to *N*,*N*-dibenzylamino-acetaldehyde-SAMP-hydrazone (*S*)-**2** (fig 2). Then the 'free diamines' can be formed from the *N*,*N*-dibenzyl *N*-acetyl diamines **4** by reductive cleavage with Raney nickel.

The first key step is the diastereoselective nucleophilic 1,2-addition of alkyl cerium or allyl Grignard reagents [12] to the C=N double bond of dibenzylamino-SAMP-hydrazone (*S*)-**2**, which occurs with high asymmetric induction. The second key step is the cleavage of the N-protected hydrazines (*R*,*S*)-**3** by lithium in ammonia [13] affording the 1,2-diamines (*R*)-**4a–g** in good yield and high enantiomeric purity (fig 3). Hydrazone (*S*)-**2** was easily prepared in excellent overall yield starting from glycine [10].

As shown in figure 3, the reaction of SAMP [14] with the aldehyde obtained in situ by Swern [15] oxidation of the amino-alcohol **1** gave quantitatively the hydrazone (*S*)-**2**. Subsequent 1,2-addition of the in situ prepared alkyl cerium reagent according to Imamoto et al [16] (method A) or allyl Grignard reagent in toluene accord-

† Dedicated to Professor Henri Kagan for his pioneering work in asymmetric synthesis

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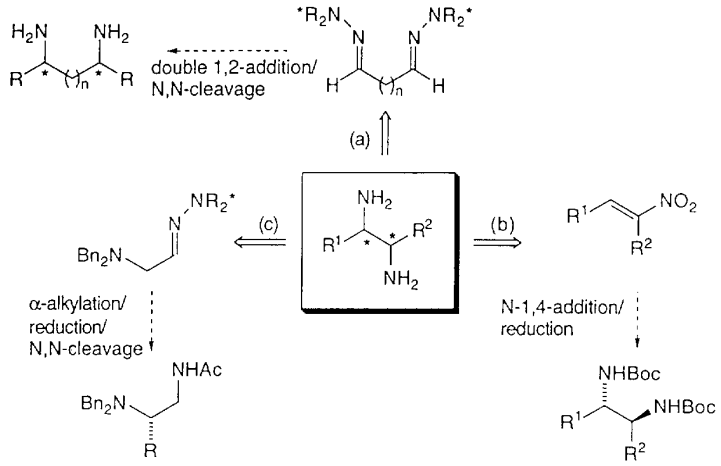


Fig 1

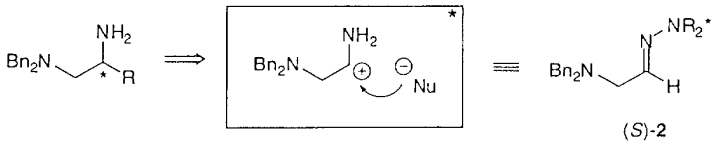
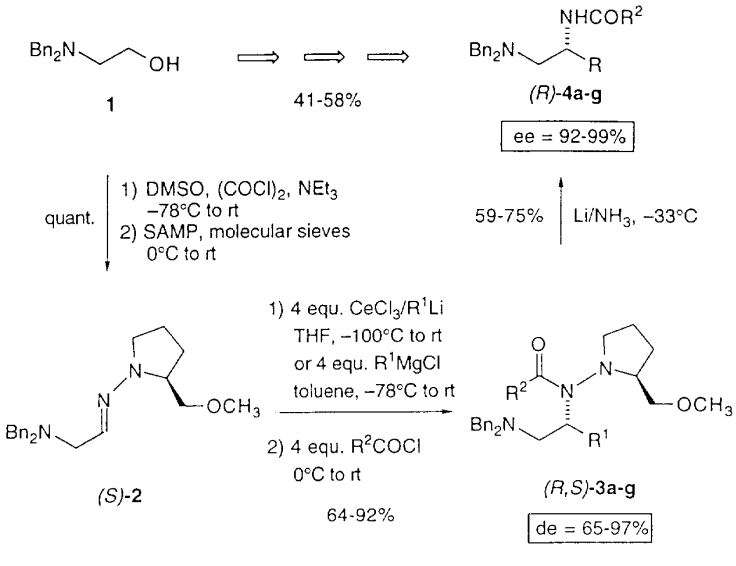


Fig 2



3-4	a	b	c	d	e	f	g
R^1	Me	Et	*n*-Pr	*n*-Bu	allyl	allyl	Ph
R^2	Me	Me	Me	Me	Me	Et	Me

Fig 3

Table I. Hydrazines **3** prepared by 1,2-addition/acylation of hydrazone **2**.

Product	R^1	R^2	*Yield*[a] *(%)*	$[\alpha]_D^{22}$ *(c, $CHCl_3$)*	*de*[b]	*Configuration*
3a	Me	Me	77	−15.7 (1.27)	95	(*R*,*S*)
3b	Et	Me	64	−19.6 (1.07)	65[c]	(*R*,*S*)
3c	*n*-Pr	Me	72	−13.8 (1.08)	71[c]	(*R*,*S*)
3d	*n*-Bu	Me	79	−9.6 (0.89)	76	(*R*,*S*)
3e	Allyl	Me	79	+3.2 (0.51)	96	(*R*,*S*)
3f	Allyl	Et	74	+1.4 (1.76)	97	(*R*,*S*)
3g	Ph	Me	92	+35.5 (0.87)	76[c]	(*R*,*S*)

[a] Yield of product **3** based on dibenzylamino-acetaldehyde-SAMP-hydrazone **2**. [b] Determined by GC-analysis. [c] Determined by ^{1}H- and ^{13}C-NMR spectroscopy.

Table II. Differently protected 1,2-diamines **4** prepared.

Product	R^1	R^2	*Yield*[a] *(%)*	$[\alpha]_D^{22}$ *(c, $CHCl_3$)*	*ee*[b]	*Configuration*
4a	Me	Me	59	+29.9 (0.90)	93	(*R*)
4b	Et	Me	64	+26.5 (1.09)	95	(*R*)
4c	*n*-Pr	Me	75	+32.1 (1.13)	92	(*R*)
4d	*n*-Bu	Me	71	+17.4 (0.89)	99	(*R*)
4e	Allyl	Me	60	+24.6 (0.99)	99	(*R*)
4f	Allyl	Et	69	+24.5 (0.64)	99	(*R*)

[a] Yield of product **4** based on the hydrazines **3**. [b] Determined by gas chromatography with chiral β-cyclodextrin phases.

ing to Alexakis et al [17] (method B) to the C=N double bond of the hydrazone (*S*)-**2** occurred with good yield (64–92%) and with high diastereoselectivities (*de* = 65–97%). The reactions were quenched with acetyl or propionyl chloride to obtain the protected hydrazines (*R*,*S*)-**3a–g** by *N*-acylation. The results are summarized in table I. The diastereoselectivity of the reactions was evaluated for the crude protected hydrazines. The absolute configuration of the products **3** is assumed to derive from *re*-face attack. One equivalent of the '$RCeCl_2$' or Grignard reagent may coordinate to the methoxymethyl group and nitrogen of the auxiliary. Then excess of the organometallic reagent delivers R to the less hindered *re* face.

This could be confirmed by an X-ray diffraction study. Crystals of **3e** (R^1 = allyl, R^2 = Me) were obtained from pentane/ether solution and the absolute configuration given as (*R*,*S*) was unambiguously determined by X-ray structure analysis. A Schakal view of this compound appears in figure 4, whereas the bond distances and angles can be found in the supplementary material.

After chromatography of the protected hydrazines **3** which allowed a separation of the minor (*S*,*S*)-diastereoisomers, (*R*,*S*)-**3a–g** were cleaved by lithium in ammonia giving the vicinal diamines (*R*)-**4a–f** in good yield (59–75%) and without much racemisation (ee = 92–99%). The acetyl group of the hydrazino function activates the N–N bond so that the reductive cleavage can proceed by treatment with an excess of lithium in liquid ammonia at −33 °C for 2 h. The ee values of these amines (*R*)-**4a–f** were determined by gas chromatography on chiral cyclodextrin phases. The results are collected in table II. In the case of **3g** (R^1 = Ph, R^2 = Me), because of the presence of the phenyl group, the cleavage by lithium in ammonia did not afford

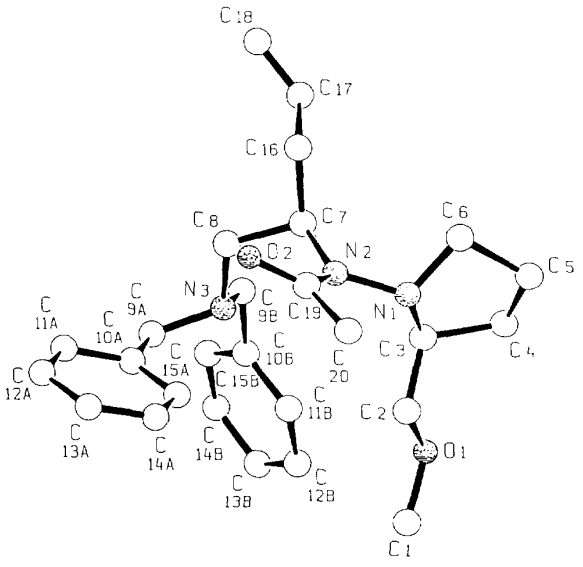


Fig 4

the expected compound **4g** but the 1-(dibenzylamino)-2-phenylethane obtained by cleavage of the CN bond.

In summary, an efficient and flexible enantioselective synthesis of differently protected unsymmetrical 1,2-diamines via nucleophilic 1,2-addition to dibenzylamino-acetaldehyde-SAMP-hydrazone **2** followed by cleavage to the corresponding vicinal diamines has been developed. An extension of this new diamine synthesis by combination with the diastereoselective α-alkylation of aldehyde SAMP-hydrazones [10] is currently being investigated in our laboratories.

Experimental section

General comments

All reagents were of commercial quality from freshly opened containers or distilled before use. The chiral auxiliary (*S*)-1-amino-2-methoxymethyl-pyrrolidine (SAMP) was prepared according to the procedure as described in the literature [18]. THF was freshly distilled from potassium-benzophenone. Analytical TLC plates (silica gel F_{254}) and silica gel 60 (230–400 mesh) were purchased from Merck. MeLi (1.6 N in *n*-hexane), *n*-BuLi (1.6 N in *n*-hexane), *t*-BuLi (1.6 N in *n*-hexane) and PhLi (1.8 N in *n*-hexane) were purchased from Aldrich. The melting point (Büchi-apparatus, system Dr Tottoli) was not corrected. Optical rotation values were measured using a Perkin-Elmer P 241 polarimeter. Microanalyses were obtained with a Heraeus CHN-O-RAPID element analyser. Mass spectra were recorded on a Varian MAT 212 (70 eV, 1 mA) spectrometer with DEI ionisation (relative intensities in parentheses) and high-resolution MS on a Finnigan MAT GmbH, MAT 95. IR spectra were obtained using a Perkin-Elmer FT 1750 spectrometer. The ^{1}H and ^{13}C NMR spectra were measured on a Varian VXR 300 (300 and 75 MHz).

*General procedures for the 1,2-addition on hydrazone (S)-**2***

• *Synthesis of **3a–d** and **3g** (method A)*

4 equiv $CeCl_3 \cdot 7H_2O$ were dried at 140 °C/0.1 torr for 2 h, suspended in THF (3 mL/mmol), stirred for 1 h and then placed in an ultrasonic bath [18] at room temperature for 1 h. Then 4 to 8 equiv of the organometallic compound in THF (1 mmol/mL) were added slowly at −78 °C (RLi) and the suspension was stirred for another 2 h at this temperature. At −100 °C a solution of SAMP-hydrazone (*S*)-**2** in THF (3 mL/mmol) was added dropwise very slowly to the suspension (10 mL/h) which was stirred for 1 h at −78 °C and was then allowed to warm up to room temperature overnight. The solution was quenched with acetyl or propionyl chloride and stirred for 4 h (TLC-control). After aqueous workup and extraction with Et_2O (3 × 30 mL) the crude hydrazines **3** were purified by flash chromatography on silica gel (ether/pentane, 1:2).

• *Synthesis of **3e–f** (method B)*

The SAMP-hydrazone (*S*)-**2** was dissolved in toluene (30 mL/mmol) and cooled to −78 °C. At this temperature 4 equiv allyl magnesium chloride in THF (1 mL/mmol) were dropped into the solution (20 mL/h). Upon warming to room temperature overnight the solution was quenched with acetyl or propionyl chloride and worked up as described in method A.

• *Synthesis of RLi [19]*

t-BuLi (2 equiv) was added at −78 °C to a solution of RI (1 equiv) in Et_2O (0.5 mL/mmol). Then, the solution was stirred for 0.5 h at −78 °C and 1 h at room temperature. The resulting RLi was used as described in method A.

*(1R,2S)-N-[2-(Dibenzylamino)-1-methylethyl]-N-[2-(methoxymethyl)pyrrolidin-1-yl]acetamide **3a***

Reaction of (*S*)-**2** (0.7 g, 2 mmol) with MeLi/$CeCl_3$ (8 mmol) and acetyl chloride (0.57 mL, 8 mmol) yielded (*R,S*)-**3a** (630 mg, 77%) as a colorless oil.

$[\alpha]_D^{22}$: −15.7 (*c* = 1.27, $CHCl_3$); de = 95%.

IR (film): 3 050, 3 020 (ArCH), 2 960, 2 920, 2 860, 2 820, 1 650 (CO), 1 490, 1 445, 1 360, 1 305, 1 195, 1 115, 1 055, 1 025, 970, 745, 695 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.39 (d, *J* = 6.7 Hz, 3H, CH_3), 1.55–1.66 (m, 4H, $NCHRCH_2$, NCH_2CH_2), 1.99 (s, 3H, CH_3CO), 2.56–2.65 (m, 2H), 2.66 (d, *J* = 3.7 Hz, 1H), 2.81–2.88 (m, 1H), 3.00–3.08 (m, 1H), 3.10–3.22 (m, 2H), 3.28 (s, 3H, OCH_3), 3.33–3.47 (m, 1H), 3.59 (s, 4H, $PhCH_2N$), 7.18–7.37 (m, 10H, CH arom).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 17.3 (CH_3), 21.0 (NCH_2CH_2), 22.4 (CH_3CO), 25.9 ($NCHRCH_2$), 50.6 (Bn_2NCH_2), 51.0 ($NCHCH_3$), 58.6 ($NCHCH_2OCH_3$), 59.0 (OCH_3), 59.1 (NCH_2), 60.3 (NCH_2Ph), 73.7 (CH_2O), 126.9, 128.2, 128.9 (CH arom), 139.7 (*C* arom), 174.6 (CO).

MS (EI, 70 eV): *m/z* 410 (0.3, M^+ + H), 318 (18.4, M^+ − $PhCH_2$), 238 (24.2), 237 (62.9), 211 (49.2), 210 (100, $Bn_2NCH_2^+$), 205 (13.8), 181 (14.5), 146 (15.5), 114 (5.1), 111 (14.1), 92 (14.3), 91 (89.8, $PhCH_2^+$), 70 (17.8), 65 (8.4).

HRMS *m/z* calc for (M^+ − $PhCH_2$): 318.2181, found: 318.2181.

*(1R,2S)-N-{1-[(1-Dibenzylamino)methyl]propyl}-N-[2-(methoxymethyl)pyrrolidin-1-yl]acetamide **3b***

Reaction of (*S*)-**2** (0.7 g, 2 mmol) with EtLi/$CeCl_3$ (16 mmol) and acetyl chloride (0.57 mL, 8 mmol) yielded (*R,S*)-**3b** (540 mg, 64%) as a colorless oil.

$[\alpha]_D^{22}$: −19.6 (*c* = 1.07, $CHCl_3$); de = 65%.

IR (film): 3 062, 3 027 (ArCH), 2 962, 2 928, 2 874, 2 828, 1 658 (CO), 1 495, 1 453, 1 417, 1 366, 1 076, 748, 700 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.79 (t, *J* = 7.7 Hz, 3H, CH_3), 1.56–1.69 (m, 6H, $NCHRCH_2$, NCH_2CH_2, CH_2CH_3), 2.02 (s, 3H, CH_3CO), 2.51–2.58 (m, 2H), 2.71 (d, *J* = 4.3 Hz, 1H), 2.78–2.88 (m, 2H), 3.12–3.17 (m, 1H), 3.31 (s, 3H, OCH_3), 3.23–3.29 (m, 2H), 3.56 (d, *J* = 13.7 Hz, 2H, $PhCH_2N$), 3.62 (d, *J* = 13.7 Hz, 2H, $PhCH_2N$), 7.25–7.36 (m, 10H, CH arom).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 11.9 (CH_3), 21.0 (NCH_2CH_2), 22.4 (CH_3CO), 23.4 (CH_2CH_3), 26.0 ($NCHRCH_2$), 51.2 (Bn_2NCH_2), 57.3 ($NCHCH_2CH_3$), 58.4 ($NCHCH_2OCH_3$), 58.5 (NCH_2), 58.7 (OCH_3), 60.2 (NCH_2Ph), 73.8 (CH_2O), 127.0, 128.2, 129.0 (CH arom), 139.6 (*C* arom), 174.7 (CO).

MS (EI, 70 eV): *m/z* 424 (0.1, M^+ + H), 332 (4.4, M^+ − $PhCH_2$), 251 (22.8), 219 (6.2), 211 (18.6), 210 (100, $Bn_2NCH_2^+$), 181 (6.0), 160 (6.2), 125 (5.9), 91 (70.2, $PhCH_2^+$), 70 (8.8).

Anal calc for $C_{26}H_{37}N_3O_2$: C, 73.76; H, 8.75; N, 9.93. Found: C, 73.44; H, 8.69; N, 9.87.

*(1R,2S)-N-{1-[(Dibenzylamino)methyl]butyl}-N-[2-(methoxymethyl)pyrrolidin-1-yl]acetamide **3c***

Reaction of (*S*)-**2** (0.7 g, 2 mmol) with *n*-PrLi/$CeCl_3$ (16 mmol) and acetyl chloride (0.57 mL, 8 mmol) gave (*R,S*)-**3c** (630 mg, 72%) as a colorless oil.

$[\alpha]_D^{22}$: −13.8 (*c* = 1.08, $CHCl_3$); de = 71%.

IR (film): 3 058, 3 023 (ArCH), 2 961, 2 926, 2 893, 2 872, 2 827, 2 807, 2 784, 1 646 (CO), 1 603, 1 495, 1 447, 1 384, 1 370, 1 327, 1 301, 1 284, 1 270, 1 257, 1 197, 1 123, 1 090, 1 080, 745, 695 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ 0.87 (t, *J* = 7.1 Hz, 3H, CH_3), 1.14–1.26 (m, 2*H*), 1.56–1.72 (m, 6H), 2.01 (s, 3H,

CH_3CO), 2.52–2.60 (m, 2H), 2.74–2.80 (m, 2H), 2.81–2.91 (m, 2H), 3.12–3.19 (m, 2H), 3.31 (s, 3H, OCH_3), 3.56 (d, J = 13.4 Hz, 2H, $PhCH_2N$), 3.62 (d, J = 13.4 Hz, 2H, $PhCH_2N$), 7.22–7.34 (m, 10H, CH arom).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 14.5 (CH_3), 20.8 (CH_2), 21.1 (CH_2), 22.4 (CH_3CO), 26.1 (CH_2), 33.3 (CH_2), 51.2 (Bn_2NCH_2), 56.1, 58.4, 59.0 ($NCHCH_2OCH_3$, $NCHCH_2$, OCH_3), 58.5 (NCH_2), 60.2 (NCH_2Ph), 73.8 (CH_2O), 127.0, 128.2, 129.1 (CH arom), 139.6 (C arom), 174.8 (CO).

MS (EI, 70 eV): m/z 438 (0.2, M^+ + H), 346 (8.2, M^+ – $PhCH_2$), 266 (13.2), 265 (35.6), 236 (8.8), 233 (7.5), 211 (22.6), 210 (100, $Bn_2NCH_2^+$), 91 (61.8, $PhCH_2^+$), 70 (9.1).

HRMS m/z calc for (M^+ – $PhCH_2$): 346.2494, found: 346.2491.

(1R,2S)-N-{1-[(Dibenzylamino)methyl]pentyl}-N-[2-(methoxymethyl)pyrrolidin-1-yl]acetamide **3d**

Reaction of (*S*)-**2** (0.68 g, 1.9 mmol) with *n*-BuLi/$CeCl_3$ (7.6 mmol) and acetyl chloride (0.55 mL, 7.6 mmol) yielded (*R,S*)-**3d** (680 mg, 79%) as a colorless oil.

$[\alpha]_D^{22}$: −9.6 (c = 0.89, $CHCl_3$); de = 76%.

IR (film): 3 060, 3 020 (ArCH), 2 945, 2 920, 2 860, 1 650 (CO), 1 492, 1 448, 1 362, 1 320, 1 245, 1 195, 1 115, 1 075, 1 025, 967, 915, 745, 698 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ 0.87 (t, J = 7.4 Hz, 3H, CH_3), 1.10–1.16 (m, 2H), 1.23–1.30 (m, 3H), 1.60–1.70 (m, 4H), 1.85–1.90 (m, 1H), 2.01 (s, 3H, CH_3CO), 2.75–2.90 (m, 4H), 3.12–3.30 (m, 4H), 3.31 (s, 3H, OCH_3), 3.56 (d, J = 13.4 Hz, 2H, $PhCH_2N$), 3.62 (d, J = 13.4 Hz, 2H, $PhCH_2N$), 7.22–7.37 (m, 10H, CH arom).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 14.7 (CH_3), 21.6 (NCH_2CH_2), 23.1 (CH_3CO), 23.6 (CH_2), 26.7 ($NCHRCH_2$), 30.4, 31.4 (CH_2), 51.8 (Bn_2NCH_2), 56.8 ($NCHCH_2CH_2CH_2$), 59.1 ($NCHCH_2OCH_3$), 59.2 (NCH_2), 59.6 (OCH_3), 60.8 (NCH_2Ph), 74.4 (CH_2O), 127.5, 128.8, 129.7 (CH arom), 140.2 (C arom), 175.3 (CO).

MS (EI, 70 eV): m/z 452 (0.2, M^+ + H), 360 (9.8, M^+ – $PhCH_2$), 280 (21.3), 279 (60.9), 247 (13.4), 236 (17.1), 211 (43.7), 210 (100, $Bn_2NCH_2^+$), 199 (9.5), 188 (5.3), 181 (10.9), 153 (11.9), 114 (7.6), 92 (12.0), 91 (88.6, $PhCH_2^+$), 70 (21.5), 65 (5.4).

Anal calc for $C_{28}H_{41}N_3O_2$: C, 74.46; H, 9.15; N, 9.30. Found: C, 74.13; H, 9.06; N, 9.18.

(1R,2S)-N-{1-[(Dibenzylamino)methyl]but-3-enyl}-N-[2-(methoxymethyl)pyrrolidin-1-yl]acetamide **3e**

Reaction of (*S*)-**2** (0.4 g, 1.14 mmol) with allyl magnesium chloride (1M in THF, 4.5 mmol, 4.5 mL) and acetyl chloride (0.33 mL, 4.6 mmol) yielded (*R,S*)-**3e** which was recrystallized from a mixture of pentane/Et_2O to give a colorless solid (390 mg ,79%).

Mp: 74 °C; $[\alpha]_D^{22}$: +3.2 (c = 0.51, $CHCl_3$); de = 96%.

IR (KBr): 3 050, 3 020 (ArCH), 2 960, 2 915, 2 860, 2 815, 1 650 (CO), 1 490, 1 360, 1 295, 1 190, 1 120, 1 025, 965, 910, 745, 699 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ 1.46–1.60 (m, 4H, $NCHRCH_2$, NCH_2CH_2), 1.92 (s, 3H, CH_3CO), 2.35–2.43 (m, 1H), 2.59–2.69 (m, 5H), 2.71–2.75 (m, 1H), 3.05–3.11 (m, 1H), 3.16–3.21 (m, 1H), 3.24 (s, 3H, OCH_3), 3.30 (dd, J = 9.1 and 13.1 Hz, 1H), 3.50 (d, J = 13.4 Hz, 2H, $PhCH_2N$), 3.56 (d, J = 13.4 Hz, 2H, $PhCH_2N$), 4.84–4.94 (m, 2H, CH_2=CH), 5.46–5.60 (m, 1H, CH_2=CH), 7.16–7.30 (m, 10H, CH arom).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.0 (NCH_2CH_2), 22.5 (CH_3CO), 26.1 ($NCHRCH_2$), 34.6 (CH_2CH=CH_2), 51.6 (Bn_2NCH_2), 55.7, 58.6 ($NCHCH_2OCH_3$, $NCHCH_2CH$=CH_2), 58.6 (NCH_2), 59.2 (OCH_3), 60.5 (NCH_2Ph), 73.9 (CH_2O), 116.8 (CH_2=CH), 127.1, 128.3, 129.1 (CH arom), 136.9 (CH_2=CH), 139.6 (C arom), 174.9 (CO).

MS (EI, 70 eV): m/z 435 (0.2, M^+), 344 (4.8, M^+ – $PhCH_2$), 264 (8.1), 263 (19.2), 211 (15.0), 210 (100, $Bn_2NCH_2^+$), 92 (5.5), 91 (62.4, $PhCH_2^+$), 70 (7.3).

Anal calc for $C_{27}H_{37}N_3O_2$: C, 74.45; H, 8.56; N, 9.64. Found: C, 74.04; H, 8.58; N, 9.48.

(1R,2S)-N-{1-[(Dibenzylamino)methyl]but-3-enyl}-N-[2-(methoxymethyl)pyrrolidin-1-yl]propanamide **3f**

Reaction of (*S*)-**2** (0.7 g, 2 mmol) with allyl magnesium chloride (1M in THF, 8 mmol, 8 mL) and propionyl chloride (0.7 mL, 8 mmol) gave (*R,S*)-**3f** (660 mg, 74%) as a colorless oil.

$[\alpha]_D^{22}$: +1.4 (c = 1.76, $CHCl_3$); de = 97%.

IR (film): 3 045, 3 020 (ArCH), 2 960, 2 920, 2 860, 2 820, 1 650 (CO), 1 490, 1 449, 1 422, 1 120, 911, 745, 699 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ 1.20 (t, J = 6.9 Hz, 3H, CH_3CH_2), 1.50–1.70 (m, 4H, $NCHRCH_2$, NCH_2CH_2), 2.35–2.80 (m, 5H), 3.20 (m, 3H), 3.31 (s, 3H, OCH_3), 3.40 (dd, 1H), 3.57 (d, J = 13.4 Hz, 2H, $PhCH_2N$), 3.64 (d, J = 13.4 Hz, 2H, $PhCH_2N$), 4.90–5.10 (m, 2H, CH_2=CH), 5.54–5.62 (ddt, J = 7.1, 10.2 and 17.3 Hz, 1H, CH_2=CH), 7.22–7.38 (m, 10H, CH arom).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 9.8 (CH_3), 21.4 (NCH_2CH_2), 26.6 ($NCHRCH_2$), 27.2 (CH_2CO), 35.2 (CH_2CH=CH_2), 52.1, 59.4 (Bn_2NCH_2, NCH_2), 56.0, 59.1 ($NCHCH_2OCH_3$, $NCHCH_2CH$=CH_2), 59.7 (OCH_3), 61.0 (NCH_2Ph), 74.4 (CH_2O), 117.2 (CH_2=CH), 127.6, 128.8, 129.6 (CH arom), 137.4 (CH_2=CH), 140.2 (C arom), 178.4 (CO).

MS (EI, 70 eV): m/z 449 (0.1, M^+), 358 (4.4, M^+ – $PhCH_2$), 264 (8.2), 263 (17.6), 245 (4.2), 211 (16.8), 210 (100, $Bn_2NCH_2^+$), 137 (5.9), 92 (7.6), 91 (87.9, $PhCH_2^+$), 70 (11.1), 57 (6.4), 55 (4.3), 45 (3.9), 42 (5.9), 41 (7.2).

Anal calc for $C_{28}H_{39}N_3O_2$: C, 74.79; H, 8.74; N, 9.34. Found: C, 74.44; H, 8.71; N, 8.95.

(1R,2S)-N-[2-(Dibenzylamino)-1-phenylethyl]-N-[2-(methoxymethyl)pyrrolidin-1-yl]acetamide **3g**

Reaction of (*S*)-**2** (0.7 g, 2 mmol) with PhLi/$CeCl_3$ (8 mmol) and acetyl chloride (0.57 mL, 8 mmol) gave (*R,S*)-**3g** (870 mg, 92%) as a colorless oil.

$[\alpha]_D^{22}$: +35.5 (c = 0.87, $CHCl_3$); de = 76%.

IR (film): 3 060, 3 020 (ArCH), 2 965, 2 920, 2 865, 2 820, 1 650 (CO), 1 490, 1 450, 1 362, 1 280, 1 195, 1 115, 1 028, 970, 912, 747, 699 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ 1.52–1.90 (m, 4H, $NCHRCH_2$, NCH_2CH_2), 2.07 (s, 3H, CH_3CO), 2.68–2.73 (m, 2H), 2.78–2.82 (m, 1H), 3.11–3.17 (m, 2H), 3.20–3.26 (m, 1H), 3.29 (s, 3H, OCH_3), 3.50 (d, J = 13.4 Hz, 2H, $PhCH_2N$), 3.58 (d, J = 13.4 Hz, 2H, $PhCH_2N$), 3.80–3.88 (m, 1H), 4.12 (dd, J = 4.4 and 9.1 Hz, 1H, $NCHPh$), 7.20–7.48 (m, 15H, CH arom).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 21.3 (NCH_2CH_2), 22.7 (CH_3CO), 26.0 ($NCHRCH_2$), 51.7 (Bn_2NCH_2), 58.6, 59.0 (OCH_3, $NCHCH_2OCH_3$), 58.8 (NCH_2), 59.8 (NCH_2Ph), 60.4 ($NCHPh$), 73.7 (CH_2O), 126.9, 127.1, 128.0, 128.1, 129.1, 129.2 (CH arom), 139.6, 141.9 (C arom), 175.4 (CO).

MS (EI, 70 eV): m/z 472 (0.01, M^+ + H), 380 (0.1, M^+ – $PhCH_2$), 211 (9.8), 210 (60.5, $Bn_2NCH_2^+$), 92 (8.9), 91 (100, $PhCH_2^+$), 70 (11.5).

Anal calc for $C_{30}H_{37}N_3O_2$: C, 76.40; H, 7.91; N, 8.91. Found: C, 76.11; H, 7.84; N, 8.80.

General procedure for the cleavage of hydrazines **3a–g**

A solution of the *N*-protected hydrazines **3a–g** in THF (1 mL/mmol) was dissolved in liquid ammonia (15 mL/mmol). Li-wire (4 equiv) was added, the solution stirred for 2 h at −33 °C and then quenched with solid NH_4Cl (5 equiv). Ammonia was evaporated, the residue dissolved in water, extracted with Et_2O (5 × 30 mL), the organic layer dried over $MgSO_4$ and purified by flash chromatography on silica gel (ether/pentane, 1:2 or 2:1).

(R)-N-[2-(Dibenzylamino)-1-methylethyl]acetamide **4a**

Following the above procedure and starting with (*R,S*)-**3a** (470 mg, 1.14 mmol), the compound (*R*)-**4a** was obtained as a colorless oil (200 mg, 59%).

$[\alpha]_D^{22}$: +29.9 (c = 0.90, $CHCl_3$); ee = 93%.

IR (film): 3 284 (NH), 3 085, 3 063, 3 028 (ArCH), 2 971, 2 930, 2 874, 2 801, 1 651 (CO), 1 603, 1 553, 1 495, 1 452, 1 373, 1 318, 1 287, 1 165, 1 125, 1 076, 1 063, 1 029, 974, 910, 735, 700 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ 1.07 (d, J = 6.7 Hz, 3H, CH_3), 1.88 (s, 3H, CH_3CO), 2.37–2.39 (m, 2H, NCH_2), 3.47 (d, J = 13.4 Hz, 2H, $PhCH_2N$), 3.64 (d, J = 13.1 Hz, 2H, $PhCH_2N$), 4.06 (m, 1H, NC*H*), 5.25 (d, J = 7.4 Hz, 1H, N*H*), 7.22–7.32 (m, 10H, C*H* arom).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 19.0 (CH_3), 23.5 (CH_3CO), 43.5 ($NCHCH_3$), 58.4 (NCH_2), 58.7 (NCH_2Ph), 127.1, 128.3, 129.0 (*C*H arom), 139.3 (*C* arom), 169.7 (*C*O).

MS (EI, 70 eV): m/z 297 (0.1, M^+ + H), 211 (10.9), 210 (57.4, $Bn_2NCH_2^+$), 205 (9.5, M^+ − $PhCH_2$), 180 (8.8), 91 (100, $PhCH_2^+$), 65 (8.4).

HRMS m/z calc for (M^+ − $PhCH_2$): 205.1340, found: 205.1340.

(R)-N-{1-[(Dibenzylamino)methyl]propyl}acetamide **4b**

Following the above procedure and starting with (*R,S*)-**3b** (360 mg, 0.84 mmol), the compound (*R*)-**4b** was obtained as a colorless oil (170 mg, 64%).

$[\alpha]_D^{22}$: +26.5 (c = 1.09, $CHCl_3$); ee = 95%.

IR (film): 3 283 (NH), 3 085, 3 063, 3 027 (ArCH), 2 966, 2 932, 2 877, 2 820, 1 650 (CO), 1 552, 1 495, 1 452, 1 373, 1 296, 1 126, 960, 753, 700 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ 1.17 (t, J = 7.1 Hz, 3H, CH_2CH_3), 1.41 (q, J = 7.3 Hz, 2H, CH_2CH_3), 1.84 (s, 3H, CH_3CO), 2.31–2.35 (m, 2H, NCH_2), 3.41 (d, J = 13.4 Hz, 2H, $PhCH_2N$), 3.57 (d, J = 13.7 Hz, 2H, $PhCH_2N$), 3.82–3.95 (m, 1H, NC*H*), 5.07 (d, J = 7.4 Hz, 1H, N*H*), 7.19–7.26 (m, 10H, C*H* arom).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 10.1 (CH_2CH_3), 23.6 (CH_3CO), 28.0 (CH_2CH_3), 48.9 (NCH), 56.7 (NCH_2), 58.9 (CH_2Ph), 127.2, 128.4, 129.1 (*C*H arom), 139.5 (*C* arom), 170.1 (*C*O).

MS (EI, 70 eV): m/z 311 (0.5, M^+ + H), 219 (12.7, M^+ − $PhCH_2$), 214 (17.7), 212 (12.4), 211 (11.5), 210 (67.0, $Bn_2NCH_2^+$), 181 (7.4), 114 (6.0), 92 (8.4), 91 (100, $PhCH_2^+$), 77 (7.1), 65 (7.4), 58 (10.5).

HRMS m/z calc for (M^+ − $PhCH_2$): 219.1497, found: 219.1495.

(R)-N-{1-[(Dibenzylamino)methyl]butyl}acetamide **4c**

Following the above procedure and starting with (*R,S*)-**3c** (450 mg, 1.02 mmol), the compound (*R*)-**4c** was obtained as a colorless oil (280 mg, 75%).

$[\alpha]_D^{22}$: +32.1 (c = 1.13, $CHCl_3$); ee = 92%.

IR (film): 3 280 (NH), 3 085, 3 063, 3 027 (ArCH), 2 957, 2 932, 2 871, 2 799, 1 646 (CO), 1 602, 1 555, 1 495, 1 452, 1 372, 1 307, 1 123, 748, 699 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ 0.80 (t, J = 7.4 Hz, 3H, CH_2CH_3), 1.12–1.43 (m, 4H, CH_2CH_2), 1.82 (s, 3H, CH_3CO), 2.30–2.33 (m, 2H, NCH_2), 3.40 (d, J = 13.4 Hz, 2H, $PhCH_2N$), 3.55 (d, J = 13.4 Hz, 2H, $PhCH_2N$), 3.96–4.02 (m, 1H, NC*H*), 5.08 (d, J = 8.0 Hz, 1H, N*H*), 7.15–7.24 (m, 10H, C*H* arom).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 14.7 (CH_2CH_3), 19.4 (CH_2CH_3), 24.1 (CH_3CO), 36.0 ($CHCH_2$), 47.9 (NCH), 57.8 (NCH_2), 59.4 (CH_2Ph), 127.6, 128.9, 129.6 (*C*H arom), 140.1 (*C* arom), 170.3 (*C*O).

MS (EI, 70 eV): m/z 325 (0.2, M^+ + H), 233 (19.2, M^+ − $PhCH_2$), 211 (21.3), 210 (100, $Bn_2NCH_2^+$), 181 (10.2), 91 (94.5, $PhCH_2^+$), 72 (5.5), 65 (6.1).

Anal calc for $C_{21}H_{28}N_2O$: C, 77.74; H, 8.71; N, 8.63. Found: C, 77.69; H, 8.41; N, 8.37.

(R)-N-{1[(Dibenzylamino)methyl]pentyl}acetamide **4d**

According to the above procedure and starting with (*R,S*)-**3d** (640 mg, 1.4 mmol), the compound (*R*)-**4d** was obtained as a colorless oil (410 mg, 71%).

$[\alpha]_D^{22}$: +17.4 (c = 0.89, $CHCl_3$); ee = 99%.

IR (film): 3 276 (NH), 3 085, 3 063, 3 027 (ArCH), 2 955, 2 930, 2 871, 2 858, 2 798, 1 643 (CO), 1 603, 1 555, 1 495, 1 452, 1 372, 1 307, 1 126, 1 029, 747, 699 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ 0.84 (t, J = 7.4 Hz, 3H, CH_3), 1.17–1.34 (m, 5H), 1.46–1.56 (m, 1H), 1.88 (s, 3H, CH_3CO), 2.32–2.45 (m, 2H, NCH_2), 3.48 (d, J = 13.1 Hz, 2H, $PhCH_2N$), 3.61 (d, J = 13.4 Hz, 2H, $PhCH_2N$), 3.99–4.11 (m, 1H, NC*H*), 5.21 (d, J = 8.1 Hz, 1H, N*H*), 7.22–7.31 (m, 10H, C*H* arom).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 14.0 (CH_3), 22.7 (CH_2CH_3), 23.5 (CH_3CO), 27.7 ($CH_2CH_2CH_3$), 32.9 ($CH_2CH_2CH_2CH_3$), 47.5 (NCH), 57.2 (NCH_2), 58.8 (NCH_2Ph), 127.0, 128.2, 129.0 (*C*H arom), 139.5 (*C* arom), 169.7 (*C*O).

MS (EI, 70 eV): m/z 338 (0.1, M^+), 247 (14.4, M^+ − $PhCH_2$), 211 (13.7), 210 (79.9, $Bn_2NCH_2^+$), 180 (8.4), 91 (100, $PhCH_2^+$), 86 (5.3).

HRMS m/z calc (M^+ − $PhCH_2$): 247.1810, found: 247.1806.

(R)-N-{1-[(Dibenzylamino)methyl]but-3-enyl}-acetamide **4e**

Starting from (*R,S*)-**3e** (650 mg, 1.5 mmol), the compound (*R*)-**4e** was obtained as a colorless oil (290 mg, 60%).

$[\alpha]_D^{22}$: +24.6 (c = 0.99, $CHCl_3$); ee = 99%.

IR (film): 3 279 (NH), 3 083, 3 063, 3 027 (ArCH), 2 928, 2 800, 1 651 (CO), 1 602, 1 554, 1 495, 1 451, 1 372, 1 297, 1 253, 1 126, 1 029, 915, 748, 699 cm^{-1}.

^1H NMR ($CDCl_3$, 300 MHz): δ 1.88 (s, 3H, CH_3CO), 2.13–2.32 (m, 2H, $CH_2CH{=}CH_2$), 2.40–2.42 (m, 2H, NCH_2), 3.53 (d, J = 13.4 Hz, 2H, $PhCH_2N$), 3.59 (d, J = 13.4 Hz, 2H, $PhCH_2N$), 4.06–4.17 (m, 1H, NC*H*), 4.93–5.00 (m, 2H, $CH_2{=}CH$), 5.23 (d, J = 7.4 Hz, 1H, N*H*), 5.49–5.63 (m, 1H, $CH_2{=}CH$), 7.21–7.31 (m, 10H, C*H* arom).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 23.4 (CH_3CO), 36.9 ($CH_2CH{=}CH_2$), 46.8 (NCH), 56.2 (NCH_2), 58.8

(CH_2Ph), 117.7 (CH_2=CH), 127.1, 128.3, 129.1 (*C*H arom), 134.3 (CH_2=*C*H), 139.3 (*C* arom), 169.7 (*C*O).

MS (EI, 70 eV): m/z 323 (0.4, M^+ + H), 231 (17.6, M^+ – $PhCH_2$), 211 (12.9), 210 (72.6, $Bn_2NCH_2^+$), 181 (8.8), 148 (5.4), 111 (5.6), 97 (7.6), 91 (100, $PhCH_2^+$), 85 (5.9), 83 (7.1), 71 (8.3), 70 (8.1), 69 (8.8), 65 (8.8), 57 (14.8), 55 (10.6).

HRMS m/z calc for (M^+ – $PhCH_2$): 231.1497, found: 231.1497.

(R)-N-{1-[(Dibenzylamino)methyl]but-3-enyl}-propanamide **4f**

Following the above procedure and starting with (*R*,*S*)-**3f** (330 mg, 0.73 mmol), the compound (*R*)-**4f** was obtained as a colorless oil (170 mg, 69%).

$[\alpha]_D^{22}$: −24.5 (c = 0.64, $CHCl_3$); ee = 99%.

IR (film): 3 292 (NH), 3 063, 3 027 (ArCH), 2 974, 2 935, 2 880, 2 802, 1 643 (CO), 1 603, 1 548, 1 495, 1 452, 1 373, 1 162, 748, 700 cm^{-1}.

^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.05 (t, J = 7.7 Hz, 3H, CH_2CH_3), 2.05 (q, J = 7.7 Hz, 2H, CH_2CH_3), 2.13–2.21 (m, 2H, CH_2CH=CH_2), 2.35 (d, J = 7.0 Hz, 2H, NCH_2), 3.46 (d, J = 13.5 Hz, 2H, $PhCH_2N$), 3.53 (d, J = 13.4 Hz, 2H, $PhCH_2N$), 4.03–4.09 (m, 1H, NC*H*), 4.87–4.93 (m, 2H, CH_2=CH), 5.12 (d, J = 7.0 Hz, 1H, N*H*), 5.42–5.56 (m, 1H, C*H*=CH_2), 7.18–7.25 (m, 10H, C*H* arom).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 10.0 (CH_2CH_3), 30.0 (CH_2CH_3), 37.1 (CH_2CH=CH_2), 46.6 (N*C*H), 56.3 (NCH_2), 58.8 (CH_2Ph), 117.7 (CH_2=CH), 127.2, 128.4, 129.1 (*C*H arom), 134.4 (*C*H=CH_2), 139.4 (*C* arom), 173.5 (*C*O).

MS (EI, 70 eV): m/z 337 (7.0, M^+ + H), 295 (6.5), 246 (12.1), 245 (64.3, M^+ – $PhCH_2$), 212 (6.0), 211 (43.8), 210 (100, $Bn_2NCH_2^+$), 181 (24.8), 140 (9.3), 118 (6.4), 92 (21.2), 91 (89.7, $PhCH_2^+$), 70 (15.8), 65 (17.9), 57 (15.8).

Anal calc for $C_{22}H_{28}N_2O$: C, 78.53; H, 8.39; N, 8.32. Found: C, 78.51; H, 8.18; N, 8.15.

1-(Dibenzylamino)-2-phenylethane **4g**

According to the above procedure, and starting with (*R*,*S*)-**3g** (640 mg, 1.35 mmol), 1-(dibenzylamino)-2-phenylethane was obtained as a colorless oil (340 mg, 84%).

^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.66–2.83 (m, 4H, CH_2CH_2), 3.63 (s, 4H, $PhCH_2N$), 7.05–7.32 (m, 15H, C*H* arom).

^{13}C NMR ($CDCl_3$, 75 MHz): δ 33.5 (CH_2Ph), 55.1 (NCH_2CH_2), 58.2 (NCH_2Ph), 125.8, 126.8, 128.1, 128.2, 128.7, 128.8 (*C*H arom), 139.7, 140.6 (*C* arom).

Supplementary material available

Supplementary material data (atomic coordinates and anisotropic thermal parameters; bond lengths and angles; a listing of observed and calculated structure factors; and full experimental details for the determination) have been deposited with the British Library, Document Supply Center at Boston Spa, Wetherby, West Yorkshire, UK, as supplementary publication N° = SUP 90454 and is available on request from the Document Supply Center.

References and notes

1 a) Corey EJ, *Pure Appl Chem* (1990) 62, 1209
b) Zhang W, Loebach JL, Wilson SR, Jacobsen EN, *J Am Chem Soc* (1990) 112, 2801
c) Irie R, Noda K, Ito Y, Katsuki T, *Tetrahedron Lett* (1991) 31, 1055
d) Alexakis A, Sedrani R, Lensen N, Mangeney P In: *Organic Synthesis via Organometallics*, Enders D, Gais HJ, Keim W, Eds, Vieweg, Braunschweig, 1993, 1
e) Nakajima M, Tomioka K, Koga K, *Tetrahedron* (1993) 49, 10807
f) Oishi T, Iida K, Hirama M, *Tetrahedron Lett* (1993) 34, 3573
g) Evans DA, Lectka T, Miller SJ, *Tetrahedron Lett* (1993) 34, 7027
h) Knochel P, Brieden W, Rozema MJ, Eisenberg C, *Tetrahedron Lett* (1993) 34, 5881
i) Davies SG, Mortlock AA, *Tetrahedron* (1993) 49, 4419
j) Stingl K, Martens J, *Liebigs Ann Chem* (1994) 243

2 Alexakis A, Frutos JC, Mutti S, Mangeney P, *J Org Chem* (1994) 59, 3326

3 Fulwood R, Parker D, *J Chem Soc, Perkins Trans 2* (1995) 2376

4 a) Roos GHP, Balasubramanian S, Doyle MP, Raab CE, *Synth Commun* (1996) 26, 2165
b) Pansare SV, Malusare MG, *Tetrahedron Lett* (1996) 37, 2859
c) Corey EJ, Lu DH, Sarshar S, *Tetrahedron: Asymmetry* (1995) 6, 3
d) Bambridge K, Begley MJ, Simpkins NS, *Tetrahedron Lett* (1994) 35, 3391
e) Dondoni A, Merchan FL, Merino P, Pejero T, Bertolasi V, *J Chem Soc, Chem Commun* (1994) 1731
f) Gmeiner P, Hummel E, *Synthesis* (1994) 1026
g) Reetz MT, Hübel M, Jaeger R, Schwickhardi R, Goddard R, *Synthesis* (1994) 733
h) Altman J, Ben-Ishai D, Beck W, *Tetrahedron: Asymmetry* (1994) 5, 887
i) Katritzky AR, Fan W-Q, Fu C, *J Org Chem* (1990) 55, 3209

5 a) Kotsuki H, Kuzume H, Gohda T, Fukuhara M, Ochi M, Oishi T, Hirama M, Shiro M, *Tetrahedron: Asymmetry* (1996) 6, 2227
b) Effenberger F, Kremser A, Stelzer U, *Tetrahedron: Asymmetry* (1996) 7, 607
c) Altman J, Beck W, *Tetrahedron* (1995) 51, 13309

6 a) Baruah B, Prajapati D, Sandhu JS, *Tetrahedron Lett* (1995) 36, 6747
b) Kalyanam N, Rao GV, *Tetrahedron Lett* (1993) 34, 1647
c) Imamoto T, Nidhimura S, *Chem Lett* (1990) 1141
d) Enholm EJ, Forbes DC, Holub DP, *Synth Commun* (1990) 20, 981
e) Cuvinot D, Mangeney P, Alexakis A, Normant JF, *J Org Chem* (1989) 54, 2420
f) Betschart C, Schmidt R, Seebach D, *Helv Chim Acta* (1988) 71, 1999

7 Ricardson PF, Nelson LTJ, Sharpless KB, *Tetrahedron Lett* (1995) 36, 9241

8 a) Enders D, Meiers M, *Angew Chem* (1996) 108, 2540
b) Enders D, Meiers M, *Angew Chem Int Ed Engl* (1996) 35, 2261

9 Enders D, Wiedemann J, *Synthesis* (1996) 1443

10 Enders D, Schiffers R, *Synthesis* (1996) 53

11 Enders D, Schankat J, Klatt M, *Synlett* (1994) 795

12 a) Imamoto T In: *Comprehensive Organic Synthesis*, Trost BM, Fleming I, Schreiber SL, Eds, Pergamon Press, New York, 1991, Vol 1, p 231.
b) Crimmins MT, Dedopoulou D, *Synth Commun* (1992) 22, 1953
c) Bartoli G, Marcantoni E, Petrini M, *Angew Chem* (1993) 105, 1115
d) Bartoli G, Marcantoni E, Petrini M, *Angew Chem*

Int Ed Engl (1993) 32, 1061
e) Enders D, Funk R, Klatt M, Raabe G, Hovestreydt ER, *Angew Chem* (1993) 105, 418
f) Enders D, Funk R, Klatt M, Raabe G, Hovestreydt ER, *Angew Chem Int Ed Engl* (1993) 32, 418
g) Enders D, Klatt M, Funk R, *Synlett* (1993) 226
h) Denmark SE, Nicaise O, *Synlett* (1993) 359

13 a) Nübling C, *Dissertation*, Technische Hochschule Aachen, 1987
b) Denmark SE, Nicaise O, Edwards JP, *J Org Chem* (1990) 55, 6219

14 a) Enders D In: *Asymmetric Synthesis*, Morrison JD, Eds, Academic Press, Orlando, 1984, Vol 3B, p 275
b) Enders D, Fey P, Kipphardt H, *Org Synth* (1987) 65, 173, 183
c) Enders D, Klatt M In: *Encyclopedia of Reagents for Organic Synthesis*, Paquette LA, Ed, Wiley, New York, 1995, p 178

15 Mancuso AJ, Huang SL, Swern DJ, *J Org Chem* (1978) 43, 2480

16 a) Imamoto T, Takiyama N, Nakamura K, *Tetrahedron Lett* (1985) 26, 4763
b) Imamoto T, Kusumoto T, Tawarayama Y, Sugiura Y, Mita T, Hatanaka Y, Yokoyama M, *J Org Chem* (1984) 49, 3904

17 Alexakis A, Lensen N, Tranchier JP, Mangeney P, *J Org Chem* (1992) 57, 4563

18 a) Enders D, Eichenauer H, *Chem Ber* (1979) 112, 2933
b) Enders D, *Chem Scripta* (1985) 25, 131
c) Enders D, Bachstädter G, Kremer KAM, Marsch M, Harms K, Boche G, *Angew Chem* (1988) 100, 1580
d) Enders D, Bachstädter G, Kremer KAM, Marsch M, Harms K, Boche G, *Angew Chem Int Ed Engl* (1988) 27, 1522

19 Greeves N, Lyford L, *Tetrahedron Lett* (1992) 33, 4759

20 Tiebes J, *Dissertation*, Technische Hochschule Aachen, 1993