Synthesis of Chiral α-Aminoalkylpyrimidines Using an Enantioselective Three-Component Reaction

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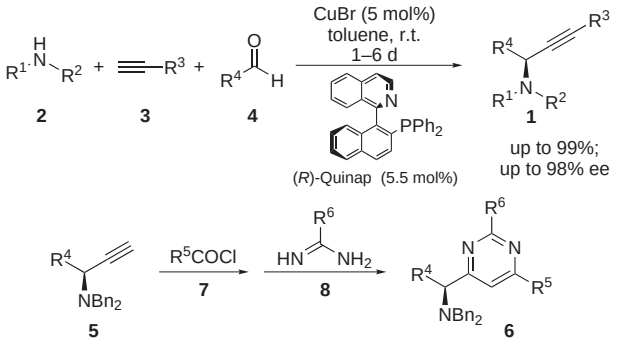
Received 5 April 2004; revised 26 April 2004

Abstract: A range of chiral α-aminoalkylpyrimidines has been prepared in a modular fashion in 5 steps with up to 98% ee. The key step is a CuBr-catalyzed enantioselective asymmetric three-component synthesis of propargylic amines.

Key words: alkynes, asymmetric synthesis, C–H activation, copper catalysis, heterocycles

Heterocyclic compounds have found numerous applications as pharmaceuticals and agrochemicals. Therefore, the development of new and efficient syntheses of complex heterocycles is an active field of research. The expeditious and modular preparation of heterocyclic rings is of special importance.[1] Recently, we have developed a new synthesis of chiral propargylamines of type **1** using three components: an amine **2**, an alkyne **3** and an aldehyde **4** (Scheme 1).[2] This reaction is efficiently catalyzed with CuBr[3] (5 mol%) and (*R*)-Quinap[4] (5.5 mol%) and produces propargylic amines of type **5** with high enantioselectivity (up to 98% ee) and good yields (82–98%).



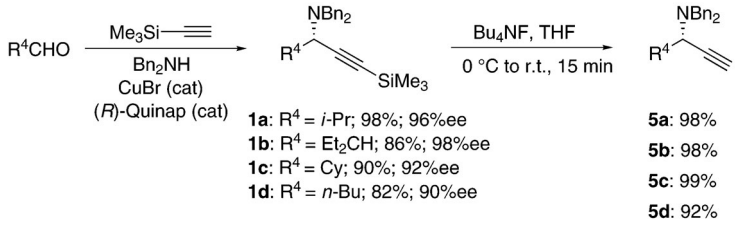
Scheme 1 Formation of chiral α-aminopyrimidines of type **6**.

Herein, we wish to report the conversion of propargylamines of type **5** (obtained by the three-component reaction) to chiral α-aminopyrimidines of type **6** by successive reaction with an acid chloride **7** and an amidine **8**. Pyrimidines are of great interest due to their potential biological activity.[5] Our approach provides a modular synthesis of a new family of pyrimidines **6**.

The reaction of various aldehydes **4** (R^4CHO) with dibenzylamine **2a** and trimethylsilylacetylene **3a** in the presence of CuBr (5 mol%) and (*R*)-Quinap (5.5 mol%) provided propargylamines **1a**–**d** in 82–98% yield and 90–98% ee. After treatment with Bu_4NF (1.0 equiv, THF, 0 °C to 25 °C, 15 min), the corresponding terminal alkynes **5a**–**d** were obtained in 92–99% yield (Scheme 2).

These terminal alkynes were subsequently acylated resulting in the formation of the alkynones **9a**–**n** in 84–97% yield (Scheme 3 and Table 1). The acylation reaction was best performed with acid chlorides **7** (R^5COCl) in the presence of $Pd(PPh_3)_2Cl_2$ (2 mol%), CuI (4 mol%) and Et_3N (1 equiv) in THF (r.t., 2 h) according to the method described by Müller.[6] This synthetic procedure is especially well suited for aromatic and heterocyclic acid chlorides **7** (Table 1, entries 1–7, 9–12, 15,16).

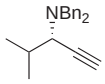
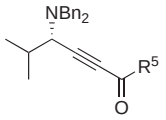
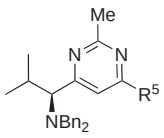
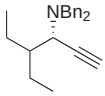
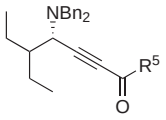
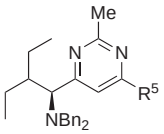
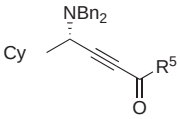
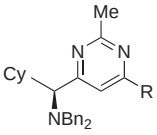
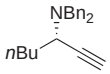
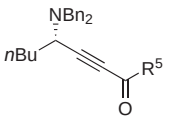
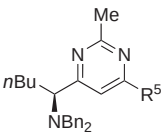
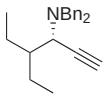
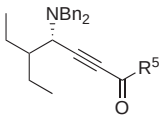
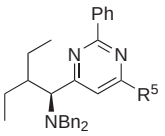
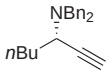
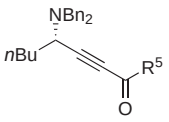
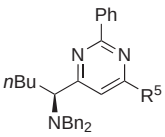
For the reaction with aliphatic acid chlorides, it was found advantageous to generate first the zinc acetylide by successive deprotonation of the propargylic amines **5** with *n*-BuLi and addition of $ZnCl_2$. The reaction of this zinc species with an acid chloride **7** (r.t., 12 h) in the absence of a palladium catalyst led to the desired alkynones **9l**–**n** in 90–92% yield (Scheme 3 and Table 1, entries 8, 13–14).[7] The ring closure of compounds **9** to the chiral pyrimidines of type **6** proceeded well with acetamidine **8a** (Table 1,



Scheme 2 Preparation of propargylamines **5** by the three-component reaction and deprotection with TBAF.

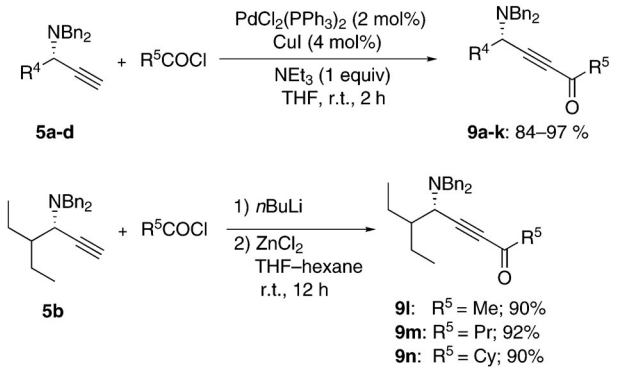
SYNTHESIS 2004, No. 12, pp 2015–2025
Advanced online publication: 01.07.2004
DOI: 10.1055/s-2004-829129; Art ID: T04104SS

Table 1 Alkynones of Type **9** Prepared from the Chiral Propargylamines **5a**–**d** and Further Transformation to 2,4,6-Substituted Pyrimidines of Type **6**

Entry	Propargyl-amine	Acid Chloride **7** (R^5COCl)	Product of Type **9**	Yield (%)[a]	Product of Type **6**	Yield (%)[a]	ee (%)
1							
	5a	**7a:** 2,4,5-$(CF_3)_3C_6H_2COCl$	**9a:** R^5 = 2,4,5-$(CF_3)_3C_6H_2$	92	**6a:** R^5 = 2,4,5-$(CF_3)_3C_6H_2$	75	96
2	**5a**	**7b:** 4-ClC_6H_4COCl	**9b:** R^5 = 4-ClC_6H_4	91	**6b:** R^5 = 4-ClC_6H_4	77	96
3	**5a**	**7c:** PhCOCl	**9c:** R^5 = Ph	84	**6c:** R^5 = Ph	82	96
							
4	**5b**	**7d**: 4-$MeOC_6H_4COCl$	**9d:** R^5 = 4-$MeOC_6H_4$	97	**6d:** R^5 = 4-$MeOC_6H_4$	78	98
5	**5b**	**7e:** 2-furylCOCl	**9e:** R^5 = 2-furyl	95	**6e:** R^5 = 2-furyl	79	98
6	**5b**	**7f:** *t*-BuCOCl	**9f:** R^5 = *t*-Bu	96	**6f:** R^5 = *t*-Bu	73	98
7	**5b**	**7c**	**9g:** R^5 = Ph	96	**6g:** R^5 = Ph	82	98
8	**5b**	**7g:** MeCOCl	**9l:** R^5 = Me	90	**6l:** R^5 = Me	79	98
							
9	**5c**	**7e**	**9h:** R^5 = 2-furyl	95	**6h:** R^5 = 2-furyl	80	92
							
10	**5d**	**7c**	**9i:** R^5 = Ph	95	**6i:** R^5 = Ph	89	90
11	**5d**	**7f**	**9j:** R^5 = *t*-Bu	94	**6j:** R^5 = *t*-Bu	81	90
12	**5d**	**7e**	**9k:** R^5 = 2-furyl	94	**6k:** R^5 = 2-furyl	90	90
							
13	**5b**	**7h:** *n*-PrCOCl	**9m:** R^5 = *n*-Pr	92	**6m:** R^5 = *n*-Pr	79	98
14	**5b**	**7i:** *c*-$C_6H_{11}COCl$	**9n:** R^5 = *c*-C_6H_{11}	90	**6n:** R^5 = *c*-C_6H_{11}	75	98
							
15	**5d**	**7c**	**9i:** R^5 = Ph	95	**6o:** R^5 = Ph	90	90
16	**5d**	**7e**	**9k**: R^5 = 2-furyl	94	**6p:** R^5 = 2-furyl	98	90

[a] Yield of analytically pure product.

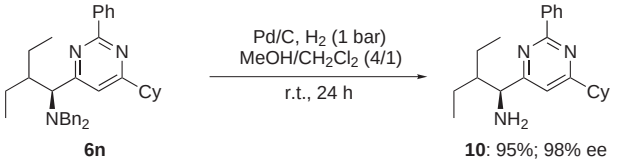
entries 1–12) or benzamidine **8b** (Table 1, entries 13–16) (1.5–2.0 equiv) and sodium carbonate (3–4 equiv) in refluxing acetonitrile (2 h–2 d) according to the method of Adlington and Baldwin[5] (Scheme 1 and Table 1).



Scheme 3 Acylation of the terminal propargylamines **5**.

We have verified that no racemization of the stereogenic center at the α-position occurs by analyzing selected pyrimidines **6** by HPLC using a chiral support (Chiracel OD-H column). In each case both the chiral and racemic product were analyzed.

The debenzylation of the amines of type **6** was readily accomplished by using Pd/C and H_2 (1 bar)[8] without affecting the heterocyclic ring leading to the primary α-aminopyrimidine **10** in 95% isolated yield (Scheme 4).



Scheme 4 Deprotection of the benzyl group leading to the chiral primary amine **10**.

In summary, we have developed a short and highly modular synthesis of new chiral aminopyrimidines of type **6** using a catalytic asymmetric three-component reaction and involving finally five readily available compounds. Further applications of this method towards the preparation of natural products are currently under way in our laboratories.

Melting points were measured on a Büchi B 540 apparatus and are uncorrected. NMR spectra were recorded in $CDCl_3$ at 300 MHz for ^1H NMR and 75 MHz for ^{13}C NMR (Varian XL 300). Chemical shifts are reported in ppm relative to TMS. IR spectra were recorded on a Perkin-Elmer FT-IR Spectrum 1000. Low-resolution mass spectra were recorded using a GC/MS combination of the type HP 6890/MSD 5973 fitted with a HP-5 column (30 m × 0.25 mm × 0.25 μm). High-resolution mass spectra were recorded on a Finnigan-MAT 95Q spectrometer (EI, 70 eV). Microanalyses were performed using a Heraeus CHN-Rapid-Elementaranalysator. Flash column chromatography purifications were carried out using silica gel 60 (silica, 0.063–0.200 mm, purchased from Merck, Darmstadt).

Unless otherwise indicated, all reactions were carried out with magnetic stirring and, with air or moisture sensitive compounds, in flame-dried glassware under N_2. Syringes were used to transfer reagents and solvents were purged with N_2 prior to use. Reactions were monitored by GC and GC-MS or TLC analysis.

Organolithium solutions were titrated using the method of Paquette.[9] $ZnCl_2$ was dried at 650 °C under high vacuum for 30 min and afterwards dissolved in anhyd THF.

General Procedures

Propargylamines (±)-1; GP 1a

In a dry and argon flushed 50 mL flask, equipped with a magnetic stirrer and a septum, CuBr (36 mg, 0.25 mmol, 5 mol%) was suspended in anhyd toluene (10 mL). Molecular sieves 4Å (2.5 g) and *n*-decane (100 mg) were added, followed by trimethylsilylacetylene (**3a**; 491 mg, 5 mmol), the aldehyde **4** (5 mmol) and dibenzylamine (**2a**; 986 mg, 5 mmol). The reaction mixture was stirred at r.t. until GC analysis showed full conversion. Molecular sieves 4Å was filtered and washed with Et_2O. The crude product was concentrated in vacuo and purified by column chromatography on silica gel.

Propargylamines (–)-1; GP 1b

In a dry and argon flushed 10 mL flask, equipped with a magnetic stirrer and a rubber septum, CuBr (3.6 mg, 0.025 mmol, 5 mol%) and (*R*)-Quinap (12.1 mg, 0.0275 mmol, 5.5 mol%) were suspended in anhyd toluene (2 mL) and stirred for 30 min. Molecular sieves 4Å (0.25 g) and *n*-decane (30 mg) were added, followed by trimethylsilylacetylene (**3a**; 49 mg, 0.5 mmol), the aldehyde **4** (0.5 mmol) and dibenzylamine (**2a**, 99 mg, 0.5 mmol). The reaction mixture was stirred at r.t. until GC analysis showed full conversion. The molecular sieves was filtered and washed with Et_2O. The crude product was concentrated in vacuo and purified by column chromatography on silica gel.

Deprotection of the TMS Group Leading to Terminal Propargylamines 5; GP 2

The TMS-protected propargylamine **1** was dissolved in anhyd THF (5 mL/mmol) and cooled to 0 °C. Bu_4NF (1 M in THF) was added dropwise. After 15 min, the conversion was complete according to GC analysis. The reaction mixture was quenched with H_2O (20 mL) and extracted with Et_2O (3 × 50 mL). The crude product was purified by column chromatography on silica gel.

Acylation of the Terminal Propargylamines 5 with Aromatic Acid Chlorides 7 Leading to Alkynones 9; GP 3

In a dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum, CuI (0.04 mmol, 4 mol%) and $PdCl_2(PPh_3)_2$ (0.02 mmol, 2 mol%) were suspended in anhyd THF (3 mL). Et_3N (0.14 mL, 1 mmol) and acid chloride **7** (1 mmol) were added, followed by the terminal propargylamine **5** (1 mmol). After stirring for 2 h at r.t., the reaction mixture was poured into H_2O (20 mL) and the aqueous phase was extracted with Et_2O (3 × 50 mL). The organic fractions were washed with brine (30 mL), dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel.

Acylation of the Terminal Propargylamines 5 with Aliphatic Acid Chlorides 7 Leading to Alkynones 9; GP 4

A dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a rubber septum, was charged with a solution of the terminal propargylamine **5** (1 mmol) in anhyd THF (2 mL) and *n*-hexane (2 mL). At –65 °C, *n*-BuLi (1.6 M in *n*-hexane, 0.75 mL, 1.2 mmol) was slowly added and the reaction mixture was stirred at this temperature for 20 min to complete the deprotonation. Then a solution of $ZnCl_2$ in THF (1 M solution in THF, 1.2 mL, 1.2 mmol) was added and the mixture was allowed to warm to r.t. The acid chloride **7** (1.5 mmol) was added and the mixture was stirred for 12 h at r.t. Af-

terwards, the mixture was quenched with H_2O (20 mL) and the aqueous phase was extracted with Et_2O (3 × 50 mL). The organic fractions were washed with brine (30 mL), dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel.

Pyrimidines 6; GP 5

A 10 mL flask, equipped with a magnetic stirrer and a reflux-condenser, was charged with the acylated propargylamine **7** (1 equiv), the amidine hydrochloride **8** (1.2–2.0 equiv), Na_2CO_3 and H_2O (cat., 1 drop) in MeCN (5 mL/mmol). This reaction mixture was heated to reflux until completion of the reaction was indicated by GC analysis. After cooling to r.t., the mixture was poured into H_2O (20 mL) and the aqueous phase was extracted with Et_2O (3 × 50 mL). The organic fractions were washed with brine (30 mL), dried ($MgSO_4$) and concentrated in vacuo. The crude product was purified by flash chromatography on silica gel.

***N,N*-Dibenzyl-4-methyl-1-(trimethylsilyl)pent-1-yn-3-amine (1a)**

Preparation according to **GP 1a** afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 99:1), (±)-**1a** as a colorless oil (1.608 g, 92%).

Preparation according to **GP 1b** afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 99:1), (–)-**1a** as a colorless oil (167 mg, 95%, 96% ee, the enantiomeric excess was determined after desilylation); $[\alpha]_D^{20}$ –268 (*c* = 0.65, $CHCl_3$).

IR (film): 2959s, 2158m, 1494m, 1454s, 1249vs, 1019s, 842vs, 746s, 698vs cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.46–7.19 (m, 10 H), 3.83 (d, 2 H, *J* = 13.7 Hz), 3.38 (d, 2 H, *J* = 13.7 Hz), 2.93 (d, 1 H, *J* = 10.2 Hz), 1.99–1.81 (m, 1 H), 1.00 (t, 6 H, *J* = 6.2 Hz), 0.28 (s, 9 H), 7.45–7.42 (m, 4 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.8, 128.9, 128.2, 126.8, 103.8, 89.9, 59.9, 55.0, 30.6, 20.9, 19.9, 0.5.

MS (70 eV, EI): *m*/*z* (%) = 307 (M^+ – *i*-Pr, 27), 306 (100), 91 (34).

HRMS (EI): *m*/*z* calcd for $C_{23}H_{30}NSi$ [M^+ – H]: 348.2148; found: 348.2166.

Anal. Calcd for $C_{23}H_{31}NSi$: C, 79.02; H, 8.94; N, 4.01. Found: C, 79.10; H, 9.17; N, 3.83.

***N,N*-Dibenzyl-4-ethyl-1-(trimethylsilyl)hex-1-yn-3-amine (1b)**

Preparation according to **GP 1a** afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 99:1), (±)-**1b** as a colorless oil (1.614 g, 86%).

IR (film): 2962s, 2158m, 1494m, 1454m, 1250s, 842vs, 747m, 698s cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.16 (m, 10 H), 3.79 (d, 2 H, *J* = 13.7 Hz), 3.34 (d, 2 H, *J* = 13.7 Hz), 3.16 (d, 1 H, *J* = 10.2 Hz), 1.75–1.18 (m, 5 H), 0.78 (t, 3 H, *J* = 7.3 Hz), 0.56 (t, 3 H, *J* = 7.5 Hz), 0.26 (s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.7, 129.1, 128.1, 126.8, 104.0, 90.0, 55.6, 55.0, 41.5, 22.1, 20.1, 10.6, 8.9, 0.5.

MS (70 eV, EI): *m*/*z* (%) = 362 (M^+ – Me, 1), 307 (30); 306 (100), 91 (29).

HRMS (EI): *m*/*z* calcd for $C_{25}H_{36}NSi$ [M^+ + H]: 378.2617; found: 378.2617.

Anal. Calcd for $C_{25}H_{36}NSi$: C, 79.51; H, 9.34; N, 3.71. Found: C, 79.49; H, 9.37; N, 3.69.

***N,N*-Dibenzyl-1-cyclohexylprop-2-yn-1-amine (1c)**

Preparation according to **GP 1a** afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 99:1), (±)-**1c** as a colorless solid (1.745 g, 90%).

IR (film): 2924s, 2852m, 2160m, 1494m, 1451m, 1248s, 1006m, 844vs, 737s, 698s cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.43–7.19 (m, 10 H), 3.80 (d, 2 H, *J* = 13.7 Hz), 3.36 (d, 2 H, *J* = 13.7 Hz), 3.03 (d, 1 H, *J* = 10.6 Hz), 2.27 (d, 1 H, *J* = 13.1 Hz), 1.99 (d, 1 H, *J* = 13.1 Hz), 1.75–1.50 (m, 4 H), 1.32–0.98 (m, 3 H), 0.89–062 (m, 2 H), 0.26 (s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.8, 128.8, 128.2, 126.8, 103.5, 90.1, 58.6, 54.9, 39.5, 31.2, 30.3, 26.6, 26.2, 25.9, 0.5.

MS (70 eV, EI): *m*/*z* (%) = 307 (M^+ – *i*-Pr, 27), 306 (100), 91 (34).

HRMS (EI): *m*/*z* calcd for $C_{26}H_{35}NSi$ [M^+]: 389.2539; found: 389.2506.

Anal. Calcd for $C_{26}H_{35}NSi$: C, 80.14; H, 9.05; N, 3.59. Found: C, 79.90; H, 9.07; N, 3.54.

***N,N*-Dibenzyl-1-(trimethylsilyl)hept-1-yn-3-amine (1d)**

Preparation according to **GP 1a** afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 99:1), (±)-**1d** as a colorless oil (1.490 g, 87%).

IR (film): 3064w, 3029w, 2958s, 2159m, 1495m, 1454m, 1250s, 842vs, 698s cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.22–7.00 (m, 10 H), 3.62 (d, 2 H, *J* = 13.7 Hz), 3.19 (d, 2 H, *J* = 13.7 Hz), 3.21–3.15 (m, 1 H), 1.59–1.35 (m, 2 H), 1.30–1.10 (m, 2 H), 1.10–0.94 (sext, 2 H, *J* = 7.3 Hz), 0.66 (t, 3 H, *J* = 7.3 Hz), 0.07 (s, 9 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.5, 128.4, 127.7, 126.4, 104.3, 88.6, 54.4, 51.9, 32.9, 28.0, 21.8, 13.5, 0.00.

MS (70 eV, EI): *m*/*z* (%) = 348 (5, M^+ – CH_3), 306 (100), 214 (4), 91 (85), 73 (12).

HRMS (EI): *m*/*z* calcd for $C_{24}H_{32}NSi$ [M^+ – H]: 362.2304; found: 362.2333.

Anal. Calcd for $C_{24}H_{33}NSi$: C, 79.28; H, 9.15; N, 3.85. Found: C, 79.19; H, 9.15; N, 3.83.

***N,N*-Dibenzyl-4-methylpent-1-yn-3-amine (5a)**

Preparation according to **GP 2** on a 4.4 mmol scale afforded, after column chromatographic purification (SiO_2, pentane), (–)-**5a** as a colorless oil (1.376 g, 99%, 96% ee); $[\alpha]_D^{20}$ –201 (*c* = 0.39, $CHCl_3$). HPLC (OD-H, 100% *n*-heptane/0% *i*-PrOH, 0.8 mL/min): t_r (min) = 8 (–), 10 (+).

IR (film): 2959m, 1495m, 1454m, 746m, 698vs cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.45–7.20 (m, 10 H), 3.84 (d, 2 H, *J* = 13.7 Hz), 3.39 (d, 2 H, *J* = 13.7 Hz), 2.93 (dd, 1 H, *J* = 10.6, 2.2 Hz), 2.86 (d, 1 H, *J* = 2.2 Hz), 2.01–1.85 (m, 1 H), 1.01 (t, 6 H, *J* = 6.6 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.6, 128.8, 128.2, 126.9, 81.2, 73.2, 59.0, 54.9, 30.6, 20.7, 19.3.

MS (70 eV, EI): *m*/*z* (%) = 235 (18), 234 (M^+ – *i*-Pr, 100), 91 (16).

HRMS (EI): *m*/*z* calcd for $C_{20}H_{22}N$ [M^+ – H]: 276.1752; found: 276.1720.

Anal. Calcd for $C_{20}H_{23}N$: C, 86.59; H, 8.36; N, 5.05: Found: C, 86.25; H, 8.20; N, 4.98.

***N,N*-Dibenzyl-4-ethylhex-1-yn-3-amine (5b)**

Preparation according to **GP 2** on a 4 mmol scale afforded, after column chromatographic purification (SiO_2, pentane), (±)-**5b** as a colorless oil (1.198 g, 98%).

IR (film): 3302m, 2963s, 2937m, 1495m, 1454m, 748m, 698s cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.43–7.18 (m, 10 H), 3.81 (d, 2 H, *J* = 13.7 Hz), 3.36 (d, 2 H, *J* = 13.7 Hz), 3.17 (dd, 1 H, *J* = 10.0, 1.6 Hz), 2.85 (d, 1 H, *J* = 2.2 Hz), 1.77–1.22 (m, 5 H), 0.77 (t, 3 H, *J* = 7.3 Hz), 0.57 (t, 3 H, *J* = 7.3 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.6, 129.0, 128.2, 126.9, 81.3, 73.4, 55.0, 54.6, 41.4, 21.9, 19.9, 10.4, 8.9.

MS (70 eV, EI): *m*/*z* (%) = 235 (20), 234 (M^+ – 1-ethylpropyl, 100), 91 (74).

HRMS (EI): *m*/*z* calcd for $C_{22}H_{26}N$ [M^+ – H]: 304.2065, found: 304.2075.

Anal. Calcd for $C_{22}H_{27}N$: C, 86.51; H, 8.91; N, 4.59: Found: C, 86.45; H, 9.07; N, 4.57.

***N*,*N*-Dibenzyl-1-cyclohexylprop-2-yn-1-amine (5c)**

Preparation according to **GP 2** on a 4.4 mmol scale afforded, after column chromatographic purification (SiO_2, pentane), (±)-**5c** as a colorless solid (1.376 g, 99%); mp 75–76 °C.

IR (film): 3302s, 2926vs, 2851s, 1495m, 1448m, 746s, 698s cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.44–7.17 (m, 10 H), 3.83 (d, 2 H, *J* = 14.0 Hz), 3.38 (d, 2 H, *J* = 14.0 Hz), 3.04 (dd, 1 H, *J* = 10.4, 2.2 Hz), 2.35 (d, 1 H, *J* = 2.2 Hz), 2.28 (d, 1 H, *J* = 13.0 Hz), 2.01, (d, 1 H, *J* = 13.0 Hz), 1.75–1.51 (m, 4 H), 1.31–0.98 (m, 3 H), 0.92–0.64 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 139.7, 128.8, 128.2, 126.8, 81.0, 73.5, 57.6, 54.8, 39.5, 31.2, 30.2, 26.5, 26.1, 25.9.

MS (70 eV, EI): *m*/*z* (%) = 235 (21), 234 (M^+ – *c*-C_6H_{11}, 100), 91 (88).

HRMS (EI): *m*/*z* calcd for $C_{23}H_{27}N$ [M^+]: 317.2143; found: 317.2139.

Anal. Calcd for $C_{23}H_{27}N$: C, 87.02; H, 8.57; N, 4.41. Found: C, 86.74; H, 8.37; N, 4.32.

***N*,*N*-Dibenzylhept-1-yn-3-amine (5d)**

Preparation according to **GP 2** on a 2 mmol scale afforded, after column chromatographic purification (SiO_2, pentane), (±)-**5d** as a colorless oil (535 mg, 92%).

IR (film): 3302m, 2956s, 2934s, 2860m, 1494m, 1454s, 746s, 698vs cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 7.41 (d, 4 H), *J* = 7.7 Hz, 7.33 (t, 4 H, *J* = 7.3 Hz), 7.25 (t, 2 H, *J* = 7.3 Hz), 3.85 (d, 2 H, *J* = 13.8 Hz), 3.46–3.40 (m, 3 H), 2.33 (d, 1 H, *J* = 1.3 Hz), 1.83–1.73 (m, 1 H), 1.71–1.63 (m, 1 H), 1.50–1.33 (m, 2 H), 1.25–1.17 (m, 2 H), 0.87 (t, 3 H, *J* = 7.3 Hz).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 139.7, 128.8, 128.2, 126.9, 82.2, 72.4, 54.7, 51.5, 33.4, 28.4, 22.2, 13.9.

MS (70 eV, EI): *m*/*z* (%) = 290 (1, M^+-H), 235 (22), 234 (98), 181 (11), 92 (100), 65 (10).

HRMS (EI): *m*/*z* calcd for $C_{21}H_{25}N$ [M^+ – H]: 290.1909; found: 290.1885.

Anal. Calcd for $C_{21}H_{25}N$: C, 86.55; H, 8.65; N, 4.81. Found: C, 86.84; H, 8.80; N, 4.97.

4-(Dibenzylamino)-5-methyl-1-(2,4,5-trifluorophenyl)hex-2-yn-1-one (9a)

Preparation according to **GP 3** afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 95:5), (±)-**9a** as a colorless oil (401 mg, 92%).

IR (film): 2199m, 1662m, 1641s, 1620s, 1514vs, 1430s, 1337s, 1295m, 1232s, 1194m, 1176m, 1146s, 797m, 748m, 699s cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.97–7.86 (m, 1 H), 7.44–7.21 (m, 10 H), 7.12–7.01 (m, 1 H), 3.92 (d, 2 H, *J* = 13.7 Hz), 3.46 (d, 2 H, *J* = 13.7 Hz), 3.20 (d, 1 H, *J* = 10.2 Hz), 2.16–1.99 (m, 1 H), 1.08–1.00 (m, 6 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 171.3, 138.8, 128.9, 128.4, 127.2, 122.3, 119.5, 119.2, 107.2, 95.3, 85.7, 59.5, 55.1, 30.4, 20.7, 19.9.

MS (70 eV, EI): *m*/*z* (%) = 433 (M^+ – 2 H, 4), 418 (5), 392 (48), 276 (1), 225 (2), 194 (3), 159 (22), 91 (100), 65 (5).

HRMS (EI): *m*/*z* calcd for $C_{27}H_{22}F_3NO$ [M^+ – 2 H]: 433.1652; found: 433.1630.

Anal. Calcd for $C_{27}H_{24}F_3NO$: C, 74.47; H, 5.55; N, 3.22. Found: C, 74.30; H, 5.59; N, 3.17.

1-(4-Chlorophenyl)-4-(dibenzylamino)-5-methylhex-2-yn-1-one (9b)

Preparation according to **GP 3** afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 97:3), (±)-**9b** as a yellow oil (379 mg, 91%).

IR (film): 2962m, 2931w, 2209m, 1650vs, 1586s, 1494w, 1454m, 1400w, 1257vs, 1170m, 1093vs, 1014m, 846w, 746s, 699s cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.08–8.03 (m, 2 H), 7.45–7.39 (m, 2 H), 7.33 (d, 4 H, *J* = 7.3 Hz), 7.25 (t, 4 H, *J* = 7.3 Hz), 7.17 (t, 2 H, *J* = 7.3 Hz), 3.87 (d, 2 H, *J* = 13.8 Hz), 3.39 (d, 2 H, *J* = 13.8 Hz), 3.15 (d, 1 H, *J* = 10.4 Hz), 2.09–0.96 (m, 1 H), 0.99 (t, 6 H, *J* = 6.3 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 176.5, 140.7, 138.8, 135.5, 130.8, 129.0, 128.9, 128.4, 127.2, 94.3, 84.3, 59.6, 55.3, 30.5, 20.8, 19.9.

MS (70 eV, EI): *m*/*z* (%) = 413 (M^+ – 2 H, 8), 398 (9), 372 (37), 281 (3), 207 (7), 139 (22), 91 (100), 65 (4).

HRMS (EI): *m*/*z* calcd for $C_{27}H_{24}ClNO$ [M^+ – 2 H]: 413.1545, found: 413.1562.

Anal. Calcd for $C_{27}H_{26}ClNO$: C, 77.96; H, 6.30; N, 3.37: Found: C, 77.49; H, 6.45; N, 3.41.

4-(Dibenzylamino)-5-methyl-1-phenylhex-2-yn-1-one (9c)

Preparation according to **GP 3** afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 98:2), (–)-**9c** as a light yellow solid (321 mg, 84%, 96% ee); mp 105–107 °C; $[\alpha]_D^{20}$ –227 (*c* = 1.06, $CHCl_3$). HPLC (OD-H, 99% *n*-heptane/1% *i*-PrOH, 0.2 mL/min): t_r(min) = 28 (–), 39 (+).

IR (film): 2963m, 2807w, 2209m, 1639vs, 1598m, 1579m, 1494w, 1451m, 1313m, 1262vs, 1173w, 1086m, 1068m, 746m, 697vs cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.25–8.19 (m, 2 H), 7.68–7.21 (m, 13 H), 3.95 (d, 2 H, *J* = 13.7 Hz), 3.49 (d, 2 H, *J* = 13.7 Hz), 3.23 (d, 1 H, *J* = 10.6 Hz), 2.18–2.03 (m, 1 H), 1.08 (d, 6 H, *J* = 6.2 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.9, 138.9, 137.0, 134.0, 129.5, 128.9, 128.6, 128.4, 127.1, 93.6, 84.6, 59.5, 55.2, 30.5, 20.9, 19.9.

MS (70 eV, EI): *m*/*z* (%) = 381 (M^+, <1), 338 (100), 246 (1), 181 (1), 115 (1), 105 (7) 91 (52), 77 (2), 65 (2).

HRMS (EI): *m*/*z* calcd for $C_{27}H_{27}NO$ [M^+]: 381.2093; found: 390.2082.

4-(Dibenzylamino)-5-ethyl-1-(4-methoxyphenyl)hept-2-yn-1-one (9d)

Preparation according to **GP 3** afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 95:5), (±)-**9d** as a yellow oil (428 mg, 97%).

IR (film): 2963m, 2934m, 2209m, 1640s, 1597s, 1509m, 1454m, 1316m, 1257vs, 1165s, 1029m, 845w, 749m, 699m cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 8.21 (d, 2 H, *J* = 8.6 Hz), 7.41 (d, 4 H, *J* = 7.5 Hz), 7.34 (t, 4 H, *J* = 7.5 Hz), 7.26 (t, 2 H, *J* = 7.5 Hz),

7.01 (d, 2 H, *J* = 8.6 Hz), 3.93 (d, 2 H, *J* = 15.1 Hz), 3.92 (s, 3 H), 3.43–3.37 (m, 3 H), 1.77–1.71 (m, 1 H), 1.71–1.59 (m, 2 H), 1.45–1.36 (m, 1 H), 1.35–1.26 (m, 1 H), 0.83 (t, 3 H, *J* = 7.3 Hz), 0.61 (t, 3 H, *J* = 7.3 Hz).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 176.6, 164.4, 139.0, 131.9, 130.5, 129.1, 128.3, 127.1, 113.9, 93.0, 84.8, 55.6, 55.3, 55.3, 41.4, 22.2, 20.0, 10.4, 8.8.

MS (70 eV, EI): *m*/*z* (%) = 439 (M^+, <1), 368 (100), 348 (1), 318 (1), 278 (3), 234 (1), 181 (2), 135 (29), 91 (79).

HRMS (EI): *m*/*z* calcd for $C_{30}H_{33}NO_2$ [M^+]: 439.2511; found: 439.2520.

Anal. Calcd for $C_{30}H_{33}NO_2$: C, 81.97; H, 7.57; N, 3.19. Found: C, 81.95; H, 7.48; N, 3.17.

4-(Dibenzylamino)-5-ethyl-1-(2-furyl)hept-2-yn-1-one (9e)
Preparation according to **GP 3** afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 9:1), (±)-**9e** as a brown oil (380 mg, 95%).

IR (film): 2963m, 2936m, 2219m, 2198m, 1638vs, 1567m, 1494m, 1463s, 1394m, 1299m, 1281m, 1168m, 1102m, 1017m, 746m, 699m cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.69 (dd, 1 H, *J* = 1.8 Hz, 0.9 Hz), 7.44–7.20 (m, 11 H), 6.62 (dd, 1 H, *J* = 3.5 Hz, 1.8 Hz), 3.91 (d, 2 H, *J* = 13.7 Hz), 3.52–3.39 (m, 3 H), 1.87–1.61 (m, 3 H), 1.54–1.27 (m, 2 H), 0.81 (t, 3 H, *J* = 7.3 Hz), 0.59 (t, 3 H, *J* = 7.3 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.7, 153.5, 147.9, 138.8, 129.0, 128.3, 127.2, 120.3, 112.6, 92.9, 84.1, 55.3, 41.3, 22.1, 20.0, 10.4, 8.8.

MS (70 eV, EI): *m*/*z* (%) = 397 (M^+ – 2 H, 1), 368 (6), 328 (16), 304 (3), 281 (1), 207 (4), 194 (3), 175 (2), 95 (18), 91 (100), 65 (7).

HRMS (EI): *m*/*z* calcd for $C_{27}H_{27}NO_2$ [M^+ – 2 H]: 397.2040; found: 397.2021.

Anal. Calcd for $C_{27}H_{29}NO_2$: C, 81.17; H, 7.32; N, 3.51: Found: C, 80.96; H, 7.38; N, 3.48.

6-(Dibenzylamino)-7-ethyl-2,2-dimethylnon-4-yn-3-one (9f)
Preparation according to **GP 3** afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 96:4), (±)-**9f** as a colorless oil (374 mg, 96%).

IR (film): 2966s, 2933m, 2876m, 2194m, 1671vs, 1454m, 1128m, 748m, 699m cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41–7.20 (m, 10 H), 3.87 (d, 2 H, *J* = 13.5 Hz), 3.44–3.32 (m, 3 H), 1.81–1.54 (m, 3 H), 1.52–1.23 (m, 2 H), 1.29 (s, 9 H), 0.78 (t, 3 H, *J* = 7.5 Hz), 0.58 (t, 3 H, *J* = 7.5 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 194.0, 138.9, 129.0, 128.3, 127.2, 92.6, 83.9, 55.3, 55.1, 44.7, 41.3, 26.3, 22.1, 20.0, 10.3, 8.8.

MS (70 eV, EI): *m*/*z* (%) = 390 (M^+ + 1 H, <1), 318 (100), 280 (3), 234 (2), 181 (2), 91 (29).

HRMS (EI): *m*/*z* calcd for $C_{27}H_{36}NO$ [M^+ + 1 H]: 390.2798; found: 390.2787.

Anal. Calcd for $C_{27}H_{35}NO$: C, 83.24; H, 9.06; N, 3.60: Found: C, 83.23; H, 9.15; N, 3.58.

4-(Dibenzylamino)-5-ethyl-1-phenylhept-2-yn-1-one (9g)
Preparation according to **GP 3** afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 95:5), **(±)-9g** as a colorless solid (395 mg, 0.96 mmol, 96%). mp.: 76-77 °C.

IR (film): 2968m, 2941m, 2209m, 1640vs, 1598m, 1579m, 1494m, 1450m, 1312m, 1261vs, 1172m, 1086m, 1069m, 748m, 734m, 697vs cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.27–8.20 (m, 2 H), 7.68–7.60 (m, 1 H), 7.58–7.49 (m, 2 H), 7.44–7.21 (m, 10 H), 3.94 (d, 2 H, *J* = 13.7 Hz), 3.54–3.43 (m, 3 H), 1.90–1.63 (m, 3 H), 1.60–1.30 (m, 2 H), 0.82 (t, 3 H, *J* = 7.3 Hz), 0.61 (t, 3 H, *J* = 7.3 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.9, 138.9, 137.1, 134.0, 129.5, 129.1, 128.6, 128.4, 127.2, 94.0, 84.5, 55.4, 55.3, 41.4, 22.2, 20.0, 10.4, 8.8.

MS (70 eV, EI): *m*/*z* (%) = 409 (M^+, <1), 338 (100), 312 (1), 246 (2), 194 (1), 181 (2), 115 (3), 105 (16), 91 (87), 77 (6), 65 (5).

HRMS (EI): *m*/*z* calcd for $C_{29}H_{31}NO$ [M^+]: 409.2406; found: 409.2443.

Anal. Calcd for $C_{29}H_{31}NO$: C, 85.04; H, 7.63; N, 3.42: Found: C, 85.44; H, 7.53; N, 3.40.

4-Cyclohexyl-4-(dibenzylamino)-1-(2-furyl)but-2-yn-1-one (9h)
Preparation according to **GP 3** afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 95:5), (±)-**9h** as a bright yellow solid (389 mg, 95%); mp 119–120 °C.

IR (film): 2929s, 2851m, 2200w, 1637vs, 1566m, 1494m, 1462s, 1396m, 1305m, 1173w, 1108m, 1015m, 884w, 739m, 699s, 594w cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.69 (dd, 1 H, *J* = 1.8, 0.9 Hz), 7.45–7.20 (m, 11 H), 6.61 (dd, 1 H, *J* = 3.5, 1.8 Hz), 3.93 (d, 2 H, *J* = 13.7 Hz), 3.48 (d, 2 H, *J* = 13.7 Hz), 3.32 (d, 1 H, *J* = 10.2 Hz), 2.30 (d, 1 H, *J* = 12.8 Hz), 2.02 (d, 1 H, *J* = 12.8 Hz), 1.85–1.55 (m, 4 H), 1.34–0.70 (m, 5 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.7, 153.4, 147.8, 138.9, 128.7, 128.3, 127.1, 120.4, 112.6, 92.4, 84.1, 58.2, 55.1, 39.3, 31.2, 30.2, 26.4, 25.9, 25.7.

MS (70 eV, EI): *m*/*z* (%) = 411 (M^+, 2), 328 (100), 302 (1), 236 (1), 181 (1), 91 (19), 65 (1).

HRMS (EI): *m*/*z* calcd for $C_{28}H_{29}NO_2$ [M^+]: 411.2198; found: 411.2214.

Anal. Calcd for $C_{28}H_{29}NO_2$: C, 81.72; H, 7.10; N, 3.40: Found: C, 81.61; H, 7.10; N, 3.34.

4-(Dibenzylamino)-1-phenyloct-2-yn-1-one (9i)
Preparation according to **GP 3** afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 98.5:1.5), (±)-**9i** as a yellow oil (376 mg, 95%).

IR (film): 3063m, 3029m, 2956m, 2932m, 2860m, 2210m, 1645vs, 1598m, 1581m, 1494m, 1451s, 1312m, 1260vs, 1174m, 1069m, 1025m, 747m, 699vs cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.24–8.17 (m, 2 H), 7.68–7.60 (m, 1 H), 7.56–7.48 (m, 2 H), 7.44–7.20 (m, 10 H), 3.95 (d, 2 H, *J* = 13.7 Hz), 3.70 (t, 1 H, *J* = 7.5 Hz), 3.51 (d, 2 H, *J* = 13.7 Hz), 1.95–1.71 (m, 2 H), 1.60–1.13 (m, 4 H), 0.87 (t, 3 H, *J* = 7.1 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 177.9, 139.1, 137.0, 134.0, 129.5, 128.8, 128.3, 127.1, 94.3, 83.6, 55.1, 52.0, 32.9, 28.4, 22.2, 13.9.

MS (70 eV, EI): *m*/*z* (%) = 395 (M^+, <1), 338 (100), 246 (1), 196 (3), 181 (1), 115 (1), 105 (9) 91 (62), 77 (2), 65 (2).

HRMS (EI): *m*/*z* calcd for $C_{28}H_{29}NO$ [M^+]: 395.2249; found: 395.2233.

Anal. Calcd for $C_{28}H_{29}NO$: C, 85.02; H, 7.39; N, 3.54. Found: C, 84.79; H, 7.42; N, 3.50.

6-(Dibenzylamino)-2,2-dimethyldec-4-yn-3-one (9j)
Preparation according to **GP 3** afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 98:2), (±)-**9j** as a colorless oil (352 mg, 94%).

IR (film): 2961s, 2870m, 2195m, 1671vs, 1494m, 1454m, 1365m, 1132s, 746m, 698s cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.20 (m, 10 H), 3.89 (d, 2 H, *J* = 13.7 Hz), 3.58 (t, 1 H, *J* = 7.7 Hz), 3.41 (d, 2 H, *J* = 13.7 Hz), 1.87–1.62 (m, 2 H), 1.52–1.12 (m, 4 H), 1.28 (s, 9 H), 0.84 (t, 3 H, *J* = 7.1 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 193.9, 139.1, 128.7, 128.3, 127.1, 93.1, 82.7, 55.1, 44.7, 32.9, 28.3, 26.2, 22.1, 13.9.

MS (70 eV, EI): *m*/*z* (%) = 375 (M^+, <1), 318 (100), 266 (5), 234 (1), 196 (2), 181 (2), 115 (1), 91 (60), 79 (2), 57 (7).

HRMS (EI): *m*/*z* calcd for $C_{26}H_{33}NO$ [M^+]: 375.2562; found: 375.2549.

Anal. Calcd for $C_{26}H_{33}NO$: C, 83.15; H, 8.86; N, 3.73. Found: C, 83.14; H, 8.82; N, 3.70.

4-(Dibenzylamino)-1-(2-furyl)oct-2-yn-1-one (9k)

Preparation according to **GP 3** afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 95:5), (±)-**9k** as a brown oil (362 mg, 94%).

IR (film): 3029m, 2956m, 2933m, 2861m, 2202m, 1640vs, 1567m, 1494m, 1463vs, 1394s, 1299m, 1168m, 1096m, 1014m, 884m, 745s, 699s cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.69 (s, 1 H), 7.42–7.36 (m, 5 H), 7.32 (t, 4 H, *J* = 7.5 Hz), 7.27–7.22 (m, 2 H), 6.63–6.59 (m, 1 H), 3.92 (d, 2 H, *J* = 13.5 Hz), 3.64 (t, 1 H, *J* = 7.7 Hz), 3.48 (d, 2 H, *J* = 13.5 Hz), 1.88–1.71 (m, 2 H), 1.51–1.34 (m, 2 H), 1.26–1.16 (m, 2 H), 0.86 (t, 3 H, *J* = 7.3 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 164.7, 153.4, 147.9, 139.0, 128.8, 128.3, 127.1, 120.5, 112.6, 93.2, 82.9, 55.0, 52.0, 32.8, 28.3, 22.1, 13.9.

MS (70 eV, EI): *m*/*z* (%) = 385 (M^+, <1), 328 (100), 302 (2), 236 (1), 196 (2), 91 (24).

HRMS (EI): *m*/*z* calcd for $C_{26}H_{27}NO_2$ [M^+]: 385.2042; found: 385.2037.

Anal. Calcd for $C_{26}H_{27}NO_2$: C, 81.01; H, 7.06; N, 3.63: Found: C, 80.56; H, 7.07; N, 3.61.

5-(Dibenzylamino)-6-ethyloct-3-yn-2-one (9l)

Preparation according to **GP 4** afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 96:4), (±)-**9l** as a bright yellow oil (312 mg, 90%).

IR (film): 2966m, 2936m, 2190m, 1679vs, 1494m, 1453m, 1356m, 1216s, 747s, 696s cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.37 (d, 4 H, *J* = 7.3 Hz), 7.32 (t, 4 H, *J* = 7.3 Hz), 7.25 (t, 2 H, *J* = 7.3 Hz), 3.85 (d, 2 H, *J* = 13.3 Hz), 3.38–3.32 (m, 3 H), 2.44 (s, 3 H), 1.75–1.66 (m, 2 H), 1.65–1.57 (m, 1 H), 1.49–1.40 (m, 1 H), 1.33–1.25 (m, 1 H), 0.79 (t, 3 H, *J* = 7.3 Hz), 0.57 (t, 3 H, *J* = 7.3 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 185.4, 138.9, 129.0, 128.3, 127.1, 91.4, 86.4, 55.2, 55.0, 41.2, 33.3, 22.1, 19.9, 10.4, 8.7.

MS (70 eV, EI): *m*/*z* (%) = 346 (M^+ – 1 H, <1), 318 (1), 304 (1), 276 (100), 234 (2), 181 (3), 142 (1), 115 (2), 91 (75), 65 (4), 43 (2).

HRMS (EI): *m*/*z* calcd for $C_{24}H_{28}NO$ [M^+ – 1 H]: 346.2170, found: 346.2152.

Anal. Calcd for $C_{24}H_{29}NO$: C, 82.95; H, 8.41; N, 4.03. Found: C, 83.21; H, 8.46; N, 4.03.

7-(Dibenzylamino)-8-ethyldec-5-yn-4-one (9m)

Preparation according to **GP 4** afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 98:2), (±)-**9m** as a colorless oil (345 mg, 92%).

IR (film): 3029w, 2964vs, 2936s, 2877m, 2197m, 1675vs, 1495m, 1454s, 1162m, 1071m, 748s, 699s cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.38 (d, 4 H, *J* = 7.2 Hz), 7.32 (t, 4 H, *J* = 7.2 Hz), 7.25 (t, 2 H, *J* = 7.2 Hz), 3.86 (d, 2 H, *J* = 13.4 Hz), 3.33–3.25 (m, 3 H), 2.63 (t, 2 H, *J* = 7.3 Hz), 1.78–1.15 (m, 7 H), 1.03 (t, 3 H, *J* = 7.5 Hz), 0.79 (t, 3 H, *J* = 7.5 Hz), 0.57 (t, 3 H), *J* = 7.3 Hz.

^{13}C NMR (75 MHz, $CDCl_3$): δ = 188.0, 138.9, 129.0, 128.3, 127.1, 91.4, 85.9, 55.2, 55.0, 47.8, 41.3, 22.1, 20.0, 17.9, 13.6, 10.4, 8.8.

MS (70 eV, EI): *m*/*z* (%) = 374 (M^+ – 1 H, <1), 304 (100), 234 (4), 181 (2), 91 (40).

HRMS (EI): *m*/*z* calcd for $C_{26}H_{32}NO$ [M^+ – 1 H]: 374.2483; found: 374.2457.

Anal. Calcd for $C_{26}H_{33}NO$: C, 83.15; H, 8.86; N, 3.73. Found: C, 83.35; H, 8.87; N, 3.66.

1-Cyclohexyl-4-(dibenzylamino)-5-ethylhept-2-yn-1-one (9n)

Preparation according to **GP 4** afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 97:3), (±)-**9n** as a colorless oil (375 mg, 90%).

IR (film): 2933vs, 2856m, 2200m, 1664vs, 1494w, 1453m, 1237w, 1162m, 1119m, 748s, 700s cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.20 (m, 10 H), 3.85 (d, 2 H, *J* = 13.7 Hz), 3.42–3.31 (m, 3 H), 2.47 (tt, 1 H, *J* = 10.9, 3.5 Hz), 2.11–2.00 (m, 2 H), 1.89–1.17 (m, 13 H), 0.78 (t, 3 H, *J* = 7.5 Hz), 0.57 (t, 3 H, *J* = 7.5 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 191.4, 138.9, 129.0, 128.3, 127.1, 92.1, 85.1, 55.2, 55.1, 52.6, 41.3, 28.5, 25.9, 25.4, 22.1, 20.0, 10.4, 8.8.

MS (70 eV, EI): *m*/*z* (%) = 386 (M^+ – CHO, 1), 344 (100), 281 (11), 234 (13), 207 (35), 194 (8), 91 (91), 83 (16).

Anal. Calcd for $C_{29}H_{37}NO$: C, 83.81; H, 8.97; N, 3.37. Found: C, 83.60; H, 8.98; N, 3.31.

***N*,*N*-Dibenzyl-2-methyl-1-[2-methyl-6-(2,4,5-trifluorophenyl)-4-pyrimidinyl]-1-propanamine (6a)**

Preparation according to **GP 5** on a 0.81 mmol scale afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 98:2), (±)-**6a** as a colorless solid (291 mg, 75%); mp 114–115 °C.

IR (film): 2960m, 1627m, 1575vs, 1541vs, 1516vs, 1495m, 1454m, 1398m, 1360m, 1208m, 1142m, 886m, 782m, 748m, 700s cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.13–8.04 (m, 1 H), 7.85 (d, 4 H, *J* = 7.5 Hz), 7.25 (t, 4 H, *J* = 7.5 Hz), 7.21–7.12 (m, 3 H), 7.03–6.94 (m, 1 H), 3.99 (d, 2 H, *J* = 14.2 Hz), 3.19 (d, 1 H, *J* = 10.7 Hz), 2.99 (d, 2 H, *J* = 14.2 Hz), 2.76 (s, 3 H), 2.61–2.49 (m, 1 H), 1.15 (d, 3 H, *J* = 6.5 Hz), 0.53 (d, 3 H, *J* = 6.5 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.1, 167.5, 157.9, 157.2, 139.9, 128.8, 128.3, 126.9, 118.8, 118.3, 118.1, 106.7, 106.5, 106.4, 106.2, 69.4, 54.1, 27.4, 26.6, 20.6, 20.2.

MS (70 eV, EI): *m*/*z* (%) = 474 (M^+ – H, <1), 432 (21), 384 (12), 341 (9), 325 (11), 280 (28), 265 (100), 196 (55), 91 (37).

HRMS (EI): *m*/*z* calcd for $C_{29}H_{27}F_3N_3$ [M^+ – H]: 474.2156; found: 474.2153.

Anal. Calcd for $C_{29}H_{28}F_3N_3$: C, 73.24; H, 8.84; N, 5.93. Found: C, 73.10; H, 8.56; N, 6.06.

***N*,*N*-Dibenzyl-1-[6-(4-chlorophenyl)-2-methyl-4-pyrimidinyl]-2-methyl-1-propanamine (6b)**

Preparation according to **GP 5** on a 0.80 mmol scale afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 98:2), (±)-**6b** as a colorless solid (279 mg, 76%); mp 58–63 °C.

IR (film): 2958m, 1582vs, 1571vs, 1534vs, 1493s, 1453m, 1403m, 1092s, 1014m, 834m, 739s, 698s cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.08–8.02 (m, 2 H), 7.54–7.47 (m, 2 H), 7.44 (d, 4 H, *J* = 7.2 Hz), 7.39–7.22 (m, 6 H), 7.08 (s, 1 H), 4.10 (d, 2 H, *J* = 14.2 Hz), 3.31 (d, 1 H, *J* = 11.1 Hz), 3.11 (d, 2 H, *J* = 14.2 Hz), 2.86 (s, 3 H), 2.76–2.57 (m, 1 H), 1.27 (d, 3 H, *J* = 6.4 Hz), 0.65 (d, 3 H, *J* = 6.4 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 168.2, 167.3, 162.0, 140.0, 136.8, 135.9, 129.2, 128.7, 128.4, 128.3, 126.9, 114.1, 69.5, 54.1, 27.4, 26.6, 20.7, 20.2.

MS (70 eV, EI): *m*/*z* (%) = 456 (M^+ + H, <1), 412 (17), 364 (10), 321 (6), 260 (50), 245 (100), 218 (12), 196 (65), 91 (78).

HRMS (EI): *m*/*z* calcd for $C_{29}H_{31}ClN_3$ [M^+ + H]: 456.2207; found: 456.2178.

Anal. Calcd for $C_{29}H_{30}ClN_3$: C, 76.38; H, 6.63; N, 9.21; Cl, 7.77. Found: C, 76.54; H, 6.61; N, 9.16; Cl, 7.74.

N,*N*-Dibenzyl-2-methyl-1-(2-methyl-6-phenyl-4-pyrimidinyl)-1-propanamine (6c)

Preparation according to **GP 5** on a 0.78 mmol scale afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 98:2), (±)-**6c** as a bright pink solid (271 mg, 82%, 96% ee); mp 95–97 °C;. $[\alpha]_D^{20}$ –192 (*c* = 1.36, $CHCl_3$). HPLC (OD-H, 98% *n*-heptane/2% *i*-PrOH, 0.5 mL/min): t_r (min) = 8 (–), 10 (+).

IR (film): 3062m, 2958m, 2925m, 1576vs, 1538vs, 1494m, 1453m, 1394m, 1366m, 1070m, 1028m, 769m, 744m, 726m, 698s, 640m cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.13–8.05 (m, 2 H), 7.56–7.49 (m, 3 H), 7.44 (d, 4 H, *J* = 7.5 Hz), 7.34 (t, 4 H, *J* = 7.5 Hz), 7.25 (t, 2 H, *J* = 7.5 Hz), 7.12 (s, 1 H), 4.09 (d, 2 H, *J* = 14.2 Hz), 3.31 (d, 1 H, *J* = 10.6 Hz), 3.12 (d, 2 H, *J* = 14.2 Hz), 2.86 (s, 3 H), 2.74–2.57 (m, 1 H), 1.26 (d, 3 H, *J* = 6.4 Hz), 0.65 (d, 3 H, *J* = 6.4 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.0, 167.0, 163.3, 140.0, 137.5, 130.6, 128.9, 128.8, 127.1, 126.8, 114.4, 114.3, 69.6, 54.1, 27.5, 26.6, 20.7, 20.2.

MS (70 eV, EI): *m*/*z* (%) = 420 (M^+ – H, 1), 378 (28), 330 (17), 287 (13), 271 (6), 226 (90), 211 (100), 196 (43), 184 (7), 91 (56), 65 (5).

HRMS (EI): *m*/*z* calcd for $C_{29}H_{30}N_3$ [M^+ – H]: 420.2439; found: 420.2482.

Anal. Calcd for $C_{29}H_{31}N_3$: C, 82.62; H, 7.41; N, 9.97. Found: C, 82.17; H, 7.34; N, 9.69.

N,*N*-Dibenzyl-2-ethyl-1-[6-(4-methoxyphenyl)-2-methyl-4-pyrimidinyl]-1-butanamine (6d)

Preparation according to **GP 5** on a 0.95 mmol scale afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 95:5), (±)-**6d** as a bright yellow solid (313 mg, 78%); mp 60–62 °C.

IR (film): 2962m, 2933m, 1609m, 1575vs, 1535s, 1513s, 1454m, 1254s, 1175m, 1029m, 835m, 746m, 698s, 574m cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 8.07 (d, 2 H, *J* = 8.6 Hz), 7.41 (d, 4 H, *J* = 7.3 Hz), 7.33 (t, 4 H, *J* = 7.3 Hz), 7.24 (t, 2 H, *J* = 7.3 Hz), 7.07 (s, 1 H), 7.04 (d, 2 H, *J* = 8.6 Hz), 4.04 (d, 2 H, *J* = 13.9 Hz), 3.89 (s, 3 H), 3.52 (d, 1 H, *J* = 10.7 Hz), 3.10 (d, 2 H, *J* = 13.9 Hz), 2.83 (s, 3 H), 2.40–2.33 (m, 1 H), 2.02–1.93 (m, 1 H), 1.71–1.62 (m, 1 H), 1.12–1.02 (m, 1 H), 1.00–0.89 (m, 1 H), 0.81 (t, 3 H, *J* = 7.1 Hz), 0.64 (t, 3 H, *J* = 7.1 Hz).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 167.8, 166.8, 162.7, 161.8, 140.1, 128.9, 128.6, 128.3, 128.2, 126.8, 114.3, 113.9, 113.6, 65.1, 55.4, 54.2, 38.4, 26.6, 21.7, 19.9, 10.3, 9.4.

MS (70 eV, EI): *m*/*z* (%) = 478 (M^+ – H, <1), 408 (16), 388 (6), 368 (5), 317 (7), 301 (5), 284 (33), 255 (100), 214 (9), 196 (5), 91 (54), 65 (4).

HRMS (EI): *m*/*z* calcd for $C_{32}H_{36}N_3O$ [M^+ – H]: 478.2858; found: 478.2868.

Anal. Calcd for $C_{32}H_{37}N_3O$: C, 80.13; H, 7.78; N, 8.76. Found: C, 79.99; H, 7.95; N, 8.43.

N,*N*-Dibenzyl-2-ethyl-1-[6-(2-furyl)-2-methyl-4-pyrimidinyl]-1-butanamine (6e)

Preparation according to **GP 5** on a 0.84 mmol scale afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 95:5), (±)-**6e** as a bright yellow solid (291 mg, 79%); mp 116–117 °C.

IR (film): 2965 (m), 2935 (m), 1604 (vs), 1564 (vs), 1538 (s), 1487 (m), 1453 (m), 1396 (m), 1012 (w), 744 (s), 698 (s).

^1H NMR (300 MHz, $CDCl_3$): δ = 7.63 (dd, 1 H, *J* = 1.8 Hz, 0.9 Hz), 7.42 (d, 4 H, *J* = 7.3 Hz), 7.37–7.20 (m, 7H), 7.11 (s, 1 H), 6.60 (dd, 1 H, *J* = 3.5 Hz, 1.8 Hz), 4.04 (d, 2 H, *J* = 14.2 Hz), 3.51 (d, 1 H, *J* = 11.5 Hz), 3.08 (d, 2 H, *J* = 14.2 Hz), 2.81 (s, 3 H), 2.41–2.28 (m, 1 H), 2.05–1.89 (m, 1 H), 1.73–1.57 (m, 1 H), 1.15–0.88 (m, 2 H), 0.79 (t, 3 H, *J* = 7.5 Hz), 0.64 (t, 3 H, *J* = 7.5 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 167.9, 167.1, 154.6, 152.3, 144.8, 140.0, 129.0, 128.2, 126.8, 112.4, 112.1, 111.7, 65.0, 54.1, 38.3, 26.6, 21.6, 19.9, 10.2, 9.4.

MS (70 eV, EI): *m*/*z* (%) = 440 (M^+ + H, 1), 368 (18), 328 (3), 277 (7), 244 (34), 215 (100), 196 (10), 174 (4), 91 (40).

HRMS (EI): *m*/*z* calcd for $C_{29}H_{34}N_3O$ [M^+ + H]: 440.2703; found: 440.2681.

Anal. Calcd for $C_{29}H_{33}N_3O$: C, 79.20; H, 7.57; N, 9.56. Found: C, 79.51; H, 7.64; N, 9.16.

N,*N*-Dibenzyl-1-(6-*tert*-butyl-2-methyl-4-pyrimidinyl)-2-ethyl-1-butanamine (6f)

Preparation according to **GP 5** on a 0.84 mmol scale afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 98:2), (±)-**6f** as a colorless oil (260 mg, 73%).

IR (film): 2963vs, 2933s, 1576vs, 1539vs, 1494m, 1454m, 1398m, 1362m, 1071w, 1028w, 743s, 698s cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.43–7.19 (m, 10 H), 6.71 (s, 1 H), 4.03 (d, 2 H, *J* = 13.9 Hz), 3.41 (d, 1 H, *J* = 11.1 Hz), 2.99 (d, 2 H, *J* = 13.9 Hz), 2.76 (s, 3 H), 2.40–2.26 (m, 1 H), 2.02–1.88 (m, 1 H), 1.72–1.57 (m, 1 H), 1.37 (s, 9 H), 1.06–0.85 (m, 2 H), 0.80 (t, 3 H, *J* = 7.5 Hz), 0.61 (t, 3 H, *J* = 7.5 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.7, 166.9, 165.9, 140.1, 128.9, 128.2, 126.8, 114.2, 65.1, 54.1, 38.4, 37.1, 29.5, 26.6, 21.7, 20.0, 10.3, 9.5.

MS (70 eV, EI): *m*/*z* (%) = 430 (M^+ + H, 3), 358 (65), 338 (29), 267 (13), 251 (10), 234 (70), 205 (100), 196 (56), 91 (68).

HRMS (EI): *m*/*z* calcd for $C_{29}H_{39}N_3$ [M^+ + H]: 430.3223; found: 430.3232.

Anal. Calcd for $C_{29}H_{39}N_3$: C, 81.07; H, 9.15; N, 9.78: Found: C, 80.53; H, 9.08; N, 9.50.

N,*N*-Dibenzyl-2-ethyl-1-(2-methyl-6-phenyl-4-pyrimidinyl)-1-butanamine (6g)

Preparation according to **GP 5** on a 0.84 mmol scale afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 98:2), (±)-**6g** as a colorless oil (260 mg, 73%).

IR (film): 2963vs, 2933s, 1576vs, 1539vs, 1494m, 1454m, 1398m, 1362m, 1071w, 1028w, 743s, 698s cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.43–7.19 (m, 10 H), 6.71 (s, 1 H), 4.03 (d, 2 H, *J* = 13.9 Hz), 3.41 (d, 1 H, *J* = 11.1 Hz), 2.99 (d, 2 H, *J* = 13.9 Hz), 2.76 (s, 3 H), 2.40–2.26 (m, 1 H), 2.02–1.88 (m, 1 H), 1.72–1.57 (m, 1 H), 1.37 (s, 9 H), 1.06–0.85 (m, 2 H), 0.80 (t, 3 H, *J* = 7.5 Hz), 0.61 (t, 3 H, *J* = 7.5 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.7, 166.9, 165.9, 140.1, 128.9, 128.2, 126.8, 114.2, 65.1, 54.1, 38.4, 37.1, 29.5, 26.6, 21.7, 20.0, 10.3, 9.5.

MS (70 eV, EI): *m*/*z* (%) = 430 (M^+ + H, 3), 358 (65), 338 (29), 267 (13), 251 (10), 234 (70), 205 (100), 196 (56), 91 (68).

HRMS (EI): *m*/*z* calcd for $C_{29}H_{39}N_3$ [M^+ + H]: 430.3223; found: 430.3232.

Anal. Calcd for $C_{29}H_{39}N_3$: C, 81.07; H, 9.15; N, 9.78. Found: C, 80.53; H, 9.08; N, 9.50.

***N*,*N*-Dibenzyl(cyclohexyl)[6-(2-furyl)-2-methyl-4-pyrimidinyl]methanamine (6h)**

Preparation according to **GP 5** on a 1.0 mmol scale afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 95:5), (±)-**6h** as a colorless solid (360 mg, 80%); mp 145–147 °C.

IR (film): 2925s, 2850m, 1604vs, 1564vs, 1538m, 1486m, 1452m, 1398w, 744m, 698m cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.62 (dd, 1 H, *J* = 1.8, 0.9 Hz), 7.42 (d, 4 H, *J* = 7.5 Hz), 7.33 (t, 4 H, *J* = 7.5 Hz), 7.28–7.20 (m, 3 H), 7.04 (s, 1 H), 6.59 (dd, 1 H, *J* = 3.5, 1.8 Hz), 4.04 (d, 2 H, *J* = 14.2 Hz), 3.38 (d, 1 H, *J* = 10.6 Hz), 3.11 (d, 2 H, *J* = 14.2 Hz), 2.80 (s, 3 H), 2.52 (d, 1 H, *J* = 11.9 Hz), 2.37–2.21 (m, 1 H), 1.85–1.73 (m, 1 H), 1.69–1.47 (m, 2 H), 1.38–0.91 (m, 5 H), 0.74–0.58 (m, 1 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.0, 166.9, 154.6, 152.2, 144.8, 140.1, 128.8, 128.2, 126.8, 112.4, 112.3, 111.8, 68.3, 54.0, 36.7, 31.0, 30.3, 26.7, 26.6, 26.1, 26.0.

MS (70 eV, EI): *m*/*z* (%) = 452 (M^+ + H, <1), 368 (11), 328 (3), 277 (3), 256 (100), 213 (24), 196 (10), 174 (10), 91 (35).

HRMS (EI): *m*/*z* calcd for $C_{28}H_{32}N_3O$ [M^+ + H]: 452.2703; found: 452.2689.

Anal. Calcd for $C_{28}H_{31}N_3O$: C, 79.79; H, 7.37; N, 9.30. Found: C, 79.62; H, 7.53; N, 8.94.

***N*,*N*-Dibenzyl-1-(2-methyl-6-phenyl-4-pyrimidinyl)-1-pentanamine (6i)**

Preparation according to **GP 5** on a 0.26 mmol scale afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 95:5), (±)-**6i** as a colorless oil (101 mg, 89%).

IR (film): 3028m, 2956m, 2929m, 1574vs, 1539vs, 1495m, 1454m, 1395m, 1073m, 1028m, 768m, 746m, 698s cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.10–8.02 (m, 2 H), 7.56–7.46 (m, 3 H), 7.42–7.19 (m, 11 H), 3.93 (d, 2 H, *J* = 14.2 Hz), 3.75 (t, 1 H, *J* = 7.3 Hz, 3.40 (d, 2 H, *J* = 14.2 Hz), 2.82 (s, 3 H), 2.12–1.91 (m, 2 H), 1.46–1.17 (m, 4 H), 0.87 (t, 3 H, *J* = 7.1 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.2, 167.8, 163.6, 140.2, 137.6, 130.5, 128.9, 128.8, 128.2, 127.2, 126.8, 113.6, 62.6, 54.2, 29.2, 28.9, 26.5, 22.7, 14.0.

MS (70 eV, EI): *m*/*z* (%) = 436 (M^+ + H, 1), 378 (4), 344 (10), 287 (2), 266 (4), 240 (53), 197 (100), 184 (6), 91 (21).

HRMS (EI): *m*/*z* calcd for $C_{30}H_{34}N_3$ [M^+ + H]: 436.2753; found: 436.2716.

***N*,*N*-Dibenzyl-1-(6-*tert*-butyl-2-methyl-4-pyrimidinyl)-1-pentanamine (6j)**

Preparation according to **GP 5** on a 0.30 mmol scale afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 95:5), (±)-**6j** as a colorless oil (101 mg, 81%).

IR (film): 3063m, 3028m, 2957vs, 2930s, 2860m, 1575vs, 1540vs, 1494m, 1454s, 1392s, 1362m, 1340m, 1232w, 1127w, 1073m, 1028m, 745s, 698vs cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.18 (m, 10 H), 6.86 (s, 1 H), 3.90 (d, 2 H, *J* = 13.9 Hz), 3.64 (t, 1 H, *J* = 7.3 Hz), 3.29 (d, 2 H, *J* = 13.9 Hz), 2.72 (s, 3 H), 2.10–1.85 (m, 2 H), 1.45–1.12 (m, 13 H), 0.87 (t, 3 H, *J* = 7.1 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 176.9, 168.0, 166.7, 140.3, 128.8, 128.2, 126.8, 113.2, 65.8, 62.5, 54.1, 37.2, 29.5, 28.9, 26.5, 22.7, 14.0.

MS (70 eV, EI): *m*/*z* (%) = 416 (M^+ + H, <1), 358 (3), 324 (10), 266 (7), 220 (50), 196 (39), 177 (100), 164 (5), 91 (26).

HRMS (EI): *m*/*z* calcd for $C_{28}H_{38}N_3$ [M^+ + H]: 416.3066; found: 416.3096.

Anal. Calcd for $C_{28}H_{37}N_3$: C, 80.92; H, 8.97; N, 10.11. Found: C, 81.06; H, 8.96; N, 10.08.

***N*,*N*-Dibenzyl-1-[6-(2-furyl)-2-methyl-4-pyrimidinyl]-1-pentanamine (6k)**

Preparation according to **GP 5** on a 0.48 mmol scale afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 9:1), (±)-**6k** as a yellow oil (183 mg, 90%).

IR (film): 2956m, 2930m, 2858m, 1605vs, 1565vs, 1539s, 1487s, 1454m, 1398m, 1011m, 885w, 745s, 698s cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.62 (d, 1 H, *J* = 1.3 Hz), 7.39 (d, 4 H, *J* = 7.1 Hz), 7.32 (t, 4 H, *J* = 7.3 Hz), 7.27–7.19 (m, 4 H), 6.59 (dd, 1 H, *J* = 1.8, 0.9 Hz), 3.92 (d, 2 H, *J* = 14.2 Hz), 3.72 (t, 1 H, *J* = 7.3 Hz), 3.37 (d, 2 H, *J* = 14.2 Hz), 2.78 (s, 3 H), 2.10–1.87 (m, 2 H), 1.49–1.14 (m, 4 H), 0.86 (t, 3 H, *J* = 7.1 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.1, 167.7, 154.9, 152.3, 144.7, 140.2, 128.8, 128.2, 126.8, 112.3, 111.6, 111.3, 62.5, 54.2, 29.3, 28.8, 26.4, 22.6, 14.0.

MS (70 eV, EI): *m*/*z* (%) = 425 (M^+, <1), 368 (2), 334 (4), 266 (3), 230 (52), 196 (5), 187 (100), 174 (9), 91 (57), 65 (5).

HRMS (EI): *m*/*z* calcd for $C_{28}H_{31}N_3O$ [M^+]: 425.2467; found: 425.2459.

Anal. Calcd for $C_{28}H_{31}N_3O$: C, 79.02; H, 7.34; N, 9.87. Found: C, 79.01; H, 7.47; N, 9.88.

***N*,*N*-Dibenzyl-1-(2,6-dimethyl-4-pyrimidinyl)-2-ethyl-1-butanamine (6l)**

Preparation according to **GP 5** on a 0.70 mmol scale afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 4:1), (±)-**6l** as a bright yellow solid (214 mg, 79%); mp 96–97 °C.

IR (film): 2962s, 2936m, 1581vs, 1546s, 1494m, 1454s, 1398m, 1360m, 1074w, 1029w, 750s, 736m, 699s cm^{-1}.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 7.40 (d, 4 H, *J* = 6.0 Hz), 7.33 (t, 4 H, *J* = 6.0 Hz), 7.25 (d, 2 H, *J* = 6.0 Hz), 6.66 (s, 1 H), 4.00 (d, 2 H, *J* = 13.3 Hz), 3.44 (d, 1 H, *J* = 10.3 Hz), 3.03 (d, 2 H, *J* = 13.3 Hz), 2.77 (s, 3 H), 2.54 (s, 3 H), 2.35–2.26 (m, 1 H), 2.00–1.91 (m, 1 H), 1.70–1.59 (m, 1 H), 1.07–0.97 (m, 1 H), 0.95–0.85 (m, 1 H), 0.78 (t, 3 H, *J* = 4.7 Hz), 0.63 (t, 3 H, *J* = 4.7 Hz).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 167.3, 166.2, 165.7, 140.0, 128.9, 128.2, 126.8, 118.1, 64.7, 54.1, 38.3, 26.3, 24.2, 21.5, 19.8, 10.2, 9.3.

MS (70 eV, EI): *m*/*z* (%) = 388 (M^+ + H, 1), 316 (35), 296 (15), 280 (2), 225 (9), 196 (34), 192 (28), 163 (100), 91 (49).

HRMS (EI): *m*/*z* calcd for $C_{26}H_{34}N_3$ [M^+ + H]: 388.2753; found: 388.2759.

***N*,*N*-Dibenzyl-2-ethyl-1-(2-phenyl-6-propyl-4-pyrimidinyl)-1-butanamine (6m)**

Preparation according to **GP 5** on a 0.65 mmol scale afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 98:2), (±)-**6m** as a colorless solid (241 mg, 79%); mp 66–68 °C.

IR (film): 2963s, 2929m, 1588m, 1570vs, 1539vs, 1453m, 1377vs, 1028w, 745m, 695s cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 8.61–8.56 (m, 2 H), 7.55–7.48 (m, 3 H), 7.42 (d, 4 H, *J* = 7.3 Hz), 7.34 (t, 4 H, *J* = 7.3 Hz), 7.25 (t, 2 H, *J* = 7.3 Hz), 6.70 (s, 1 H), 4.12 (d, 2 H, *J* = 14.1 Hz), 3.53 (d, 1 H, *J* = 11.1 Hz), 3.12 (d, 2 H, *J* = 14.1 Hz), 2.84 (t, 2 H, *J* = 7.7 Hz), 2.48–2.38 (m, 1 H), 2.06–1.97 (m, 1 H), 1.96–1.85 (m, 2 H), 1.74–1.62 (m, 1 H), 1.07 (t, 3 H, *J* = 7.4 Hz), 1.11–0.8 (m, 2 H), 0.82 (t, 3 H, *J* = 7.4 Hz), 0.62 (t, 3 H, *J* = 7.4 Hz).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 170.0, 166.2, 163.7, 140.1, 138.5, 130.3, 129.0, 128.4, 128.3, 128.2, 126.8, 118.8, 64.9, 54.4, 40.0, 38.7, 22.2, 21.6, 20.0, 13.9, 10.2, 9.6.

MS (70 eV, EI): *m*/*z* (%) = 476 (M^+ – H, <1), 406 (20), 386 (12), 315 (5), 299 (5), 282 (30), 253 (100), 224 (4), 196 (13), 104 (5), 91 (53).

HRMS (EI): *m*/*z* calcd for $C_{33}H_{38}N_3$ [M^+ – H]: 476.3065; found: 476.3060.

Anal. Calcd for $C_{33}H_{39}N_3$: C, 82.97; H, 8.23; N, 8.80. Found: C, 83.19; H, 8.37; N, 8.68.

N,*N*-Dibenzyl-1-(6-cyclohexyl-2-phenyl-4-pyrimidinyl)-2-ethyl-1-butanamine (6n)

Preparation according to **GP 5** on a 0.83 mmol scale afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 98:2), (±)-**6n** as a colorless solid (322 mg, 75%); mp 118–119 °C.

IR (film): 2962m, 2928s, 2852m, 1588m, 1569s, 1538vs, 1451m, 1380s, 1028w, 745w, 698vs cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 8.61 (d, 2 H, *J* = 6.5 Hz), 7.55–7.46 (m, 3 H), 7.43 (d, 4 H, *J* = 7.3 Hz), 7.35 (t, 4 H, *J* = 7.3 Hz), 7.26 (t, 2 H, *J* = 7.3 Hz), 6.69 (s, 1 H), 4.12 (d, 2 H, *J* = 14.0 Hz), 3.52 (d, 1 H, *J* = 10.7 Hz), 3.11 (d, 2 H, *J* = 14.0 Hz), 2.77 (tt, 1 H, *J* = 11.8, 3.4 Hz), 2.47–2.40 (m, 1 H), 2.13–1.89 (m, 5 H), 1.82 (d, 1 H, *J* = 12.9 Hz), 1.74–1.58 (m, 3 H), 1.56–1.45 (m, 2 H), 1.40–1.31 (m, 1 H), 1.10–1.01 (m, 1 H), 0.99–0.91 (m, 1 H), 0.83 (t, 3 H, *J* = 7.3 Hz), 0.63 (t, 3 H, *J* = 7.3 Hz).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.2, 163.4, 140.2, 138.6, 130.3, 129.0, 128.4, 128.3, 128.2, 126.8, 117.1, 109.3, 64.9, 54.3, 46.0, 38.6, 32.4, 32.1, 26.4, 26.3, 26.1, 21.6, 20.0, 10.2, 9.5.

MS (70 eV, EI): *m*/*z* (%) = 518 (M^+ + H, <1), 446 (29), 426 (16), 355 (6), 322 (20), 293 (100), 265 (2), 196 (6), 91 (19).

HRMS (EI): *m*/*z* calcd for $C_{36}H_{44}N_3$ [M^+ + H]: 518.3536; found: 518.3528.

Anal. Calcd for $C_{36}H_{43}N_3$: C, 83.51; H, 8.37; N, 8.12. Found: C, 83.10; H, 8.33; N, 7.92.

N,*N*-Dibenzyl-1-(2,6-diphenyl-4-pyrimidinyl)-1-pentanamine (6o)

Preparation according to **GP 5** on a 0.78 mmol scale afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 98:2), (±)-**6o** as a bright yellow oil (348 mg, 90%).

IR (film): 3062m, 3028m, 2927m, 1590m, 1568s, 1533s, 1494m, 1453m, 1376m, 1027w, 746w, 691s cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.73–8.65 (m, 2 H), 8.29–8.21 (m, 2 H), 7.62–7.49 (m, 6 H), 7.47–7.21 (m, 11 H), 4.04 (d, *J* = 13.9 Hz, 2 H), 3.86 (t, *J* = 7.1 Hz, 1 H), 3.47 (d, 2 H, *J* = 13.9 Hz), 2.20–2.09 (m, 2 H), 1.57–1.25 (m, 4 H), 0.90 (t, 3 H, *J* = 7.1 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.4, 163.9, 163.5, 140.3, 138.3, 137.5, 130.7, 130.7, 128.9, 128.8, 128.5, 128.4, 128.3, 127.2, 126.9, 114.3, 62.5, 54.3, 29.3, 29.0, 22.8, 14.1.

MS (70 eV, EI): *m*/*z* (%) = 498 (M^+ + H, 1), 406 (5), 302 (48), 259 (100), 246 (9), 196 (12), 91 (23).

HRMS (EI): *m*/*z* calcd for $C_{35}H_{36}N_3$ [M^+ + H]: 498.2910; found: 498.2884.

Anal. Calcd for $C_{35}H_{35}N_3$: C, 84.47; H, 7.09; N, 8.44. Found: C, 84.17; H, 7.02; N, 8.28.

N,*N*-Dibenzyl-1-[6-(2-furyl)-2-phenyl-4-pyrimidinyl]-1-pentanamine (6p)

Preparation according to **GP 5** on a 0.87 mmol scale afforded, after column chromatographic purification (SiO_2, pentane–Et_2O, 98:2), (±)-**6p** as a colorless oil (413 mg, 98%).

IR (film): 3063w, 3028w, 2955m, 2930m, 1604vs, 1558vs, 1534vs, 1486s, 1454m, 1386s, 1368s, 1073w, 1028m, 1008m, 747vs, 699vs cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.49–8.57 (m, 2 H), 7.58–7.12 (m, 16 H), 6.54 (dd, 1 H, *J* = 3.4, 1.7 Hz), 3.92 (d, 2 H, *J* = 14.0 Hz), 3.74 (t, 1 H, *J* = 7.3 Hz), 3.34 (d, 2 H, *J* = 14.0 Hz), 2.06–1.95 (m, 2 H), 1.42–1.14 (m, 4 H), 0.79 (t, 3 H, *J* = 7.1 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.3, 163.8, 155.3, 152.7, 144.7, 140.3, 138.1, 130.5, 128.9, 128.4, 128.3, 128.2, 126.8, 112.4, 112.1, 111.9, 62.4, 54.3, 29.4, 28.9, 22.7, 14.0.

MS (70 eV, EI): *m*/*z* (%) = 488 (M^+ + H, <1), 430 (2), 396 (5), 339 (2), 292 (50), 249 (100), 236 (13), 196 (11), 91 (42).

HRMS (EI): *m*/*z* calcd for $C_{33}H_{34}N_3O$ [M^+ + H]: 488.2703; found: 488.2747.

Anal. Calcd for $C_{33}H_{33}N_3O$: C, 81.28; H, 6.82; N, 8.62. Found: C, 80.87; H, 6.89; N, 8.42.

1-(6-Cyclohexyl-2-phenyl-4-pyrimidinyl)-2-ethyl-1-butanamine (10)

In a 10 mL flask, the dibenzyl protected amine **6p** (246 mg, 0.48 mmol) was dissolved in MeOH (3 mL) and CH_2Cl_2 (2 mL), and 10% Pd/C (120 mg) was added. After stirring for 2 d under H_2 atmosphere (1 bar), the reaction was complete according to TLC analysis. Pd/C was filtered through Celite and washed with Et_2O. The solvents were evaporated and the crude product was purified by column chromatography (SiO_2, CH_2Cl_2–MeOH, 9: 1) affording **10a** as a yellow oil (155 mg, 95%).

IR (film): 2961m, 2929vs, 2854m, 1590s, 1571s, 1540vs, 1450m, 1379s, 1028w, 864w, 767w, 697s cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ = 8.53–8.48 (m, 2 H), 7.49–7.43 (m, 3 H), 6.98 (s, 1 H), 3.96 (d, 1 H, *J* = 5.5 Hz), 2.70 (tt, 1 H, *J* = 11.9, 3.5 Hz), 2.04–1.24 (m, 17 H), 0.93 (t, 3 H, *J* = 7.5 Hz), 0.85 (t, 3 H *J* = 7.5 Hz).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 174.5, 172.6, 163.4, 138.4, 130.2, 128.3, 128.3, 114.0, 57.9, 47.3, 46.1, 32.2, 32.1, 26.3, 26.0, 22.7, 21.0, 11.7, 11.5.

MS (70 eV, EI): *m*/*z* (%) = 335 (M^+ – 2 H, 1), 266 (100), 252 (1), 211 (4), 157 (1), 104 (3), 80 (1), 41 (1).

HRMS (EI): *m*/*z* calcd for $C_{22}H_{29}N_3$ [M^+ – 2 H]: 335.2360; found: 335.2361.

Acknowledgment

We thank the Fonds der Chemischen Industrie, the DFG (SPP 1118 ‘Sekundäre Wechselwirkungen als Steuerungsprinzip zur gerichteten Funktionalisierung reaktionsträger Substrate’) for a fellowship for N. G. We thank the Chemetall GmbH (Frankfurt), Degussa AG (Frankfurt), BASF AG (Ludwigshafen) and Wacker AG (Munich) for the generous gift of chemicals.

References

(1) (a) Joule, J. A.; Mills, K.; Smith, G. F. *Heterocyclic Chemistry*, 3rd ed.; Stanley Thornes (Publishers) Ltd: London, **1998**. (b) Wang, Y.; Dong, X.; Larock, R. C. *J. Org. Chem.* **2003**, *68*, 3090. (c) Larock, R. C.; Roesch, K. R. *J. Org. Chem.* **2002**, *67*, 86. (d) Larock, R. C.; Pace, P.; Yang, H.; Russel, C. E. *Tetrahedron* **1998**, *54*, 9961. (e) Larock, C. L.; Yum, E. K.; Doty, M. J.; Sham, K. K. C. *J. Org. Chem.* **1995**, *60*, 3270. (f) Larock, R. C.; Yang, H. *J. Org. Chem.* **1994**, *59*, 4172. (g) Lindsay, D. M.; Dohle, W.; Jensen, A. E.; Kopp, F.; Knochel, P. *Org. Lett.* **2002**, *4*, 1819.

(2) (a) Gommermann, N.; Koradin, C.; Polborn, K.; Knochel, P. *Angew. Chem. Int. Ed.* **2003**, *42*, 5763. (b) For related reactions, see: Akullian, L. C.; Snapper, M. L.; Hoveyda, A. H. *Angew. Chem. Int. Ed.* **2003**, *42*, 4244. (c) See also: Wei, C.; Li, C. *J. Am. Chem. Soc.* **2003**, *125*, 9584. (d) Wei, C.; Li, Z.; Li, C. *Org. Lett.* **2003**, *5*, 4473. (e) See also: Wei, C.; Li, C. *J. Am. Chem. Soc.* **2002**, *124*, 5638. (f) See also: Li, C.; Wei, C. *Chem. Commun.* **2001**, 268.

(3) For related reactions, see: (a) Koradin, C.; Gommermann, N.; Polborn, K.; Knochel, P. *Chem.–Eur. J.* **2003**, *9*, 2797. (b) See also: Wei, C. M.; Li, C. J. *J. Am. Chem. Soc.* **2002**, *124*, 5638. (c) See also: Anand, N. K.; Carreira, E. M. *J. Am. Chem. Soc.* **2001**, *123*, 9687. (d) See also: Wei, C. M.; Li, C. J. *J. Am. Chem. Soc.* **2003**, *125*, 9584. (e) See also: Sakaguchi, S.; Kubo, T.; Ishii, Y. *Angew. Chem. Int. Ed.* **2001**, *40*, 2534. (f) See also: Kabalka, G. W.; Wang, L.; Pagni, R. M. *Synlett* **2001**, 676.

(4) (a) Valk, J. M.; Whitlock, G. A.; Layzell, T. P.; Brown, J. M. *Tetrahedron: Asymmetry* **1995**, *6*, 2593. (b) Fernandez, E.; Maeda, K.; Hooper, M. W.; Brown, J. M. *Chem.–Eur. J.* **2000**, *6*, 1840.

(5) (a) Adlington, R. M.; Baldwin, J. E.; Catterick, D.; Pritchard, G. J. *Chem. Commun.* **1997**, 1757. (b) Adlington, R. M.; Baldwin, J. E.; Catterick, D.; Pritchard, G. J. *J. Chem. Soc., Perkin Trans. 1* **1999**, 855. (c) Adlington, R. M.; Baldwin, J. E.; Pritchard, G. J.; Spencer, K. C. *Tetrahedron Lett.* **2000**, *41*, 575. (d) Bennet, G. B.; Mason, R. B.; Alden, L. J.; Roach, J. B. *J. Med. Chem.* **1978**, *21*, 623. (e) Gilligan, P. J.; He, L.; Culp, S.; Fitzgerald, L.; Tam, S. W.; Wong, Y. N. *Bioorg. Med. Chem.* **1999**, *7*, 2321. (f) Norman, M. H.; Chen, N.; Chen, Z.; Fotsch, C.; Hale, C.; Han, N.; Hurt, R.; Jenkins, T.; Kincaid, J.; Liu, L.; Lu, Y.; Moreno, O.; Santora, V. J.; Sonnenberg, J. D.; Karbon, W. *J. Med. Chem.* **2000**, *43*, 4288. (g) Tanaka, K.; Konno, Y.; Kuraishi, Y.; Kimura, I.; Suzuki, T.; Kiniwa, M. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 623. (h) Heaney, F.; Burke, C.; Cunningham, D.; McArdle, P. *J. Chem. Soc., Perkin Trans. 1* **2001**, 622. (i) Medwid, J. B.; Paul, R.; Baker, J. S.; Brockman, J. A.; Du, M. T.; Hallett, W. A.; Hanifin, J. W.; Hardy, R. A. Jr.; Tarrant, M. E.; Torley, L. W.; Wrenn, S. *J. Med. Chem.* **1990**, *33*, 1230. (j) Gudmundsson, K. S.; Johns, B. A. K. *Org. Lett.* **2003**, *5*, 1369.

(6) Karpov, A. S.; Müller, T. J. J. *Org. Lett.* **2003**, *5*, 3451.

(7) Fürstner, A.; Szillat, H.; Gabor, B.; Mynott, R. *J. Am. Chem. Soc.* **1998**, *120*, 8305.

(8) For related deprotections, see: (a) Gray, B. D.; Jeffs, P. W. *J. Chem. Soc., Chem. Commun.* **1987**, 1329. (b) Amin, B. E.; Anantharamaiah, G. M.; Royer, G. P.; Means, G. E. *J. Org. Chem.* **1979**, *44*, 3442.

(9) Lin, H.-S.; Paquette, L. A. *Synth. Commun.* **1994**, *24*, 2503.