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Asymmetric synthesis of *N*-phenylethyl-2-phenyldecahydroquinolin-4-ones via Lewis acid catalyzed imino-Diels–Alder reaction

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Abstract

The asymmetric synthesis of *N*-phenylethyl-2-phenyldecahydroquinolin-4-ones was performed via a Lewis acid catalyzed imino-Diels–Alder reaction between the enantiopure (*R*)-*N*-phenylethylbenzylideneimine and the trimethylsilyl enol ether of acetylcyclohexene. The regio- and stereoselective formation of intermediary bicyclic enoxysilanes, followed by their stereoselective protonation was evidenced. The initial stereoselectivity was kept only if the reaction mixture was treated using controlled basic conditions. Three enantiopure title compounds were isolated with a 5–15% yield.

1. Introduction

Hetero Diels–Alder reactions with imino-dienophiles and activated dienes under Lewis acid catalysis have received increasing interest after the pioneer work of Danishefsky, since they play an important role in the synthesis of nitrogen heterocycles.[1–4] The asymmetric version has been investigated by different groups using either chiral imines[5–8] or chiral Lewis acids;[9,10] more recently, the chirality was introduced on both partners.[11]

We have previously reported the reaction of trimethylsilyl enol ethers of acetylcyclopentene and acetylcyclohexene with various *N*-substituted imines in the presence of Lewis acids which provides an easy access to *N*-substituted octahydropyrindin-4- and decahydroquinolin-4-ones, respectively.[12–14]

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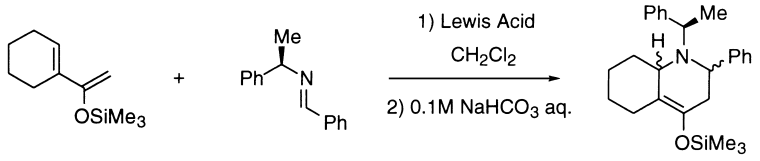
Herein, we describe the asymmetric synthesis of *N*-phenylethyl-2-phenyldecahydroquinolin-4-ones starting from the trimethylsilyl enol ether of acetylcyclohexene **1** and the (*R*)-*N*-phenylethyl benzylideneimine **2** in the presence of achiral and chiral Lewis acids.

2. Results

To a methylene chloride solution of imine **2** (1 equiv.) (Scheme 1), were added at 25°C, the Lewis acid (0.1 or 1 equiv.) and, after 0.5 h, diene **1** (1.1 equiv.) at various temperatures; the condensation was then carried out at various times (Table 1). The reaction mixture was quenched with a 0.1 M $NaHCO_3$ aqueous solution followed by usual workup.



1 **2** **3-4**

Scheme 1.

Table 1
Lewis acid promoted reaction of diene **1** and imine **2**

entry	Lewis Acid (eq.)	Conditions[a]	**3/4**[b]	conversion (%)[c]
1	$AlCl_3$ (1)	-40°C, 0.25h	[d]	[d]
2	$AlCl_3$ (1)	-40°C, 5h	[e]	20
3	$AlCl_3$ (1)	25°C, 2h	33 / 67	84
4	$AlCl_3$ (1)	25°C, 48h	50 / 50	55
5	TfOSTBDM (1)	25°C, 3h	57 / 43	72
6	TfOSTM (1)	25°C, 2h	46 / 54	72
7	TfOSTM (1)	25°C, 48h	38 / 62	95
8	$TiCl_2(OiPr)_2$ (0.1)(*R*)-BINOL (0.1)	25°C, 0.25h	[f]	[f]
9	$TiCl_2(OiPr)_2$ (0.1)(*R*)-BINOL (0.1)	25°C, 0.5h	38 / 62	52
10	$TiCl_2(OiPr)_2$ (0.1)(*R*)-BINOL (0.1)	25°C, 1h	[f]	[f]
11	$TiCl_2(OiPr)_2$ (0.1)(*S*)-BINOL (0.1)	25°C, 0.5h	40 / 60	31

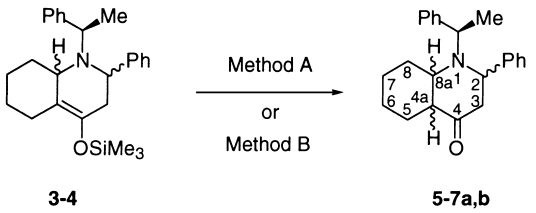
[a] Imine **2** complexation was performed with Lewis acid at 25°C during 0.5 h. [b] Cycloadducts **3-4** were obtained after quenching the reaction mixture by a 0.1M $NaHCO_3$ aqueous solution; **3/4** ratio was estimated by ^1H NMR analysis. [c] Conversion % of the **3-4** mixture was determined from ^1H NMR analysis. [d] Only starting materials were recovered in the crude product. [e] Undetermined. [f] Starting materials were recovered next to traces of bicyclic ketones.

The IR data (ν (C=C-O): 1660 cm^{-1}) of the crude product was consistent with an enoxysilane structure and the ^1H NMR analysis allowed to characterize only two diastereomers **3** and **4** next to the starting materials, as reported in our previous work.[12,13]

The conversions for the **3** and **4** mixtures and the **3**:**4** ratios were estimated by ^1H NMR and given in Table 1. With $AlCl_3$ (1 equiv.) at low temperature (–40°C), the reaction did not take

place or led to low conversion after 0.25 or 5 h, respectively (Table 1, entries 1 and 2). This conversion was increased to 84% by carrying out the reaction at 25°C over 2 h (Table 1, entry 3) while it fell down to 55% after a longer reaction time (48 h) (Table 1, entry 4). TBDMSOTf (1 equiv.) or TMSOTf (1 equiv.) led to a 72% conversion at 25°C during 3 h or 2 h respectively (Table 1, entries 5 and 6); TMSOTf (1 equiv.) improved it up to 95% by increasing the reaction time (48 h) (Table 1, entry 7). The reaction carried out over 0.5 h with the chiral (*R*)- or (*S*)-BINOL–titanium complexes[15,16] (0.1 equiv.) led to 52 or 31% conversion, respectively (Table 1, entries 9 and 11). Only starting materials were recovered for reaction times of 0.25 and 1.5 h using the (*R*)-titanium complex (Table 1, entries 8 and 10).

The crude product was treated at 25°C with either a $MeOH/Et_3N$ mixture during 15 h (method A) or a 1 M THF solution of n-Bu_4NF during 4 h (method B). Under these conditions, the cycloadducts **3** and **4** were completely converted into a mixture of six diastereomeric ketones **5**–**7a**,**b** (Scheme 2). The IR (ν (C=O): 1720 cm^{-1}), the ^1H NMR analysis as well as the mass spectrometry data of the crude product are in agreement with the *N*-phenylethyldecahydroquinolin-4-one structure.



3-4 **5-7a,b**

Scheme 2.

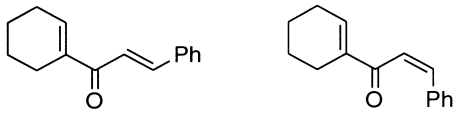
The yields of isolated **5**–**7a**,**b** mixtures, obtained after the starting material elimination by a rapid silica gel chromatography, and the **5a**/**5b**/**6a**/**6b**/**7a**/**7b** proportions, determined from the ^1H NMR analysis of the crude product, are given in Table 2.

Table 2
Formation of the decahydroquinolin-4-ones **5**–**7a**,**b** and facial stereoselectivities

entry[a]	Lewis Acid (eq.)	**5a/5b/6a/6b/7a/7b**[b,c]	**de$_{exo}$**[d] (%)	**de$_{endo}$**[e] (%)	**5-7a,b** yield(%)[f]
1	TfOSTM (1)	27/11/36/7/15/4	56	64	95
2	$TiCl_2(OiPr)_2$ (0.1) (*R*)-BINOL (0.1)	32/6/27/6/24/5	68	66	52
3	$TiCl_2(OiPr)_2$ (0.1) (*S*)-BINOL (0.1)	28/12/38/-/22/-	40	>98	31

[a] For the entries 1-3 in Table 2, the cycloaddition was performed under the conditions indicated in entries 7, 9 and 11 in Table 1 respectively. [b] The protonation of the cycloadducts was performed by the method A or B. [c] The ratios were determined by ^1H NMR analysis. [d] Diastereomeric excess corresponding to the facial stereoselectivity in the *exo* approach, determined from the **5a/5b** ratio. [e] Diastereomeric excess corresponding to the facial stereoselectivity in the *endo* approach, determined from the **6-7a/6-7b** ratio. [f] Yield % of the **5-7a,b** isolated mixture, obtained after treatment of the cycloadducts **3-4a,b** by method A or B followed by rapid silicagel column chromatography.

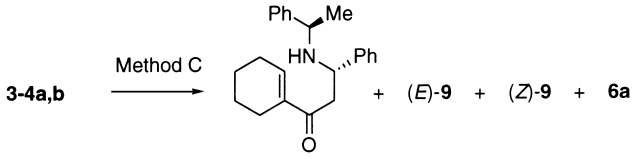
Only the predominant ketones **5a**, **6a** and **7a** were isolated as pure compounds by recrystallization. Actually, **5b** and **6b** were only obtained next to **5a**, **6a** and the monocyclic α,β-unsaturated ketones (*E*)-**9** and (*Z*)-**9**[17] (Scheme 3) which were formed in the course of the silica gel column or flash chromatography. Compound **7b** was only detected in the crude product.



(*E*)-**9** (*Z*)-**9**

Scheme 3.

Acidic quenching by 1N HCl aq./MeOH of the **3**,**4** mixture during 15 h at 25°C (method C) afforded predominantly the γ-amino-α,β-unsaturated ketone **8a** (Scheme 4) as in our previous work[12,13] but in this case, it was accompanied by (*E*)-**9**, (*Z*)-**9** compounds and the bicyclic ketone **6a**.



Scheme 4.

Stereochemical assignments of the *N*-phenylethyldecahydroquinolin-4-ones were first given by ^{1}H NMR analysis (Table 3). The *cis* ring junction stereochemistry of **5a**,**b** and **6a**,**b** was established either by the ^3JH8aH4a coupling constant value (2.9–5.6 Hz) or by the H8a half bandwidth

Table 3
Main ^{1}H NMR parameters of decahydroquinolin-4-ones **5**–**7a**,**b** ($CDCl_3$, 250 MHz)

compound	δ H2	$^3J_{H2-H3}$	δ H8a ($\omega_{1/2}$)	$^3J_{H8a-H8}$	$^3J_{H8a-H4a}$
5a	4.45	9.6, 4.4	3.05	12.5, 5.1	3.7
5b	4.40	8.1, 5.9	3.40	14.0, 5.1	2.9
6a	4.45	12.5, 3.7	3.05 (20.0)	11.8, 5.5	5.5
6b	4.60	7.5, 3.1	4.10 (18.7)	-	-
7a	4.20	11.9, 4.0	3.50 (24.4)	10.3, 5.1	10.3
7b	4.32	7.8, 5.6	-	-	-

δ in ppm, J and $\omega_{1/2}$ in Hz.

value (18.7–20.0 Hz). On the other hand, the ^{3}JH8aH4a coupling constant value of 10.3 Hz as well as the H8a half bandwidth value of 24.4 Hz indicated a *trans* ring junction for **7a**. A *trans* ring junction was expected for compound **7b**, which was not fully characterized by ^{1}H NMR. The ^{3}JH2H3 coupling constant values of **5**–**7a**,**b** indicated clearly that the privileged position of the C-2 phenyl group is equatorial or quasi-equatorial, depending on the heterocycle conformation.

Structure of **5a** and **6a** was then unambiguously established by single-crystal X-ray analysis; the main X-ray data are listed in Table 4, and the solid state structures are shown in Figs. 1 and 2, respectively. A *trans* relationship between the C2H2 and C8H8a bonds (*exo* configuration) was assigned to **5a** and a *cis* relationship between these two bonds (*endo* configuration) was attributed to **6a**. The heterocycle ring adopted a chair conformation in **5a** whereas it adopted a quasi-boat form in **6a**. The *cis* ring junction was confirmed. The agreement between the X-ray and the ^{1}H NMR data indicated thus a similarity of the preferred conformations in the solid state and in solution. Finally, the X-ray analysis of **5a** and **6a** based on the known *R*-configuration of the starting imine **2** gives their absolute configuration: compound **5a**: 2*S*,4a*S*,8a*R*,11*R*; compound **6a**: 2*S*,4a*R*,8a*S*,11*R*.

Table 4
Main X-ray data of **5a** and **6a**

Compound	**5a**	**6a**
	Selected Bond Angles (deg.)	
C8aN1C2	112.2	117.1
C8aN1C11	117.3	114.1
C2N1C11	114.8	113.1
Σ	344.3	344.3
	Selected Dihedral Angles (deg.)	
C5C6C7C8	-55.54	60.71
C6C7C8C8a	56.50	-61.29
C7C8C8aC4a	-54.89	61.83
C8C8aC4aC5	53.86	-59.09
C8aC4aC5C6	-53.67	55.53
C4aC5C6C7	53.25	-57.97
N1C2C3C4	-48.56	-55.69
C2C3C4C4a	42.48	12.71
C3C4C4aC8a	-44.28	42.02
C4C4aC8aN1	53.89	-55.60
C4aC8aN1C2	-65.60	12.87
C8aN1C2C3	61.40	42.48
C8aN1C2C21	-177.64	159.77
H4aC4aC8aH8a	52.31	-57.27
H2C2C3H31	-50.64	-56.22
H2C2C3H32	-169.26	-175.95
	Distance from C2N1C8a Plane (Å)	
H2	-0.810	+0.888
C8	-1.262	-1.401
H8a	+0.034	+0.685

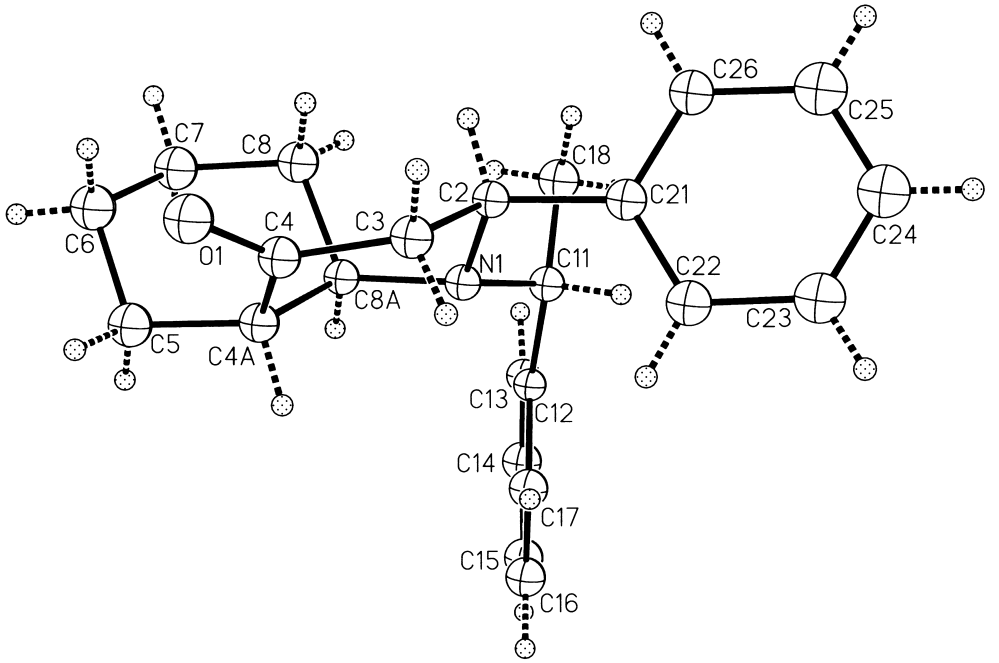


Figure 1. ORTEP drawing of compound **5a**. Displacement ellipsoids are shown at the 40% probability level

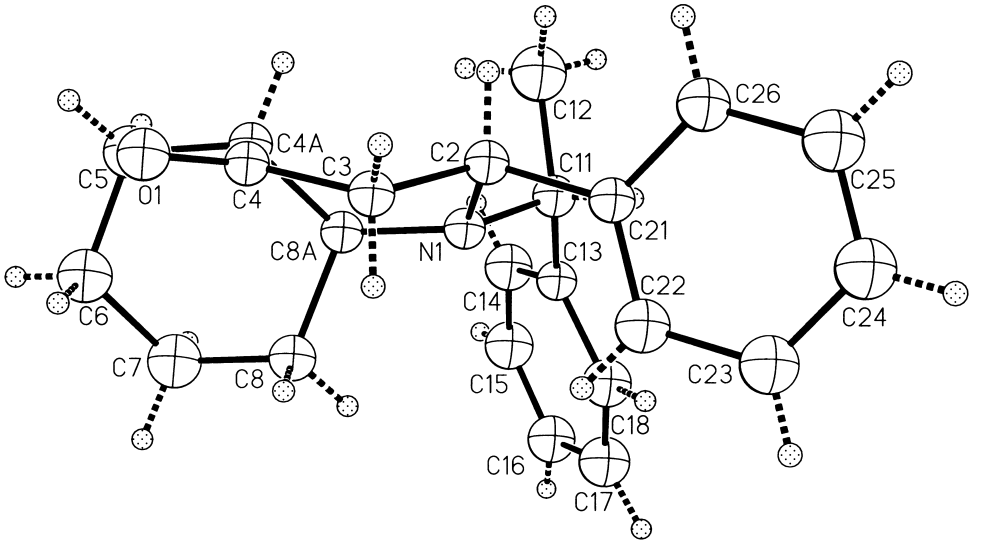
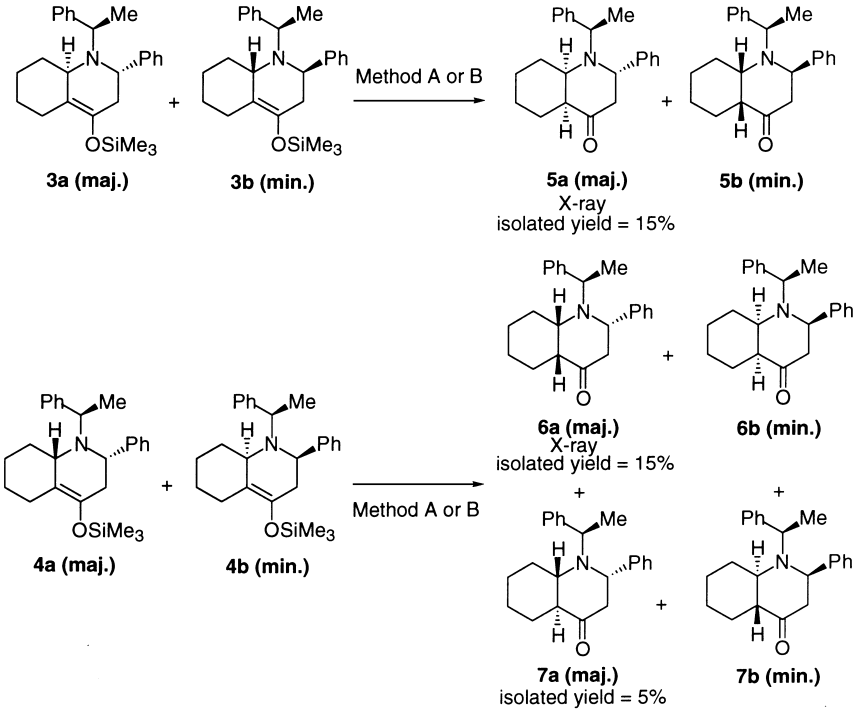


Figure 2. ORTEP drawing of compound **6a**. Displacement ellipsoids are shown at the 40% probability level

Considering the ketones ratio values **5a**,**b**/**6**–**7a**,**b** (38:62 for entries 1 and 2 and 40:60 for entry 3) deduced from the **5a**/**5b**/**6a**/**6b**/**7a**/**7b** proportions given in Table 2 and comparing these data with the cycloadduct ratio values **3**/**4** (Table 1, entries 7, 9 and 11), it appears that **5a** and **b** derive from the cycloadduct **3** while **6a**, **7a**, **6b** and **7b** derive from **4**. Thus, **3** and **4** are formed probably by two diastereomers **3a**,**b** and **4a**,**b**, respectively (**3a** and **4a** being predominant), although their ^{1}H NMR spectra were not distinguished.

On one hand, from the assumption that **5a** and **b** result from **3a** and **b**, respectively, the *exo* configuration is assigned to the ketone **5b** and to the cycloadducts **3a** and **b**. On the other hand, **6**–**7a** and **6**–**7b** deriving from **4a** and **b**, respectively, the *endo* configuration is attributed to the ketones **6b** and **7a**,**b** and to the cycloadducts **4a** and **b**. The absolute configurations of **3**–**4a**,**b**, **5**–**6b** and **7a**,**b** are shown in Scheme 5.



Scheme 5.

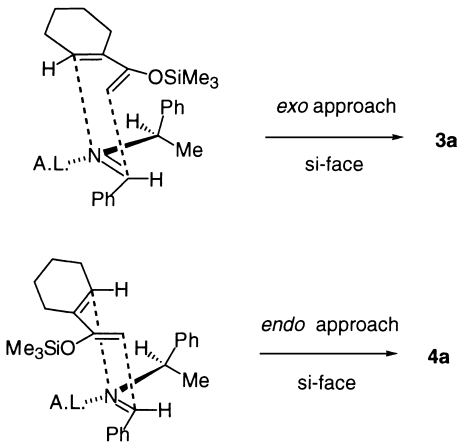
The *exo* and *endo* diastereomeric excesses (de_{exo} and de_{endo}) are given in Table 2. The use of an achiral Lewis acid as TMSOTf provided a poor diastereofacial recognition for the *exo* compounds (de = 56%) and for the *endo* ones (de = 64%) (Table 2, entry 1); same results were obtained with $AlCl_3$ or TBDMSOTf. The use of the (*R*)-BINOL–titanium complex led only to a small increase of the *exo* diastereomeric excess (de = 68%) while the (*S*)-BINOL–titanium complex highly improved the *endo* one up to 98% (Table 2, entries 2 and 3).

3. Discussion

A high regioselectivity was shown in the reaction of the diene **1** and the imine **2** promoted by $AlCl_3$, TMSOTf, TBDMSOTf and (*R*)- or (*S*)-BINOL–titanium complexes. The use of achiral Lewis acids led to high conversion rates (72–95%) as described previously,[12] while with the chiral Lewis acids, low conversions were observed according to the literature data.[11] Actually, the

treatment of the reaction mixture by a 0.1 M $NaHCO_3$ aqueous solution resulted in the exclusive formation of bicyclic trimethylsilylenol ethers **3**–**4a**,**b**.

Conversely, a very low or negligible *exo* versus *endo* stereoselectivity was observed, the **3a**,**b**:**4a**,**b** ratio values varying in the 33:67 to 57:43 range, whatever the reaction conditions (Lewis acid nature, time and temperature). Such a lack of *exo*/*endo* stereoselectivity when the subtituent on the nitrogen is a benzyl group, was evidenced in our previous work.[12] Thus, the kinetic control of the condensation may be reasonably put forward, **3**–**4a**,**b** being the primary products of the reaction. These observations are consistent with a nonsynchronous concerted process, as previously reported by our group and others.[5,12–14,18–21] *exo* and *endo* Approaches involving a Lewis acid–imine complex, in a *trans* geometry, are thus considered (Scheme 6).[11,18,25,26]



Scheme 6.

The imino-Diels–Alder process is strengthened since α,β-unsaturated ketones **8a**, (*E*)-**9** and (*Z*)-**9** were only observed when the reaction mixture was treated under acidic conditions. The high regioselectivity of the condensation is well explained by the FMO theory.[22,23] The poor *exo* versus *endo* stereoselectivity is consistent with a loose transition state.[18,19,24]

The diastereofacial selectivity was determined only after $MeOH/Et_3N$ or nBu_4NF treatments of the crude cycloadducts providing the six diastereomeric ketones **5**–**7a**,**b**. This protonation step converted the **3a**,**b** enoxysilanes into the *cis* ring fused *exo* ketones **5a**,**b** exclusively and the **4a**,**b** enoxysilanes into the *cis* ring fused *endo* ketones **6a**,**b**. Compounds **7a** and **b** were probably formed by epimerization of **6a** and **b**, respectively, during these treatments. A similar isomerization was previously described.[12,13]

The predominant *cis* ring fused ketones **5a** and **6a** resulted from the *exo* and *endo* approaches of the diene **1** on the *si*-face of the Lewis acid–imine complex, respectively. It is unlikely that the minor diasteromers **5b** and **6b** corresponded to the attack of the *re*-face of the same complex. Similar diastereofacial selectivity was reported by Yamamoto in the case of the condensation of the Danishefsky's diene with the same imine.[11]

A high matched effect was observed with the (*S*)-BINOL–titanium complex for the *endo* approach (de = 98%) while the (*R*)-one led to a mismatched effect (de = 66%), the result being analogous to that obtained with achiral Lewis acids. In the *exo* approach, whatever the achiral or chiral Lewis acids used, the facial recognition varied unsignificantly (de = 40–68%).

The PM3 calculation of the TMS–imine **2** (1/1) complex, performed with the Hyperchem program,[27] shows that, in the privileged conformation, the phenyl group occupies the *si*-face while the methyl group lies on the *re*-one (Fig. 3). This may reflect the low diastereofacial selectivity observed with this Lewis acid, the two faces being sterically hindered. This model is insufficient to account for the sterically demanding of the (*S*)-BINOL–titanium complex which led to a very high facial recognition in the *endo* approach**.** Moreover, the structure of the involved Lewis acid–imine complexes was likely to exhibit various stoichiometries.[28]

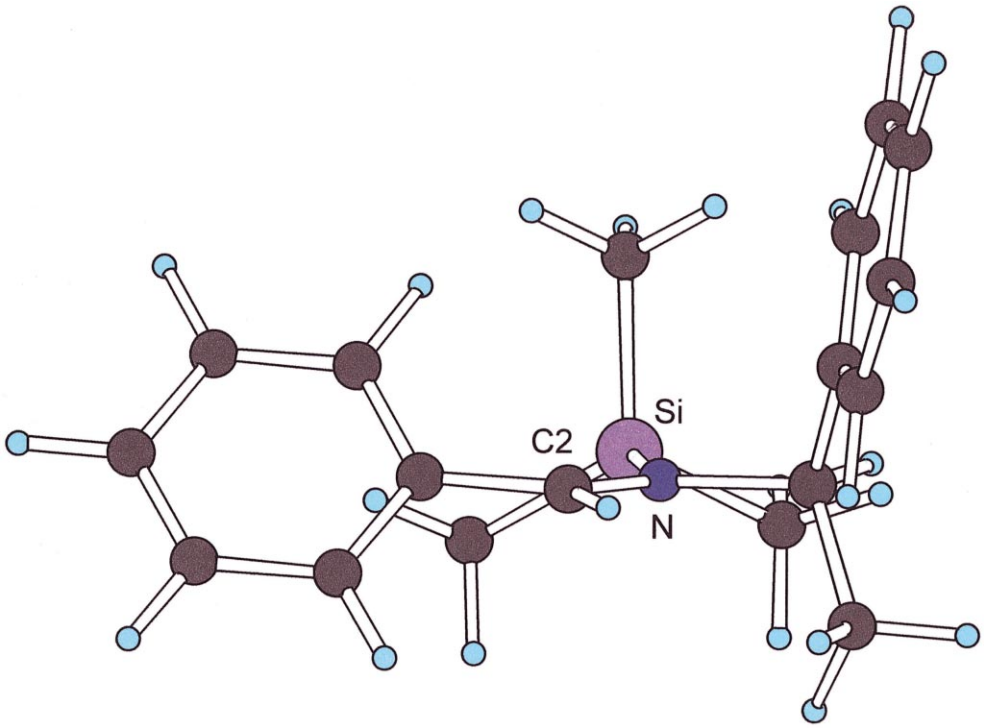


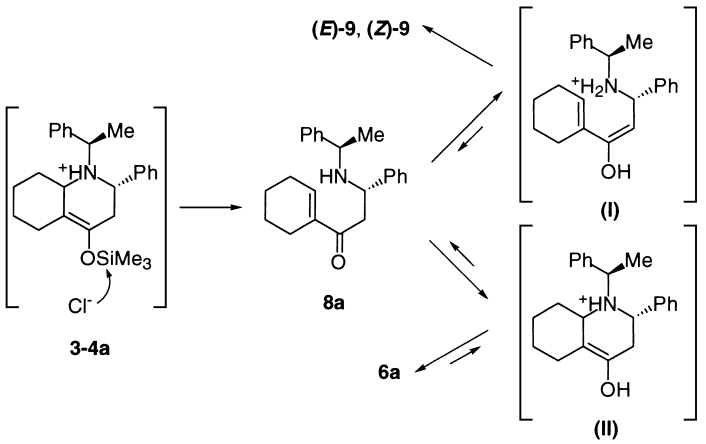
Figure 3. PM3 minimized structure of TMS–imine **2** complex

The formation of **8a**, (*E*)-**9**, (*Z*)-**9** and **6a** obtained by acidic treatment of the crude enoxysilanes is explained as follows: the γ-amino-α,β-unsaturated ketone **8a** resulted from a ring opening of the major enoxysilanes **3a** and **4a**. This ketone led, on one hand, to (*E*)-**9** and (*Z*)-**9** by desamination of the intermediate dienol **I**, and, on the other hand, to the most stable ketone **6a** by succesive ring closure/opening processes via the bicyclic enol **II** (Scheme 7).[3,5,7,8,12–14]

Furthermore, attempts of purification of **8a** by chromatography gave mixtures of (*E*)-**9**, (*Z*)-**9** and **6a**. Compound **8b**, proceeding from the minor cycloadducts **3b** and **4b**, was not detected probably due to its decomposition into the (*E*)-**9** and (*Z*)-**9** mixture.

The formation of (*E*)-**9** and (*Z*)-**9** in the course of silica gel chromatography of **5**–**7a**,**b** probably took place via the intermediates **8a** and **II**.

The cycloadducts **3**–**4a**,**b** as well as the ketones **5**–**7a**,**b** appeared to be very unstable under acidic conditions.



Scheme 7.

4. Conclusion

The condensation of the chiral imine **2** with the silyloxydiene **1** promoted by various Lewis acids allowed the asymmetric synthesis of *N*-phenylethyl-2-phenyldecahydroquinolin-4-ones **5**–**7a**,**b** and the preparation of the enantiopure predominant ketones **5**–**7a**. The best diastereofacial selectivity was obtained with the (*S*)-BINOL–titanium complex. This study had revealed a privileged attack of the *si*-face of the Lewis acid–imine complex. Moreover, all the results are in the framework of a concerted nonsynchronous process. The obtention of the α,β-unsaturated ketones **8a**, (*E*)-**9** and (*Z*)-**9** by acidic treatment of the reaction mixture, strengthened this mechanism and demonstrated the importance of the basic quenching to keep the initial selectivity.

5. Experimental

5.1. X-Ray crystal structure determinations for **5a** and **6a**

Diffraction data for both compounds were collected at room temperature on an Enralf–Nonius CAD4 diffractometer using graphite-monochromatized Mo–Kα radiation with the w-2q scan technique. Data were corrected for Lorentz-polarisation effects and decay (loss of 0.6% in 26 h **5a**, 0.7% in 29 h **6a**, linearly corrected).[29] The structures were solved by direct method[30] and refined by full matrix least squares (F2) with isotropic thermal parameters. H atoms were introduced at calculated positions as riding atoms with an anisotropic displacement parameter equal to 1.2(CH) or 1.5(CH3) times that of the parent atom.[31] Crystallographic data for **5a**: orthorhombic, P 21 21 21, $a=8.594(6)$ Å, $b=13.737(2)$ Å, $c=16.305(6)$ Å, $V=1925(1)$ Å3, $Z=4$, $D_{calc}=1.151$ g cm^{-3}, 950 reflections with $I>2(I)$ out of 1395 unique reflections, $R=0.0675$, $Rw=0.1986$. For **6a**: monoclinic, P 21, $a=6.855(6)$ Å, $b=26.3870(19)$ Å, $c=10.996(6)$ Å, $V=1989(2)$ Å3, $Z=4$, $D_{calc}=1.114$ g cm^{-3}, 1340 reflections with $I>2(I)$ out of 2174 unique reflections, $R=0.0729$, $Rw=0.2111$.

5.2. General

Cycloadditions were run in a three necked flask equipped with a magnetic stirrer, a thermometer, a rubber septum cap and under argon. Methylene chloride was distilled over CaH_2 and diethyl ether over $LiAlH_4$. Tetrahydrofuran was distilled under argon over benzophenone-ketyl and hexane over P_4O_{10}. Triethylamine was distilled over KOH. Ethanol and methanol were purchased from Carlo Erba. 0.1 M Tetra-*n*-butylammonium fluoride in THF was purchased from Acros. $AlCl_3$ was sublimed and *tert*-butyldimethylsilyltriflate and trimethylsilyltriflate were distilled under argon. 1-(1-Cyclohexen-1-yl)ethenyloxy)trimethylsilane **1** was prepared according to literature.[32] (*R*)-*N*-Phenylethylbenzylideneimine **2** was synthesized according to the procedure of F. Texier-Boullet;[33] their enantiomeric purity (ee $>99\%$) was controlled by ^{13}C NMR analysis using a methylene chloride solution of poly(γ-benzyl L-glutamate) as solvent as it was described by J. Courtieu et al.[34,35] Column chromatography was performed with silica gel SDS (70–200). Flash chromatography was carried out with silica gel SDS (35–70). The ^1H NMR spectra were recorded on a Bruker AM250 or AM400 spectrometers. The ^{13}C NMR spectra were recorded on a Bruker AM250 spectrometer. δ Values are reported in ppm. IR spectra were achieved on a Perkin–Elmer Model 682 infrared spectrometer and wavelenghts are given in cm^{-1}. Mass spectra were recorded on a mass spectrometer coupled with a Nermag R10-10 capillary chromatograph. High resolution mass spectra were recorded on a MAT 95S. Melting points were obtained on a Mettler FP5 capillary melting point apparatus. Microanalyses were done by the service of microanalysis of CNRS. Optical rotation values were measured using a Perkin–Elmer P.241 polarimeter.

5.3. General procedure for cycloaddition reactions of imine **2** with diene **1** catalyzed by Lewis acids

5.3.1. In the presence of achiral Lewis acids

To a solution of 180 μL of imine **2** (1 mmol) in anhydrous methylene chloride (10 mL), under argon, was added the Lewis acid (1 mmol), at 25°C. After 0.5 h of stirring, 240 μL of 1-(1-cyclohexen-1-yl)ethenyloxy)trimethylsilane **1** (1.2 mmol) was then added dropwise at different temperatures for various times (Table 1). The reaction mixture was quenched by addition of a 0.1 M $NaHCO_3$ aqueous solution, until reaching a pH value of 8–9 and extracted with methylene chloride (2×20 mL). The combined layers were washed with a 0.1 M $NaHCO_3$ aqueous solution and brine, dried over $MgSO_4$ and concentrated under vacuum. The crude product was analysed by IR (neat, C=C-O 1660). The 200 MHz ^1H NMR analysis indicated the signals of only two cycloadducts **3** and **4** which correspond to the superposed spectra of the compounds **3a**,**b** and **4a**,**b**, respectively.

(2*S*,8a*R*,11*R*)-2-Phenyl-1-(1-phenylethyl)-4-trimethylsilyloxy-Δ4-decahydroquinolin **3a**. 200 MHz ^1H NMR ($CDCl_3$) δ 0.05 (s, 9H), 1.00 (d, J = 7.3 Hz, 3H), 0.80–2.60 (m, 8H), 2.70–3.00 (m, 2H), 3.40–3.55 (m, 1H), 3.75–3.90 (m, 1H), 4.10–4.20 (m, 1H), 7.00–7.60 (m, 10H).

(2*S*,8a*S*,11*R*)-2-Phenyl-1-(1-phenylethyl)-4-trimethylsilyloxy-Δ4-decahydroquinolin **4a**. 200 MHz ^1H NMR ($CDCl_3$) δ 0.20 (s, 9H), 1.40 (d, J = 7.3 Hz, 3H), 0.80–2.60 (m, 8H), 2.70–3.00 (m, 1H), 3.00–3.15 (m, 1H), 3.15–3.30 (m, 1H), 3.90–4.10 (m, 2H), 7.00–7.60 (m, 10H).

(2*R*,8a*S*,11*R*)-2-Phenyl-1-(1-phenylethyl)-4-trimethylsilyloxy-Δ4-decahydroquinolin **3b**. The 200 MHz ^1H NMR spectra was superposed to that of the diastereomer **3a**.

(2*R*,8a*R*,11*R*)-2-Phenyl-1-(1-phenylethyl)-4-trimethylsilyloxy-Δ4-decahydroquinolin **4b**. The 200 MHz ^1H NMR spectra was superposed to that of the diastereomer **4a**.

*5.3.2. In the presence of (*R*)- or (*S*)-BINOL–titanium complexes*[16]

A solution of $TiCl_2(OiPr)_2$ was previously prepared under argon from 20 mL of methylene chloride, 55 μL of $TiCl_4$ (0.5 mmol) and 150 μL of $Ti(OiPr)_4$ (0.5 mmol) and stirred during 10 min, at 25°C. To a 2 mL of this solution of $TiCl_2(OiPr)_2$) (0.1 mmol) introduced in a three necked flask and cooled at –65°C, a solution of 28.6 mg of (*R*) or (*S*)-BINOL (0.1 mmol) in 5 mL of methylene chloride was added. After 1 h of stirring at 25°C, 180 μL of imine **2** (0.1 mmol) were added to the deep red obtained solution (0.1 mmol of the chiral Lewis acid) and stirred during 0.5 h. Then, 240 μL of diene **1** (1.2 mmol) were introduced dropwise at different temperatures for various times (Table 1). The reaction medium was treated as above.

5.4. General procedure for treatment of enoxysilanes ***3–4a,b***

5.4.1. Method A

A mixture of MeOH (250 μL) and Et_3N (250 μL) was added to the crude enoxysilanes obtained from 1 mmol of imine **2**, at 25°C. The reaction medium was stirred during 15 h at 25°C. After removal of the solvents under reduced pressure, the crude residue was purified by column or flash chromatography.

5.4.2. Method B

The crude enoxysilanes obtained from 1 mmol of imine **2** were diluted in 4 mL of THF and treated with 4 mL of a 1 M nBu_4NF in THF solution during 4 h, at 25°C. The reaction medium was diluted with Et_2O (10 mL), washed with water (10 mL). The organic layer was dried over $MgSO_4$. The purification was performed as above.

5.4.3. Method C

A 1N HCl aqueous solution (15 mL) was added, at 25°C, to the reaction mixture, obtained from 1 mmol of imine **2** and diluted with MeOH (15 mL). After stirring during 15 h, at 25°C, the reaction medium was quenched by addition of a 0.1 M $NaHCO_3$ aqueous solution until a pH value of 8–9 was obtained, extracted with Et_2O (2×15 mL), dried over $MgSO_4$ and concentrated under vacuum.

*5.4.4. (2*S*,4a*S*,8a*R*,11*R*)-2-Phenyl-1-(1-phenylethyl)decahydroquinolin-4-one* ***5a***

Obtained from method A or B; the solid isolated after silica gel column chromatography (hexane:Et_2O, 4:1) was recrystallized from EtOH to give white crystals in a 15% yield: mp 109°C; R_f (hexane:Et_2O, 4:1) 0.53; IR (CCl_4) C=O 1720; 200 MHz ^{1}H NMR ($CDCl_3$) δ 1.00–1.20 (m, 2H), 1.25 (d, J = 7.3 Hz, 3H), 1.30–1.5 (m, 2H), 1.5–1.65 (m, 1H), 1.65–1.9 (m, 2H), 2.15–2.25 (m, 1H), 2.5–2.75 (m, 3H), 3.05 (dq, J = 3.7, 5.1 and 12.5 Hz, 1H), 4.05 (q, J = 7.3 Hz, 1H), 4.45 (dd, J = 4.4 and 9.6 Hz, 1H), 7.20–7.55 (m, 10H); 62 MHz ^{13}C NMR ($CDCl_3$) δ 15.5, 21.4, 25.1, 25.6, 28.1, 50.3, 51.8, 55.0, 56.3, 59.1, 126.8, 127.4, 127.7, 127.9, 128.2, 128.8, 130.8, 142.5, 210.8; GC t_R (180°C+10°C/min) 8 min 31 s; MS (EI) *m*/*z* 333 (M^+, 2.11%), 105 (100%); $[\alpha]_D^{25}$ = +66.8 (*c* 0.82, EtOH). Anal. calcd for $C_{23}H_{27}NO$: C, 82.84; H, 8.16; N, 4.20; O, 4.80. Found: C, 82.79; H, 8.11; N, 4.17; O, 4.80.

*5.4.5. (2*R*,4a*R*,8a*S*,11*R*)-2-Phenyl-1-(1-phenylethyl)decahydroquinolin-4-one* ***5b***

Prepared from method A or B and obtained after silica gel column chromatography (hexane:Et_2O, 4:1) as an oil next to **5a**, (*E*)-**9** and (*Z*)-**9** in the following ratio determined by ^{1}H NMR: **5a**:**5b**:(*E*)-

9:(*Z*)-**9**, 59:22:18:1. IR and ^{1}H NMR data of **5b** were deduced from the spectra of this mixture. IR (CCl_4) C=O 1720; 200 MHz ^{1}H NMR ($CDCl_3$) δ 0.90–1.20 (m, 2H), 1.20–1.40 (m, 2H), 1.45 (d, J = 7.3 Hz, 3H), 1.50–1.90 (m, 3H), 2.25–2.45 (m, 1H), 2.50–2.65 (m, 2H), 2.90 (m, 1H), 3.40 (dq, J = 2.9, 5.1 and 14.0 Hz, 1H), 4.10 (m, 1H), 4.40 (dd, J = 8.1 and 5.9 Hz, 1H), 7.20–7.55 (m, 10H); GC t_R (180°C+10°C/min) 7 min 21 s; MS (EI) *m*/*z* 333 (M^+, 10.56%), 105 (100%); HRMS (EI) calcd for $C_{23}H_{27}NO$ (M+): 333.2092, found: 333.2081.

*5.4.6. (2*S*,4a*R*,8a*S*,11*R*)-2-Phenyl-1-(1-phenylethyl)decahydroquinolin-4-one* ***6a***

Obtained from method A or B; the solid isolated after silica gel column chromatography (hexane:Et_2O, 4:1) was recrystallized from EtOH to give white crystals in a 15% yield: mp 116°C; R_f (hexane:Et_2O, 4:1) 0.27; IR (CCl_4) C=O 1720; 200 MHz ^{1}H NMR ($CDCl_3$) δ 0.80–1.40 (m, 8H), 1.45 (d, J = 7.3 Hz, 3H), 2.30–2.45 (m, 1H), 2.55 (dd, J = 3.7 and 17.5 Hz, 1H), 2.70 (dd, J = 12.5 and 17.5 Hz, 1H), 2.75–2.90 (m, 1H), 3.00 (dt, J = 5.5 and 11.8 Hz, $\omega_{1/2}$ = 20.0 Hz, 1H), 3.90 (q, J = 6.6 Hz, 1H), 4.45 (dd, J = 3.7 and 12.5 Hz, 1H), 7.15–7.65 (m, 10H); 62 MHz ^{13}C NMR ($CDCl_3$) δ 8.8, 21.5, 24.9, 25.5, 36.7, 48.2, 48.4, 52.9, 55.9, 59.1, 126.7, 127.5, 127.6, 127.7, 128.0, 128.2, 128.7, 143.4, 144.3, 211.6; GC t_R (180°C+10°C/min) 7 min 3 s; MS (EI) *m*/*z* 333 (M^+, 15.99%), 105 (100%); $[\alpha]_D^{25}$ = –142.3 (c 0.70, EtOH). Anal. calcd for $C_{23}H_{27}NO$: C, 82.84; H, 8.16; N, 4.20; O, 4.80. Found: C, 82.80; H, 8.13; N, 4.19; O, 4.80.

*5.4.7. (2*R*,4a*S*,8a*R*,11*R*)-2-Phenyl-1-(1-phenylethyl)decahydroquinolin-4-one* ***6b***

Prepared from method A or B and obtained after silica gel column chromatography (hexane:Et_2O, 4:1) as an oil next to **5b**, **6a**, (*E*)-**9** and (*Z*)-**9** in the following ratio determined by ^{1}H NMR: **5b**:**6a**:**6b**:(*E*)-**9**:(*Z*)-**9**, 3:36:24:12:25. IR and ^{1}H NMR data of **6b** were deduced from the spectra of this mixture. IR (CCl_4) C=O 1720; 250 MHz ^{1}H NMR ($CDCl_3$) δ 1.40 (d, J = 7.3 Hz, 3H), 4.15 (m, $\omega_{1/2}$ = 18.7 Hz, 1H), 4.60 (dd, J = 3.1 and 7.5 Hz, 1H), 4.70 (q, J = 6.6 Hz, 1H); GC t_R (180°C+10°C/min) 7 min 9 s; MS (EI) *m*/*z* 333 (M^+, 17.87%), 105 (100%); HRMS (EI) calcd for $C_{23}H_{27}NO$ (M+): 333.2092, found: 333.2100.

*5.4.8. (2*S*,4a*S*,8a*S*,11*R*)-2-Phenyl-1-(1-phenylethyl)decahydroquinolin-4-one* ***7a***

Obtained from method A or B; the solid isolated after silica gel column chromatography (hexane:Et_2O, 4:1) was recrystallized from EtOH to give white crystals in a 5% yield: mp 119°C; R_f (hexane:Et_2O, 4:1) 0.39; IR (CCl_4) C=O 1720; 200 MHz ^{1}H NMR ($CDCl_3$) δ 0.80–1.20 (m, 2H), 1.20–1.35 (m, 2H), 1.45 (d, J = 7.3 Hz, 3H), 1.55–1.85 (m, 2H), 1.85–2.10 (m, 2H), 2.10–2.35 (m, 1H), 2.40 (dd, J = 4.0 and 17.5 Hz, 1H), 2.55 (dd, J = 11.9 and 17.5 Hz, 1H), 3.50 (dt, J = 5.1 and 10.3 Hz, $\omega_{1/2}$ = 24.4 Hz, 1H), 3.80 (q, J = 6.6 Hz, 1H), 4.25 (dd, J = 4.0 and 11.9 Hz, 1H), 7.15–7.60 (m, 10H); 62 MHz ^{13}C NMR ($CDCl_3$) δ 19.5, 21.5, 25.0, 25.9, 38.5, 47.3, 48.7, 52.4, 57.2, 58.9, 66.8, 127.0, 127.3, 127.6, 128.2, 128.8, 140.1, 144.6, 211.5; GC t_R (180°C+10°C/min) 6 min 39 s; MS (EI) *m*/*z* 333 (M^+, 15.20%), 105 (100%); $[\alpha]_D^{25}$ = +188.4 (*c* 1.00, EtOH). Anal. calcd for $C_{23}H_{27}NO$: C, 82.84; H, 8.16; N, 4.20; O, 4.80. Found: C, 82.69; H, 7.99; N, 4.20; O, 4.77.

*5.4.9. (2*R*,4a*R*,8a*R*,11*R*)-2-Phenyl-1-(1-phenylethyl)decahydroquinolin-4-one* ***7b***

Prepared from method A or B, this compound was detected (< 2%) in the ^{1}H NMR spectrum of the crude product by a signal at δ 4.32 (dd, J = 5.6 and 7.8 Hz, 1H); GC t_R (180°C+10°C/min) 7 min 17 s; MS (EI) *m*/*z* 333 (M^+, 15.78%), 105 (100%).

5.4.10. (3S,11R)-1-(1-Cyclohexenyl)-3-phenyl-3-(1-phenylethylamino)pro-pan-1-one ***8a***

Obtained from method C as an oil next (*E*)-**9** and (*Z*)-**9** and **6a** in the following ratio determined by ^{1}H NMR: **8a**:**6a**:(*E*)-**9**:(*Z*)-**9**: 56:16:21:6. IR and ^{1}H NMR data were deduced from the spectra of this mixture. IR (CCl_4) C=O 1660; 200 MHz ^{1}H NMR ($CDCl_3$) δ 1.40 (d, J = 6.6 Hz, 3H), 2.95 (dd, J = 4.8 and 16.9 Hz, 1H), 3.05 (dd, J = 7.3 and 16.9 Hz, 1H), 3.65 (q, J = 7.3 Hz, 1H), 4.35 (dd, J = 4.8 and 7.3 Hz, 1H), 6.75–6.85 (m, 1H), 7.05–7.50 (m, 10H). GC and MS data were not obtained because of decomposition.

*5.4.11. 1-(1-Cyclohexenyl)-3-phenyl-propen-1-one (*E*)-9*[17] *and (*Z*)-9*

The two isomers were isolated, as an oil, in a (*E*)-**9**:(*Z*)-**9**, 66:33 ratio determined by ^{1}H NMR, in the course of the purification of **5**–**7a**,**b** by silica gel column or flash chromatography (hexane:Et_2O, 4:1). IR, ^{1}H and ^{13}C NMR data were deduced from the spectra of this mixture. IR (CCl_4) C=O 1650; 200 MHz ^{1}H NMR ($CDCl_3$) (*E*)-**9** δ 0.80–2.50 (m, 8H), 7.00–7.10 (m, 1H), 7.27 and 7.62 (AB, J = 18 Hz, 2H), 7.10–7.60 (m, 5H), (*Z*)-**9** δ 0.80–2.50 (m, 8H), 6.30 and 6.80 (AB, J = 10.4 Hz, 2H), 6.85–6.95 (m, 1H), 7.10–7.60 (m, 5H); 62 MHz ^{13}C NMR δ 21.6, 21.8, 21.9, 22.7, 22.8, 22.9, 23.5, 25.1, 25.9, 26.1, 26.2, 29.7, 64.1, 66.7, 66.8, 121.4, 128.3, 129.9, 135.2, 135.7, 136.7, 139.3, 140.3, 140.9, 142.4, 143.7, 190.9, 197.1; GC t_R (150°C+10°C/min) (*E*)-**9** 3 min 27 s, (*Z*)-**9** 4 min 49 s; MS (EI) *m*/*z* (*E*)-**9** 212 (M^+, 100%), (*Z*)-**9** 212 (M^+, 94.89%), 211 (100%).

Supplementary material available: tables of X-ray data for **5a** and **6a**.

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