Asymmetric Synthesis of 3,4-Annulated Cyclopentenones from Cycloalkenyl Ketones and Vinyl Carbamates by Diastereoselective Carbonyl Addition/ Conrotatory 4π Ring Closure

Michael Siemer, Roland Fröhlich, Dieter Hoppe*

Organisch-Chemisches Institut, Westfälische Wilhelms-Universität Münster, Corrensstr. 40, 48149 Münster, Germany
Fax +49(251)8336531; E-mail: dhoppe@uni-muenster.de

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Abstract: 1-Lithiated *O*-vinyl carbamates add with high induced diastereoselectivity onto enantiomerically pure cycloalk-1-enyl (1-dibenzylamino)alkyl ketones. Subsequent *O*-carbamoyl migration, followed by a torquoselective, antarafacial 4π ring closure, leads to homochiral 2-substituted bicyclo[n.3.0]alk-1-ene-2-ones.

Key words: carbanion, cyclopentenones, asymmetric synthesis, electrocyclic reaction, torquoselectivity

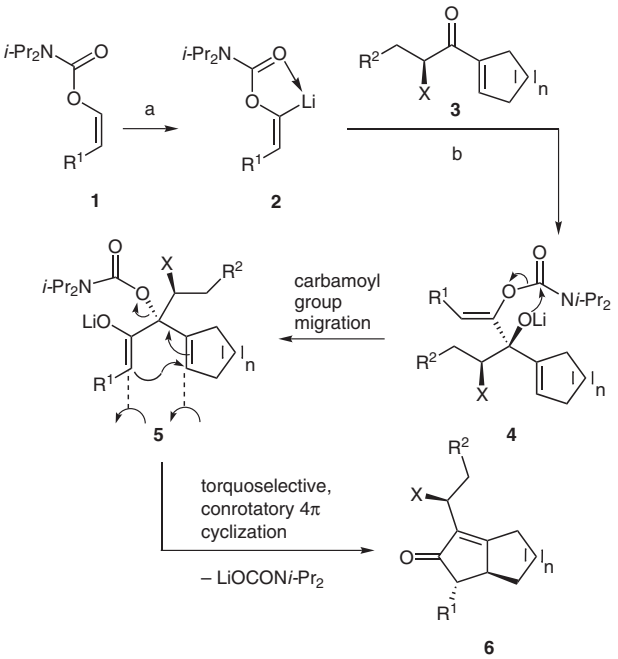
The synthesis of cyclopent-2-en-1-ones finds considerable interest due to their occurrence in physiologically active compounds[1] or their utilization in synthesis.[2] There is no 'silver bullet' for the construction of enantiopure cyclopentenones from two starting materials by formation of two C–C bonds. The latter was accomplished by Pauson–Khand reaction[3] ([2+2+1] mode), the Nazarov cyclization from an in situ generated divinyl ketone[4] ([3+2] mode), or by the Danheiser method ([4+1] mode) by nucleophilic attack of a d^1-synthon onto a silylketene and subsequent ring formation to yield racemic cyclopentenones.[5]

A novel addition-cyclization reaction, leading to 5-alkylidenecyclopent-2-en-1-ones, utilizing 1-lithioallenyl carbamates and ketones, following the [3+2] mode, had been developed in a cooperation between the Tius research group and our own.[6] Quantum chemical calculation by Lera et al.[7] substantiated our previous assumption that the 4π process does not proceed through a Nazarov intermediate, but is better described as a hybrid of a pericyclic and an ionic process, which is the origin of the observed high torquoselectivity.

This publication deals with the highly diastereoselective cyclopentenone annulation onto chiral 1-acylcycloalk-1-enes **3** making use of a 4π cyclization step. (*Z*)-Alk-1-enyl carbamates **1** are rapidly deprotonated in the vinylic position by means of alkyllithium (Scheme 1).[8] Enantioenriched ketones **3** were prepared by acylation of cycloalk-1-enyllithiums with the appropriate *N*-methoxy-*N*-methylcarboxamides according to the Weinreb method.[9]

To the 1-lithioalk-1-enyl carbamate **2** (1.5 equiv) and LiCl (1.5 equiv) in THF solution was added at –78 °C the enone **3** and the reaction mixture was allowed to warm up slowly to room temperature. During this period, the alkoxide **4**, formed with high substrate-directed diastereoselectivity,[10] rearranges by carbamoyl migration[6] to release two hidden reactive functionalities from **4**, namely a lithium enolate and an allylic carbamoyloxy group in **5**.

The intramolecular substitution step proceeds as a pericyclic 4π electrocyclization with strict conrotatory torquoselectivity in which the substitution of the carbamoyloxy group in the allylic position takes place as an antarafacial process; bicyclic cyclopentenones **6** result with complete diastereoselectivity (Scheme 1, Table 1).



Scheme 1 Synthesis of highly substituted, enantiopure cyclopentenones **6**. *Reagents and conditions*: a) *s*-BuLi, LiCl, THF, –78 °C, 1 h; b) –78 °C, 10 h, r.t., 2 h.

The products **6** usually are obtained with an essentially perfect diastereomeric ratio (dr >98:2). The high stereoselectivity is the result of the efficient diastereofacial selection at the carbonyl group adjacent to a dibenzylamino group (enones **3a–d**,**g**,**j**) or a *tert*-butyldiphenylsilyloxy group (enones **3e**,**f**) combined with a stereocontrolled pericyclic reaction. Only compound **6ca** is a notable ex-

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Table 1 Enones **6** Prepared

Entry	**1**	R^1	**3**	R^2	**6**	n	X	Yield (%)	dr[a]
1	**a**	Et	**a**	Ph	**aa**	2	NBn_2	85	>98:2
2	**a**	Et	**b**	Ph	**ab**	1	NBn_2	72	>98:2
3	**a**	Et	**c**	*i*-Pr	**ac**	2	NBn_2	63	>98:2
4	**a**	Et	**d**	*i*-Pr	**ad**	1	NBn_2	49	>98:2
5	**a**	Et	**e**	H	**ae**	2	OTPS[b]	88	>98:2
6	**a**	Et	**f**	H	**af**[c]	1	OTPS[b]	60	>98:2
7	**b**	H	**a**	Ph	**ba**	2	NBn_2	85	>98:2
8	**b**	H	**g**	H	**bg**	1	NBn_2	85	>98:2
9	**b**	H	**j**	OBn	**bj**	1	NBn_2	69	>98:2
10	**c**	Me	**a**	Ph	**ca**	2	NBn_2	82	93:7[d]
11	**d**	Bn	**a**	Ph	**da**	2	NBn_2	94	>98:2

[a] In the ^{1}H NMR spectrum of each enone (except for **6ca**), only one diastereomer was observed.
[b] TPS = *t*-$BuPh_2Si$.
[c] X-ray crystal structure analysis.
[d] Minor product: epimer at C-3.

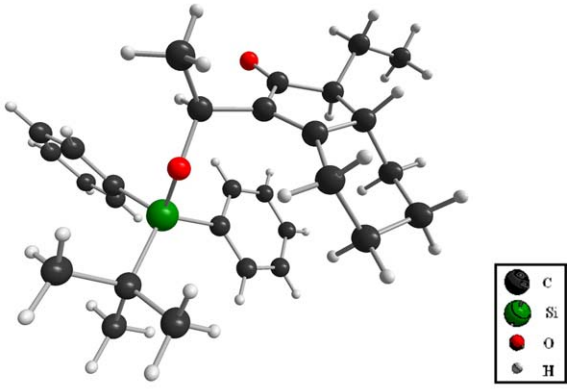
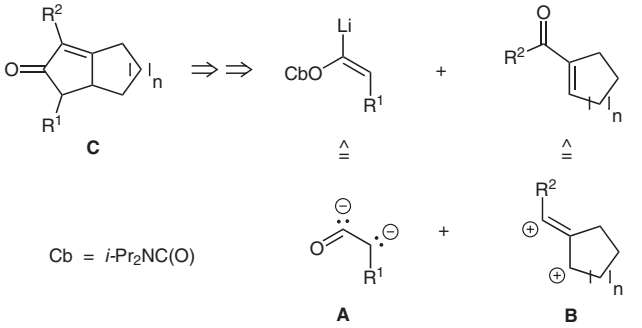


Figure 1 Structure of enone **6af**

ception, dr = 93:7.[11] The structure of bicyclic enone **6af**, and, thus, the mechanistic pathway, was confirmed by an X-ray crystal structure analysis under anomalous dispersion (Figure 1).[12]

From the view of synthesis strategy (Scheme 2), the new reaction corresponds to the cycloaddition of a d^1d^2 synthon **A** and an a^1a^3 synthon **B**, thereby shifting the enone moiety into the newly attached five-membered ring **C**. All together, the method represents a unique and simple route for the construction of chiral bicyclic cyclopentenones.



Scheme 2 Retrosynthetic presentation of the reaction

Reactions with organometallic reagents were carried out under argon in flasks, sealed with a rubber septum. *n*-Pentane (P), Et_2O (E), and toluene were dried by refluxing over sodium wire. THF was dried over potassium metal. CH_2Cl_2 was distilled over CaH_2. *s*-BuLi (~1.3 M in hexanes) was purchased from Acros, filtered (under argon) through Kieselgur, and the concentration was determined by titration against diphenylacetic acid.[13] Vinyllithium reagents were titrated with butan-2-ol in anhyd xylene against phenanthrolidine as indicator.[14] Silica gel (40–63 µm) for flash chromatography[15] was purchased from E. Merck Company (Darmstadt). TLC analysis: silica gel cards 60 F_{254}, detection by UV light (254 nm) and stained with vanillin reagent, $KMnO_4$ reagent, I_2 vapor, or molybdatophosphoric acid. GC analysis: HP 6890 (Hewlett-Packard) on the capillary column HP 5 (30 m, ∅ 0.3 mm, Phase 0.25 µm). Determination of er: column Chira Grom ODH, 250 × 2 mm or on HPLC (Waters 717). Mps: MFB 595, Gallenkamp, or Stuart Melting Point Apparatus SMP3; Bibby, UK; not corrected. Optical rotations: polarimeter PerkinElmer 341. Mass spectra: EI, Finnigan MAT 8200; HRMS, Varian Saturn II. NMR: ARX 300, AM 360, or AMX 400 (Bruker, Karlsruhe), in $CDCl_3$ with TMS or $CHCl_3$ as internal standard, assignment of ^{13}C signals (in part) by 90° and 135° DEPT, (H,H)- or (H,C)-COSY experiments. The numbering used for the interpretation of NMR data of compounds **6** are shown in Figure 2.

Crystallographic data: Data sets were collected with a Nonius KappaCCD diffractometer. Programs used: data collection COLLECT (Nonius B.V., 1998), data reduction Denzo-SMN,[16] absorption correction SORTAV,[17] Denzo,[18] structure solution SHELXS-97,[19] structure refinement SHELXL-97,[20] graphics Mopict.[21]

The (*Z*)-alk-1-enyl carbamates **1a**,[22] **1c**,[23] and **1d**[22,24] are reported. Compound **1b**[8b] was prepared by base-induced elimination (vide infra).[25] Some of the Weinreb amides, used for ketone preparation, are known: (*S*)-2-(dibenzylamino)-*N*′-methoxy-*N*′-methylpropane amide,[26] (*S*)-2-(dibenzylamino)-*N*′-methoxy-4,*N*′-dimethylpentane amide,[27] (*S*)-2-(dibenzylamino)-*N*′-methoxy-*N*′-methyl-3-phenylpropane amide,[28] (*S*)-3-benzyloxy-2-(dibenzylamino)-*N*′-methoxy-*N*′-methylpropane amide,[28] and 2-(*tert*-butyldiphenylsilyloxy)-*N*-methoxy-*N*-methylpropane amide.[29]

Vinyl *N*,*N*-Diisopropylcarbamate (1b)

2-Chloroethyl *N*,*N*-diisopropylcarbamate (31.15 g, 0.15 mol) was added dropwise to a solution of *t*-BuOK (33.7 g, 0.30 mol) in THF (400 mL). After stirring for 24 h at r.t., H_2O (200 mL) was added and the phases were separated. The aqueous phase was extracted with *tert*-butyl methyl ether (3 × 100 mL), the combined organic phases were dried ($MgSO_4$), and the solvent was distilled off at 100 mbar. Short-path distillation (63 °C/5 mbar) yielded pure **1b**; yield: 21.8 g (85%); colorless oil.

^{1}H NMR (400 MHz): δ = 1.24 [d, $^3J_{(CH3)2CH,(CH3)2CH}$ = 7.2 Hz, 12 H, $(H_3C)_2CH$], 3.85 [ps-s, 1 H, $(H_3C)_2CH$], 4.05 [ps-s, 1 H, $(H_3C)_2CH$], 4.41 (dd, $^2J_{2a,2b}$ = 1.4 Hz, $^3J_{1,2a}$ = 6.1 Hz, 1 H, H-2a), 4.75 (dd, $^3J_{1,2b}$ = 13.9 Hz, 1 H, H-2b), 7.25 (dd, 1 H, H-1).

Ketones 3; General Procedure (GP)

Cycloalk-1-en-1-yllithium (6.0 mmol, 0.1–0.65 M in Et_2O) in THF (15 mL) under argon was cooled to –40 °C before the Weinreb

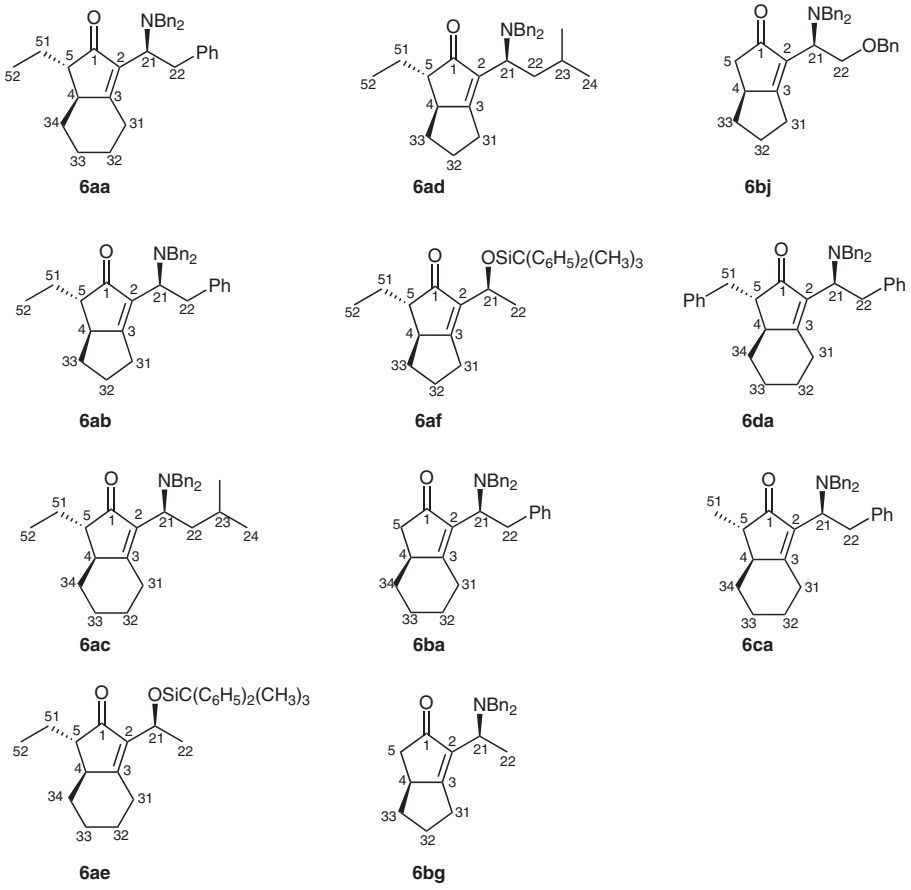


Figure 2

amide (3.0 mmol) dissolved in THF (6 mL) was added. Stirring at –40 °C was continued for 5 h. For workup, the mixture was quenched with aq sat. NH_4Cl (20 mL) and H_2O (20 mL). Extraction of the aqueous phase with *tert*-butyl methyl ether (3 × 20 mL), drying ($MgSO_4$), filtration, removal of solvent, and column chromatographic purification on silica gel (P:E, 20–3:1) afforded ketones **3**.

(*S*)-1-Cyclohex-1-en-1-yl-2-(dibenzylamino)-3-phenylpropan-1-one (3a)

According to GP, **3a** was obtained from (*S*)-2-(dibenzylamino)-*N*′-methoxy-*N*′-methyl-3-phenylpropane amide[28] and cyclohex-1-en-1-yllithium;[30] yield: 80%; colorless oil; $[\alpha]_D^{20}$ +9.3 (*c* = 1.0, $CHCl_3$).

IR (film): 3084, 3062, 3026, 2939, 2856, 2838, 1740, 1662, 1637, 1601 cm^{-1}.

^1H NMR (400 MHz): δ = 1.42–1.65 (m, 4 H, CH_2), 1.86–2.23 (m, 4 H, CH_2), 3.0 (dd, $^2J_{PhCHH,PhCHH}$ = 13.6 Hz, $^3J_{CH,PhCHH}$ = 5.3 Hz, 1 H, PhC*H*H), 3.17 (dd, $^3J_{CH,PhCHH}$ = 8.9 Hz, 1 H, PhCH*H*), 3.67 (d, $^2J_{HaNBn,HbNBn}$ = 14.2 Hz, 2 H, C*H*aNBn), 3.77 (d, 2 H, C*H*bNBn), 4.26 (dd, 1 H, CNH), 6.00–6.10 (m, 1 H, C=CH), 7.07–7.33 (m, 15 H, C_6H_5).

^{13}C NMR (100 MHz): δ = 21.4, 21.9, 23.0, 25.7 (CH_2), 32.0 (Ph*C*H_2), 54.3 (*C*H_2NBn), 60.8 (CNH), 125.9, 126.9, 128.0, 128.1, 128.8, 129.4, 139.2 (C_6H_5), 139.7 (*C*=CH), 140.2 (C=*C*H), 200.9 (C=O).

Anal. Calcd for $C_{29}H_{31}NO$: C, 85.04; H, 7.63; N, 3.42. Found: C, 84.96; H, 7.71; N, 3.29.

(*S*)-1-Cyclopent-1-en-1-yl-2-(dibenzylamino)-3-phenylpropan-1-one (3b)

According to GP, **3b** was obtained from (*S*)-2-(dibenzylamino)-*N*′-methoxy-*N*′-methyl-3-phenylpropane amide[28] and cyclopent-1-en-1-yllithium;[31] yield: 58%; viscous oil; $[\alpha]_D^{20}$ +5.4 (*c* = 0.8, $CHCl_3$).

IR (KBr): 3084, 3062, 3027, 2924, 2837, 1659, 1608 cm^{-1}.

^1H NMR (400 MHz): δ = 1.65–1.83 (m, 1 H, CH_2), 2.14–2.41 (m, 4 H, CH_2), 2.93 (dd, $^2J_{PhCHH,PhCHH}$ = 13.5 Hz, $^3J_{CH,PhCHH}$ = 5.4 Hz, 1 H, PhC*H*H), 3.09 (dd, $^2J_{PhCHH,PhCHH}$ = 13.5 Hz, $^3J_{CH,PhCHH}$ = 9.0 Hz, 1 H, PhCH*H*), 3.64 (d, $^2J_{HaNBn,HbNBn}$ = 14.0 Hz, 2 H, C*H*aNBn), 3.72 (d, 2 H, C*H*bNBn), 4.13 (dd, 1 H, CNH), 5.84 (m, 1 H, H-1), 7.00–7.25 (m, 15 H, C_6H_5).

^{13}C NMR (100 MHz): δ = 22.6 (CH_2), 30.4 (CH_2), 32.2 (CH_2), 33.8 (Ph*C*H_2), 54.4 (*C*H_2NBn), 63.1 (CHN), 125.9, 126.9, 128.1, 128.2, 128.8, 129.4, 139.0, 139.7 (C_6H_5), 144.2 (C=*C*H), 145.6 (*C*=CH), 198.5 (C=O).

Anal. Calcd for $C_{28}H_{29}NO$: C, 85.02; H, 7.39; N, 3.54. Found: C, 84.76; H, 7.48; N, 3.33.

(*S*)-1-Cyclohex-1-en-1-yl-2-(dibenzylamino)-4-methylpentan-1-one (3c)

According to GP, **3c** was obtained from (*S*)-2-(dibenzylamino)-*N*′-methoxy-4,*N*′-dimethylpentane amide[27] and cyclohex-1-en-1-yllithium;[30] yield: 52%; colorless oil; $[\alpha]_D^{20}$ +1.5 (*c* = 1.0, $CHCl_3$).

IR (film): 3084, 3062, 3028, 2932, 2866, 1663, 1635, 1603 cm^{-1}.

^1H NMR (400 MHz): δ = 0.81 [d, $^3J_{(CHa3)2CH,(CH3)2CH}$ = 6.2 Hz, 3 H, (C*H*a$_3$)$_2$CH], 0.84 [d, $^3J_{(CHb3)2CH,(CH3)2CH}$ = 6.2 Hz, 3 H, (C*H*b$_3$)$_2$CH], 1.44–1.73 [m, 7 H, $(H_3C)_2CH$, CH_2], 1.93–2.12, 2.15–2.25 (m, 4 H, CH_2), 3.59 (d, $^2J_{HaNBn,HbNBn'}$ = 14.0 Hz, 2H, C*H*aNBn), 3.75 (d, 2 H,

C*H*bNBn), 4.06 (dd, $^3J_{CNH,CH2}$ = 5.9 Hz, $^3J_{CNH,CH2}$ = 7.7 Hz, 1 H, CNH), 6.15–6.25 (m, 1 H, C=CH), 7.17–7.41 (m, 10 H, C_6H_5).

^{13}C NMR (100 MHz): δ = 22.0, 22.5, 23.1, 23.3, 23.5, 25.4 [$(H_3C)_2$CH, CH_2], 26.3 [$(H_3C)_2C$H], 35.9 (CH_2), 54.7 (CH_2NBn), 57.0 (CNH), 127.2, 128.5, 129.3, 140.2 (C_6H_5), 139.8 (C=CH), 140.7 (C=CH), 203.1 (C=O).

Anal. Calcd for $C_{26}H_{33}NO$: C, 83.15; H, 8.86; N, 3.73. Found: C, 82.94; H, 8.99; N, 3.64.

(*S*)-1-Cyclopent-1-en-1-yl-2-(dibenzylamino)-4-methylpentan-1-one (3d)

According to GP, **3d** was obtained from (*S*)-2-(dibenzylamino)-*N*′-methoxy-4,*N*′-dimethylpentane amide[27] and cyclopent-1-en-1-yllithium;[31] yield: 73%; colorless oil; $[\alpha]_D^{20}$ +1.3 (*c* = 1.2, $CHCl_3$).

IR (film): 3084, 3062, 3028, 2956, 2868, 2839, 2806, 1663, 1609 cm^{-1}.

^{1}H NMR (400 MHz): δ = 0.81 [d, $^3J_{(CHa3)2CH,(CH3)2CH}$ = 5.0 Hz, 3 H, $(CHa_3)_2$CH], 0.85 [d, $^3J_{(CHb3)2CH,(CH3)2CH}$ = 5.2 Hz, 3 H, $(CHb_3C)_2$CH], 1.53–1.71 [m, 3 H, CH_2, $(H_3C)_2CH$], 1.82–1.99 (m, 2 H, CH_2), 2.36–2.60 (m, 4 H, CH_2), 3.64 (d, $^2J_{HaNBn,HbNBn}$ = 14.2 Hz, 2 H, CHaNBn), 3.79 (d, 2 H, CHbNBn), 4.01 (dd, $^3J_{CNH,CHaHb}$ = 5.6 Hz, $^3J_{CNH,CHaHb}$ = 7.3 Hz, 1 H, CNH), 6.05 (s, 1 H, C=CH), 7.19–7.34 (m, 10 H, C_6H_5).

^{13}C NMR (100 MHz): δ = 22.5 (CH_2), 22.6 [$(H_3C)_2$CH], 24.9 [$(H_3C)_2C$H], 27.8 [$(H_3C)_2$CH], 30.5 (CH_2), 33.9 (CH_2), 35.7 (CH_2), 54.3 (CH_2NBn), 59.0 (CNH), 122.7, 126.8, 128.0, 128.8 (C_6H_5), 143.5 (C=CH), 145.6 (C=CH), 200.0 (C=O).

Anal. Calcd for $C_{25}H_{31}NO$: C, 83.06; H, 8.64; N, 3.87. Found: C, 82.67; H, 8.62; N, 3.74.

2-(*tert*-Butyldiphenylsilyloxy)-1-cyclohex-1-en-1-ylpropan-1-one (3e)

According to GP, **3e** was obtained from 2-(*tert*-butyldiphenylsilyloxy)-*N*-methoxy-*N*-methylpropane amide and cyclohex-1-en-1-yllithium;[30] yield: 65%; colorless oil; $[\alpha]_D^{20}$ –17.9 (*c* = 1.1, $CHCl_3$).

IR (film): 3071, 2933, 2858, 1680, 1635 cm^{-1}.

^{1}H NMR (400 MHz): δ = 1.08 [s, 9 H, $C(CH_3)_3$], 1.35 (d, $^3J_{CHOSi,CH3}$ = 6.8 Hz, 3 H, CH_3), 1.47–1.58 (m, 4 H, CH_2), 1.90–2.28 (m, 4 H, CH_2), 6.68 (s, 1 H, C=CH), 7.31–7.46, 7.60–7.72 (m, 10 H, C_6H_5).

^{13}C NMR (100 MHz): δ = 19.1 [$C(CH_3)_3$], 21.2, 21.4, 23.2, 25.80 (CH_2), 21.8 (CH_3), 26.8 [$C(CH_3)_3$], 69.0 (CHOSi), 127.4, 127.5, 129.5, 129.6, 133.2, 133.70, 135.7, 135.9 (C_6H_5), 136.6 (C=CH), 140.3 (C=CH) 201.6 (C=O).

Anal. Calcd for $C_{25}H_{32}O_2Si$: C, 76.48; H, 8.22. Found: C, 76.23; H, 8.32.

2-(*tert*-Butyldiphenylsilyloxy)-1-cyclopent-1-en-1-ylpropan-1-one (3f)

According to GP, **3f** was obtained from 2-(*tert*-butyldiphenylsilyloxy)-*N*-methoxy-*N*-methylpropane amide and cyclopent-1-en-1-yllithium;[31] yield: 55%; slightly yellow oil; $[\alpha]_D^{20}$ –21.1 (*c* = 1.4, $CHCl_3$).

IR (film): 3071, 2958, 2932, 2893, 2858, 1679, 1611 cm^{-1}.

^{1}H NMR (300 MHz): δ = 1.00 [s, 9 H, $C(CH_3)_3$], 1.27 (d, $^3J_{CHOSi,CH3}$ = 6.8 Hz, 3 H, CH_3), 1.70–1.76 (m, 2 H, CH_2), 2.21–2.47 (m, 4 H, CH_2), 4.54 (q, 1 H, CHOSi), 6.59 (t, $^3J_{C=CH,CH2}$ = 4.3 Hz, 1 H, C=CH), 7.15–7.40, 7.48–7.64 (m, 10 H, C_6H_5).

^{13}C NMR (75 MHz): δ = 19.6 [$C(CH_3)_3$], 22.4 (CH_3), 22.5, 31.5, 34.6 (CH_2), 27.3 [$C(CH_3)_3$], 73.7 (CHOSi), 127.0, 128.0, 130.1, 133.6, 134.1, 136.2, 136.3, 142.5, 144.8 (C_6H_5, C=CH), 142.5 (C=CH), 200.0 (C=O).

Anal. Calcd for $C_{24}H_{30}O_2Si$: C, 76.14; H, 7.99. Found: C, 76.03; H, 8.21.

[6*S*,7*S*,9(1*S*)]-9-[1-(Dibenzylamino)-2-phenylethyl]-7-ethylbicyclo[4.3.0]non-1(9)-en-8-one (6aa); Typical Procedure (TP)

A round-bottomed flask sealed with a septum containing LiCl (21 mg, 0.5 mmol, 1.5 equiv) was flame-dried in vacuum and filled with argon. To this were added THF (2 mL) and (*Z*)-but-1-enyl carbamate (**1a**; 100 mg, 0.5 mmol, 1.5 equiv) by a syringe. After cooling to –78 °C, a 1.38 M solution of *s*-BuLi in hexane–cyclohexane (92:8) (0.31 mL, 0.43 mmol, 1.3 equiv) was added. After 1 h, ketone **3a** (135 mg (0.33 mmol, 1.0 equiv) dissolved in THF (2 mL) was slowly injected. After 10 h at –78 °C, the mixture was allowed to warm to r.t. over 2 h followed by 2 h stirring at r.t. H_2O (5 mL) was added, the phases were separated, and the aqueous phase was extracted with *tert*-butyl methyl ether (3 × 5 mL). After drying the organic phases ($MgSO_4$), the crude product was purified by flash chromatography (E:P = 1:30); yield: 130 mg (85%); colorless solid; mp 81 °C; $[\alpha]_D^{20}$ –9.5 (*c* = 0.8, $CHCl_3$); dr >98:2.

IR (KBr): 3083, 3061, 3025, 2924, 2856, 2796, 1688, 1623, 1601 cm^{-1}.

^{1}H NMR (400 MHz): δ = 0.23 (m, 1 H, H-32a), 0.52 (m, 1 H, H-34a), 0.88 (t, $^3J_{51,52}$ = 7.4 Hz, 3 H, H-52), 1.19 (m, 1 H, H-33a), 1.39 (m, 1 H, H-51a), 1.44 (m, 1 H, H-33b), 1.47 (m, 1 H, H-32b), 1.60 (m, 1 H, H-5), 1.64 (m, 1H, H-31a), 1.66 (m, 1 H, H-51b), 1.92 (m, 1 H, H-34b), 1.99 (m, 1 H, H-31b), 2.10 (m, 1 H, H-4), 3.15 (dd, $^2J_{22a,22b}$ = 12.7 Hz, $^3J_{21,22a}$ = 5.2 Hz, 1 H, H-22a), 3.29 (d, $^2J_{HaNBn,HbNBn}$ = 14.6 Hz, 2 H, NCHa), 3.47 (dd, 1 H, $^3J_{21,22b}$ = 10.8 Hz, H-22b), 3.70 (dd, 1 H, H-21), 3.99 (d, 2 H, NCHb), 6.92–7.25 (m, 15 H, C_6H_5).

^{13}C NMR (100 MHz): δ = 11.5 (C-52), 24.3 (C-51), 25.1 (C-33), 26.5 (C-32), 28.9 (C-31), 35.2 (C-34), 35.7 (C-22), 46.5 (C-5), 53.8 (C-4), 55.3 (CH_2NBn), 57.0 (C-21), 125.6, 126.4, 127.9, 128.0, 128.3, 129.2, 140.2, 140.8 (C_6H_5), 132.9 (C-2), 180.5 (C-3), 210.8 (C-1).

Anal. Calcd for $C_{33}H_{37}NO$: C, 85.48; H, 8.04; N, 3.02. Found: C, 85.23; H, 8.15; N, 2.97.

[4*S*,5*S*,2(1*S*)]-2-[1-(Dibenzylamino)-2-phenylethyl]-4-ethylbicyclo[3.3.0]oct-1-en-3-one (6ab)

According to TP, **6ab** was obtained from carbamate **1a** and ketone **3b**; yield: 72%; colorless solid; mp 92 °C (E–P); $[\alpha]_D^{20}$ –8.3 (*c* = 1.3, $CHCl_3$); dr >98:2.

IR (KBr): 3080, 3059, 3023, 2964, 2928, 2865, 2789, 2715, 1692, 1642 cm^{-1}.

^{1}H NMR (400 MHz): δ = 0.72 (m, 1 H, H-33a), 0.98 (t, $^3J_{51,52}$ = 7.3 Hz, 3 H, H-52), 1.45 (m, 1 H, H-51a), 1.70 (m, 1 H, H-31a), 1.77–1.87 (m, 3 H, H-5, H-32), 1.94 (m, 1 H, H-51b), 2.03 (m, 1 H, H-33b), 2.18 (m, 1 H, H-31b), 2.48 (m, 1 H, H-4), 3.23 (dd, $^2J_{22a,22b}$ = 13.2 Hz, $^3J_{21,22a}$ = 6.4 Hz, 1 H, H-22a), 3.33 (dd, $^3J_{21,22b}$ = 9.4 Hz, 1 H, H-22b), 3.42 (d, $^2J_{CHaNBn,\ CHbNBn}$ = 14.3 Hz, 2 H, NCHa), 3.72 (dd, 1 H, H-21), 4.04 (d, 2 H, NCHb), 6.99–7.31 (m, 15 H, C_6H_5).

^{13}C NMR (100 MHz): δ = 11.9 (C-52), 22.3 (C-51), 25.68, 25.73 (C-31, C-32), 31.3 (C-33), 35.4 (C-22), 50.6 (C-5), 55.3 (NCH_2), 56.3 (C-4), 58.1 (C-21), 125.7, 127.1, 127.8, 127.9, 128.3, 129.1, 139.9, 140.6 (C_6H_5), 133.1 (C-2), 187.1 (C-3), 211.6 (C-1).

Anal. Calcd for $C_{32}H_{35}NO$: C, 85.48; H, 7.85; N, 3.12. Found: C, 85.20; H, 7.86; N, 2.99.

[6*S*,7*S*,9(1*S*)]-9-[1-(Dibenzylamino)-3-methylbutyl]-7-ethylbicyclo[4.3.0]non-1(9)-en-8-one (6ac)

According to TP, **6ac** was obtained from carbamate **1a** and ketone **3c**; yield: 63%; amorphous solid; $[\alpha]_D^{20}$ –11.2 (*c* = 0.9, $CHCl_3$); dr >98:2.

IR (KBr): 3084, 3062, 3028, 2957, 2930, 2860, 2801, 1694, 1622 cm^{-1}.

^1H NMR (400 MHz): δ = 0.67 (d, $^3J_{23,24a}$ = 6.7 Hz, 3 H, H-24a), 0.73 (d, $^3J_{23,24b}$ = 6.5 Hz, 3 H, H-24b), 0.92 (m, 3 H, H-52), 0.99 (m, 1 H, H-32a), 1.01 (m, 1 H, H-34a), 1.32–1.46, 1.71–1.82 (m, 4 H, H-31, H-51), 1.64 (m, 1 H, H-22a), 1.81 (m, 1 H, H-34b), 1.87 (m, 1 H, H-33a), 2.10 (m, 1 H, H-22b), 2.15 (m, 1 H, H-32b), 2.24 (m, 1 H, H-4), 2.37 (m, 1 H, H-33b), 3.17 (d, $^2J_{CHaNBn,CHbNBn}$ = 14.3 Hz, 2 H, NCHa), 3.56 (dd, $^3J_{21,22a}$ = 9.6 Hz, $^3J_{21,22b}$ = 6.2 Hz, 1 H, H-21), 3.86 (d, 2 H, NCHb), 7.01–7.27 (m, 5 H, C_6H_5).

^{13}C NMR (100 MHz): δ = 12.3 (C-52), 22.8 (C-24a), 24.0 (C-24b), 24.9, 26.0, 26.1 (C-23, C-31, C-51), 27.7 (C-34), 30.0 (C-33), 36.1 (C-32), 39.0 (C-22), 47.3 (C-4), 54.5 (C-21), 55.6 (C-5), 55.7 (NCH_2), 127.1, 128.5, 128.6, 129.0, 129.1, 129.3, 141.7 (C_6H_5), 134.6 (C-2), 180.2 (C-3), 211.5 (C-1).

Anal. Calcd for $C_{30}H_{39}NO$: C, 83.87; H, 9.15; N, 3.26. Found: C, 83.56; H, 9.00; N, 3.33.

[2(1*S*),4*S*,5*S*]-2-[1-(Dibenzylamino)-3-methylbutyl]-4-ethylbicyclo[3.3.0]oct-1-en-3-one (6ad)

According to TP, **6ad** was obtained from carbamate **1a** and ketone **3d**; yield: 49%; amorphous solid; $[\alpha]_D^{20}$ –7.0 (*c* = 1.1, $CHCl_3$); dr >98:2.

IR (KBr): 3085, 3062, 3028, 2957, 2931, 2869, 2801, 1698, 1641, 1603 cm^{-1}.

^1H NMR (400 MHz): δ = 0.64 (d, $^3J_{23,24a}$ = 6.5 Hz, 3 H, H-24a), 0.67 (d, $^3J_{23,24b}$ = 6.7 Hz, 3 H, H-24b), 0.93 (dd, $^3J_{51,52}$ = 7.2 Hz, 3 H, H-52), 0.98 (m, 1 H, H-33a), 1.33–1.48 (m, 2 H, H-51a, H-23), 1.62–1.82 (m, 2 H, H-22), 1.84–1.96 (m, 4 H, H-5, H-51b, H-32), 2.06–2.13 (m, 1 H, H-33b), 2.18 (ddd, $^2J_{31a,31b}$ = 19.0 Hz, $^3J_{31a,32a}$ = 8.1 Hz, $^3J_{31a,32b}$ = 8.5 Hz, 1 H, H-31a), 2.37 (ddd, $^3J_{31b,32a}$ = 7.4 Hz, $^3J_{31b,32b}$ = 6.4 Hz, 1 H, H-31b), 2.47 (m, 1 H, H-4), 3.25 (d, $^2J_{NCHa,\ NCHa'}$ = 14.2 Hz, 2 H, NCHa), 3.49 (dd, $^3J_{21,22a}$ = 6.8 Hz, $^3J_{21,22b}$ = 8.4 Hz, 1 H, H-21), 3.78 (d, 2 H, NCHb), 7.08–7.18 (m, 2 H, $CH_{arom\text{-}para}$), 7.16–7.23 (m, 4 H, $CH_{arom\text{-}ortho}$), 7.26–7.31 (m, 4 H, $CH_{arom\text{-}meta}$).

^{13}C NMR (100 MHz): δ = 11.9 (C-52), 22.3 (C-51), 22.4 (C-24b), 22.7 (C-24a), 25.1 (C-23), 26.0 (C-32), 26.3 (C-31), 31.6 (C-33), 38.3 (C-22), 51.1 (C-5), 53.2 (C-21), 55.1 (NCH_2), 56.3 (C-4), 126.4 ($CH_{arom\text{-}para}$), 127.8 ($CH_{arom\text{-}ortho}$), 128.5 ($CH_{arom\text{-}meta}$), 134.0 (C-2), 140.8 ($C_{arom\text{-}ipso}$), 185.2 (C-3), 211.8 (C-1).

Anal. Calcd for $C_{29}H_{37}NO$: C, 83.81; H, 8.97; N, 3.37. Found: C, 84.02; H, 9.15; N, 3.11.

[4*S*,7*S*,9(1*S*)]-9-[1-(*tert*-Butyldiphenylsilyloxy)ethyl]-7-ethylbicyclo[4.3.0]non-1(9)-en-8-one (6ae)

According to TP, **6ae** was obtained from carbamate **1a** and ketone **3e**; yield: 60%; colorless solid; mp 103 °C; $[\alpha]_D^{20}$ –59 (*c* = 0.34, $CHCl_3$); dr >98:2.

IR (film): 3071, 3051, 2931, 2858, 1694, 1646, 1428, 1110, 910, 760, 823, 735, 704, 471 cm^{-1}.

^1H NMR (400 MHz): δ = 0.81 (t, $^3J_{51,52}$ = 6.8 Hz, 3 H, H-52), 0.99 [s, 9 H, $C(CH_3)_3$], 1.18 (d, $^3J_{21,22}$ = 6.6 Hz, 3 H, H-22), 1.12–2.06, 3.44 (m, 12 H, H-4, H-5, H-31, H-32, H-33, H-34, H-51), 4.76 (q, 1 H, H-21), 7.17–7.35, 7.46–7.57 (m, 10 H, C_6H_5).

^{13}C NMR (100 MHz): δ = 11.5 (C-52), 23.5, 25.3, 26.0, 28.6, 29.6, 34.6 [C-31, C-32, C-33, C-34, C-51, $C(CH_3)_3$], 23.9 (C-22), 26.9 [$C(CH_3)_3$], 46.9 (C-4), 53.2 (C-5), 63.8 (C-22), 127.3, 127.4, 129.4, 129.5, 133.9, 133.9, 135.6, 135.7, 135.8, 135.8, 139.3 (C_6H_5), 133.9 (C-2), 175.8 (C-3), 207.9 (C-1).

Anal. Calcd for $C_{29}H_{38}O_2Si$: C, 77.97; H, 8.57. Found: C, 77.71; H, 8.31.

[2(1*S*),4*S*]-2-[1-(*tert*-Butyldiphenylsilyloxy)ethyl]-4-ethylbicyclo[3.3.0]oct-1-en-4-one (6af)

According to TP, **6af** was obtained from carbamate **1a** and ketone **3f**; yield: 88%; amorphous solid; $[\alpha]_D^{20}$ –66 (*c* = 0.9, $CHCl_3$); dr >98:2.

IR (film): 3071, 3041, 2962, 2859, 1702, 1662, 1431, 1375, 1287, 1256, 1108, 1072, 1002, 947, 913, 822, 736, 704, 436 cm^{-1}.

^1H NMR (400 MHz): δ = 1.19 (t, $^3J_{51,52}$ = 7.5 Hz, 3 H, H-52), 1.53 (d, $^3J_{21,22}$ = 6.4 Hz, 3 H, H-22), 1.33 [s, 9 H, $C(CH_3)_3$], 1.86–3.14 (m, 10 H, H-4, H-5, H-31, H-32, H-33, H-51), 5.07 (q, 1 H, H-21), 7.52–7.71, 7.82–8.01 (m, 10 H, C_6H_5).

^{13}C NMR (100 MHz): δ = 112.0 (C-52), 18.3 (C-22), 22.1 [$C(CH_3)_3$], 24.0, 26.4, 27.0, 30.9 (C-31, C-32, C-33, C-51), 27.0 [$C(CH_3)_3$], 51.8 (C-4), 55.4 (C-5), 64.7 (C-21), 122.7, 127.3, 127.4, 127.6, 129.4, 129.5, 133.9, 134.0, 134.4, 134.7, 135.6, 135.7 (C_6H_5), 138.1 (C-2), 181.9 (C-3), 209.7 (C-1).

Anal. Calcd for $C_{28}H_{36}O_2Si$: C, 77.73; H, 8.39. Found: C, 77.92; H, 8.51.

[6*S*,9(1*S*)]-9-[1-(Dibenzylamino)-2-phenylethyl]bicyclo[4.3.0]non-1(9)-en-8-one (6ba)

According to TP, **6ba** was obtained from carbamate **1b** and ketone **3a**; yield: 75%; amorphous solid; $[\alpha]_D^{20}$ –13.4 (*c* = 0.9, $CHCl_3$); dr = 99:1.

IR (KBr): 3081, 3062, 3015, 2932, 2865, 2799, 1695, 1614, 1605 cm^{-1}.

^1H NMR (400 MHz): δ = 0.21 (m, 1 H, H-32a), 0.56 (m, 1 H, H-34a), 1.23–1.95 (m, 8 H, H-5, H-31, H-32b, H-33, H-34b), 2.12 (m, 1 H, H-4), 3.09 (dd, $^2J_{22a,22b}$ = 12.6 Hz, $^3J_{21,22a}$ = 5.4 Hz, 1 H, H-22a), 3.23 (d, $^2J_{HaNBn,HbNBn}$ = 14.6 Hz, 2 H, NCHa), 3.56 (dd, $^3J_{21,22b}$ = 10.6 Hz, 1 H, H-22b), 3.77 (dd, 1 H, H-21), 4.01 (d, 2 H, NCHb), 6.75–7.18 (m, 15 H, C_6H_5).

^{13}C NMR (100 MHz): δ = 23.2, 26.7, 29.3 (C-31, C-32, C-33), 34.9 (C-34), 36.6 (C-22), 46.3 (C-5), 55.1 (C-4), 55.4 (CH_2NBn), 56.2 (C-21), 125.8, 126.3, 127.9, 128.1, 128.2, 129.9, 140.3, 140.8 (C_6H_5), 133.2 (C-2), 180.6 (C-3), 212.2 (C-1).

Anal. Calcd for $C_{31}H_{33}NO$: C, 85.48; H, 7.64; N, 3.22. Found: C, 85.11; H, 7.55; N, 3.23.

[2(1*S*),5*S*]-2-[1-(Dibenzylamino)ethyl]bicyclo[3.3.0]oct-1-en-3-one (6bg)

According to TP, **6bg** was obtained from carbamate **1b** and ketone **3g**; yield: 85%; colorless oil; $[\alpha]_D^{20}$ –25.3 (*c* = 1.2, $CHCl_3$); dr >98:2.

IR (film): 3083, 3059, 3027, 2963, 2869, 2802, 1697, 1642, 1601 cm^{-1}.

^1H NMR (300 MHz): δ = 0.86 (m, 1 H, H-33a), 1.37 (d, $^3J_{21,22}$ = 7.1 Hz, 3 H, H-22), 1.89 –2.00 (m, 2 H, H-32), 1.96 (dd, $^2J_{5a,5b}$ = 17.3 Hz, $^3J_{4,5a}$ = 3.2 Hz, 1 H, H-5a), 2.07 (m, 1 H, H-33b), 2.33–2.52 (m, 2 H, H-31), 2.57 (dd, $^3J_{4,5b}$ = 6.3 Hz, 1 H, H-5b), 2.73 (m, 1 H, H-4), 3.51 (d, $^2J_{HaNBn,HbNBn}$ = 14.4 Hz, 2 H, C*H*aNBn), 3.72 (d, 1 H, H-21), 3.74 (d, 2 H, C*H*bNBn), 7.14–7.38 (m, 10 H, C_6H_5).

^{13}C NMR (75 MHz): δ = 14.6 (C-22), 25.7 (C-32), 26.3 (C-31), 31.1 (C-33), 42.5 (C-5), 44.5 (C-4), 50.8 (C-21), 55.1 (CH_2NBn), 126.5, 127.9, 128.3, 140.7 (C_6H_5), 136.3 (C-2), 186.3 (C-3), 210.1 (C-1).

Anal. Calcd for $C_{24}H_{27}NO$: C, 83.44; H, 7.88; N, 4.05. Found: C, 83.32; H, 8.16; N, 3.81.

[2(1*S*),5*S*]-2-[1-(Dibenzylamino)-2-benzyloxyethyl]bicyclo[3.3.0]oct-1-en-3-one (6bj)

According to TP, **6bj** was obtained from carbamate **1b** and ketone **3j**; yield: 69%; colorless oil; $[\alpha]_D^{20}$ –23.1 (c = 0.6, CH_2Cl_2); dr = 98:2.

IR (film): 3082, 3061, 3028, 2957, 2865, 2799, 1696, 1643, 1608 cm^{-1}.

^1H NMR (300 MHz): δ = 0.91 (m, 1 H, H-33a), 1.81–1.93 (m, 2 H, H-32), 1.99 (dd, $^2J_{5a,5b}$ = 17.8 Hz, $^3J_{4,5a}$ = 3.2 Hz, 1 H, H-5a), 2.07 (m, 1 H, H-33b), 2.16–2.46 (m, 2 H, H-31), 2.59 (dd, $^3J_{4,5b}$ = 6.5 Hz, 1 H, H-5b), 2.78 (m, 1 H, H-4), 3.41 (d, $^2J_{HaNBn,HbNBn}$ = 14.1 Hz, 2 H, C*H*aNBn), 3.78 (t, $^3J_{21,22b}$ = 7.2 Hz, 1 H, H-21), 3.87 (d, 2 H, C*H*bNBn), 3.92 (dd, $^2J_{22a,22b}$ = 9.6 Hz, $^3J_{21,22a}$ = 7.2 Hz, 1 H, H-22a), 3.93 (dd, 2 H, H-22b), 4.40 (s, 2 H, CH_2OBn), 7.10–7.35 (m, 15 H, C_6H_5).

^{13}C NMR (100 MHz): δ = 25.6 (C-32), 26.2 (C-31), 31.2 (C-33), 42.5 (C-5), 44.8 (C-4), 55.5 (C-21), 55.7 (*C*H_2NBn), 69.4 (C-22), 73.0 (*C*H_2OBn), 126.6, 126.8, 127.3, 127.4, 128.0, 128.2, 128.4, 128.8, 128.9, 138.7, 140.5 (C_6H_5), 133.1 (C-2), 188.8 (C-3), 210.2 (C1).

Anal. Calcd for $C_{31}H_{33}NO_2$: C, 82.45; H, 7.37; N, 3.10. Found: C, 82.21; H, 7.12; N, 3.33.

[6*S*,7*S*,9(1*S*)]-9-[1-(Dibenzylamino)-2-phenylethyl]-7-methylbicyclo[4.3.0]non-1(9)-en-8-one (6ca)

According to TP, **6ca** was obtained from **1c** and ketone **3a**; yield: 82%; colorless solid; $[\alpha]_D^{20}$ –5.4 (c = 0.9, $CHCl_3$); dr = 93:7.

IR (KBr): 3090, 3056, 3020, 2927, 2858, 2795, 1691, 1619 cm^{-1}.

^1H NMR (400 MHz): δ = 0.29 (m, 1 H, H-32a), 0.49 (m, 1 H, H-34a), 0.91–2.13 (m, 11 H, H-4, H-5, H-31, H-32b, H-33, H-34b, H-51), 3.17 (dd, $^2J_{22a,22b}$ = 12.5 Hz, $^3J_{21,22a}$ = 5.4 Hz, 1 H, H-22a), 3.30 (d, $^2J_{HaNBn,HbNBn}$ = 14.5 Hz, 2 H, NCHa), 3.43 (dd, $^3J_{21,22b}$ = 10.6 Hz, 1 H, H-22b), 3.70 (dd, 1 H, H-21), 3.97 (d, 2 H, NCHb), 6.85–7.31 (m, 15 H, C_6H_5).

^{13}C NMR (100 MHz): δ = 15.9 (C-51), 24.9, 26.4, 28.5 (C-31, C-32, C-33), 34.3, 35.6 (C-22, C-34), 47.4 (C-5), 49.0 (C-4), 55.3 (*C*H_2NBn), 57.0 (C-21), 125.6, 126.5, 127.9, 128.1, 128.4, 129.0, 140.8 (C_6H_5), 132.3 (C-2), 179.8 (C-3), 211.8 (C-1).

Anal. Calcd for $C_{32}H_{35}NO$: C, 85.48; H, 7.85; N, 3.12. Found: C, 85.33; H, 7.99; N, 3.55.

[6*S*,7*S*,9(1*S*)]-7-Benzyl-9-[1-(dibenzylamino)-2-phenylethyl]bicyclo[4.3.0]non-1(9)-en-8-one (6da)

According to TP, **6da** was obtained from **1d** and ketone **6a**; yield: 94%; colorless solid; $[\alpha]_D^{20}$ –15.6 (c = 1.1, $CHCl_3$); dr = 99:1.

IR (KBr): 3085, 3055, 3028, 2927, 2852, 2801, 1690, 1622, 1605 cm^{-1}.

^1H NMR (400 MHz): δ = 0.17 (m, 1 H, H-32a), 0.41 (m, 1 H, H-34a), 1.01–1.61, 1.91 (m, 7 H, H-5, H-31, H-32b, H-33, H-34b), 2.11 (m, 1 H, H-4), 2.51 (dd, $^2J_{51a,51b}$ = 9.9 Hz, $^3J_{5,51a}$ = 7.4 Hz, 1 H, H-51a), 3.09 (dd, $^2J_{22a,22b}$ = 12.6 Hz, $^3J_{21,22a}$ = 5.1 Hz, 1 H, H-22a), 3.17 (dd, $^3J_{5,51b}$ = 4.9 Hz, 1 H, H-51b), 3.29 (d, $^2J_{HaNBn,HbNBn}$ = 14.6 Hz, 2 H, NCHa), 3.47 (dd, 1 H, H-22b), 3.69 (dd, $^3J_{21,22b}$ = 11.0 Hz, 1 H, H-21), 3.99 (d, 2 H, NCHb), 6.81–7.16 (m, 20 H, C_6H_5).

^{13}C NMR (100 MHz): δ = 24.9, 26.3, 28.9 (C-31, C-32, C-33), 34.7, 35.6, 36.8 (C-34, C-22, C-51), 46.0 (C-5), 54.1 (C-4), 55.3 (*C*H_2NBn), 57.1 (C-21), 125.7, 125.9, 126.2, 126.5, 127.9, 128.0, 128.2, 128.27, 128.33, 129.2, 139.7, 140.1, 140.7 (C_6H_5), 133.0 (C-2), 180.7 (C-3), 209.5 (C-1).

Anal. Calcd for $C_{38}H_{39}NO$: C, 86.82; H, 7.48; N, 2.66. Found: C, 86.47; H, 7.54; N, 2.33.

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