DOI: 10.1002/ejoc.201101462

Studies on the Diastereoselective Intramolecular Pauson–Khand Reaction on Regioisomeric Chiral Perhydrobenzoxazines Derived from (–)-8-Aminomenthol

Alicia Maestro,[a] Rafael Pedrosa,*[a] Alfonso Pérez-Encabo,[a] and Juan J. Pérez-Rueda[a]

Keywords: Asymmetric synthesis / Cyclization / Enynes / Stereoselective synthesis

Chiral perhydrobenzoxazines derived from (–)-8-aminomenthol and containing a 1,6-enyne moiety participate in intramolecular diastereoselective Pauson–Khand reactions with diastereoselection that depends on the nature of the starting compounds. 3-Propargyl-2-vinyl-substituted perhydrobenzoxazines yielded the cyclization products with low diastereoselectivity except for compounds where the double bond was 1,2-disubstituted. Regioisomeric perhydrobenzoxazines with the acetylenic bond at C-2 and an allyl substituent at the nitrogen atom gave much better stereochemical discrimination.

Introduction

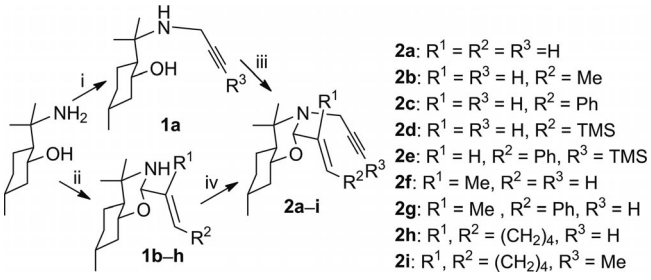
Cyclization of an alkene, an alkyne, and carbon monoxide in the presence of dicobalt octacarbonyl, named the Pauson–Khand reaction (PKR), is one of the most powerful and flexible methods available to construct polysubstituted cyclopentenone derivatives.[1] Other metal carbonyls have been also used for similar carbocyclizations leading to cyclopentenones.[2] The intermolecular version of the PKR presents some problems associated with the poor reactivity of common alkenes and, in some cases, the low regioselectivity of the process when a combination of unsymmetrically substituted alkenes and alkynes are used.

More interesting is the intramolecular version of the PKR, because it is regioselective, thermodynamically more favored, and allows the synthesis of polycyclic cyclopentenone derivatives. The development of the stereoselective intramolecular PKR is especially important. One of the most studied methods uses chiral auxiliaries attached to both the alkene or alkyne components of the reaction,[3] but it has been demonstrated that the presence of substituents at the tether chain, making the C-3 and C-5 atoms stereogenic centers, also promotes diastereoselective PKRs. Both approaches have been widely employed in the synthesis of natural products.[4]

Perhydrobenzoxazines derived from (–)-8-aminomenthol have been shown to be excellent chiral templates in a series of intramolecular reactions such as radical cyclizations,[5] Diels–Alder[6] and dipolar cycloadditions,[7] or anionic cyclizations,[8] and now we reasoned that this structure could act as a chiral template in diastereoselective intramolecular PKRs. The attachment of a vinyl substituent at C-2 and a propargyl group at the nitrogen atom of the perhydrobenzoxazine nucleus allows the construction of chiral 1,6-enynes, which could lead to pirrolyl cyclopentenone derivatives diastereoselectively. To this end, we have prepared a series of 1,6-enynes tethered by the nitrogen atom to form part of a chiral structure derived from (–)-8-aminomenthol and then studied the diastereoselective PKR.

Results and Discussion

Enantiopure 2-vinyl-3-propargyl-substituted perhydrobenzoxazines **2a**–**i** were prepared, in two steps, from (–)-8-aminomenthol by condensation with the corresponding aldehyde followed by alkylation with propargyl bromides or by reaction with propargyl bromides and condensation with acrolein or methacrolein for **2a** and **2f** (Scheme 1).

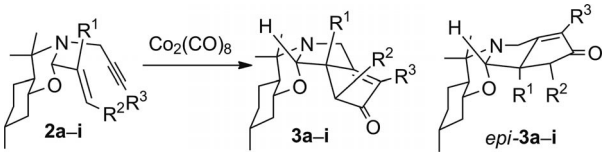


Scheme 1. Reagents and conditions: (i) propargyl bromide, K_2CO_3, MeCN, r.t.; (ii) aldehyde, DCM, r.t.; (iii) acrolein or methacrolein, sealed tube, 120 °C; (iv) propargyl bromides, K_2CO_3, MeCN, reflux.

[a] Instituto CINQUIMA (Centro de Innovación en Química y Materiales Avanzados) and Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Valladolid
Dr. Mergelina s/n, 47011 Valladolid. Spain
Fax: +34-983-186324
E-mail: pedrosa@qo.uva.es

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/ejoc.201101462.

Initially, parent compound **2a** was selected to study the reaction, and it was subjected to cyclization with dicobalt octacarbonyl under different conditions (Scheme 2 and Table 1).



Scheme 2. Pauson–Khand reaction of 2-vinyl-3-propargylperhydrobenzoxazines.

Table 1. Pauson–Khand reaction for **2a** under different conditions.

Entry	Solvent	Additive	*T* [°C]	Time [h]	Yield[a] [%]	*dr* (**3a**/*epi*-**3a**)
1	toluene	–	110	2	28	40:60
2	DCM	NMO[b]	25	24	45	48:52
3	DCM	TMANO[b]	25	24	50	47:53
4	DCM	TMANO[c]	25	4	84	48:52
5	DCM	TMANO[c]	0	10	60	50:50
6	DME	$CyNH_2$	60	9	20	50:50
7	DME	$CyNH_2$	60	4	85	50:50

[a] Isolated yield. [b] 6 equiv. of amine oxide. [c] 8 equiv. of TMANO and 8 equiv. of 3 Å MS.

Complete disappearance of the starting compound was observed when an equimolar mixture of **2a** and $Co_2(CO)_8$ was heated in refluxing toluene for 2 h, but a lot of decomposition products were formed and only 28% of cyclization diastereoisomers **3a** and *epi*-**3a** was isolated as a 2:3 mixture (Table 1, Entry 1). The yield was improved to 45–50% when an equimolar mixture of **2a** and $Co_2(CO)_8$ in DCM and NMO or trimethylamine *N*-oxide (TMANO, 6 equiv.) was allowed to stand at room temperature for 24 h, but the diastereoisomers were isolated as a near equimolar mixture (Table 1, Entries 2 & 3). A much better yield, although without an improvement in the diastereoselectivity, was observed for the reaction in which 8 equiv. of TMANO and 8 equiv. of 3 Å molecular sieves was used (Table 1, Entry 4). Under the same reaction conditions, 60% of an equimolar mixture of diastereoisomers was obtained when the reaction was carried out at 0 °C, but the reaction time had to be increased to 10 h (Table 1, Entry 5).

The catalytic version of the reaction was also tested by heating a 0.1 M solution of **2a** and a catalytic amount of dicobalt octacarbonyl in DME with 20% of cyclohexylamine under atmospheric carbon monoxide pressure (balloon of CO) at 60 °C. The reaction took place only if the solution was saturated with CO previous to the addition of the catalyst, and the yield was highly dependent on the catalyst loading. In the presence of 5 mol-% of $Co_2(CO)_8$, a mixture of diastereoisomers was obtained in only 20% yield, but the yield increased to 85% when using 10 mol-% of the catalyst, although no diastereoselection was observed in any case (Table 1, Entries 6 & 7).

The influence of the substitution pattern at both the olefinic and acetylenic components in the diastereoselection was studied in compounds **2b**–**i** by using the described stoichiometric and catalytic reaction conditions, and the results are summarized in Table 2. The reaction of perhydrobenzoxazines **2b**–**d** with a substituent at the outer position of the vinyl group led to equimolar mixtures of diastereoisomers independent of the size of the substituents (Table 2, Entries 1–6). Only a very low diastereoselection was observed for monosubstituted vinyl derivatives when an additional bulky group (TMS) was attached to the acetylenic bond (i.e., **2e**; Table 2, Entries 6 & 7).

Table 2. Stoichiometric and catalytic Pauson–Khand reactions of perhydrobenzoxazines **2b**–**i**.

Entry	Compd.	$R^1/R^2/R^3$	Cond.[a]	Yield[b] [%]	*dr* (**3**/*epi*-**3**)
1	**2b**	H/Me/H	A	74	50:50
2	**2b**	H/Me/H	B	85	50:50
3	**2c**	H/Ph/H	A	68	50:50
4	**2c**	H/Ph/H	B	88	50:50
5	**2d**	H/TMS/H	A	36[c]	50:50
6	**2d**	H/TMS/H	B	55[d]	50:50
7	**2e**	H/Ph/TMS	A	77	60:40
8	**2e**	H/Ph/TMS	B	30	55:45
9	**2f**	Me/H/H	A	40	62:38
10	**2f**	Me/H/H	B	75	55:45
11	**2g**	Me/Ph/H	A	56	75:25
12	**2g**	Me/Ph/H	B	73	67:33
13	**2h**	$–(CH_2)_4–$/H	A	75	90:10
14	**2h**	$–(CH_2)_4–$/H	B	70	80:20
15	**2i**	$–(CH_2)_4–$/Me	A	68	90:10
16	**2i**	$–(CH_2)_4–$/Me	B	40	80:20

[a] Conditions A: Stoichiometric reaction. Conditions B: catalytic reaction. [b] Isolated yield. [c] 30% of desilylation products **3a** and *epi*-**3a** were isolated. [d] 17% of desilylation products **3a** and *epi*-**3a** were isolated.

Interestingly, the substitution at the *endo* position of the double bond made the reaction more diastereoselective, especially for the stoichiometric reaction (Table 2, Entry 9 vs. 10). Much better diastereoselection was obtained for the reaction of **2g** with two substituents at the double bond (Table 2, Entries 11 & 12), and the best stereochemical results were obtained in the cyclization of cyclohexene carboxaldehyde derivatives **2h** (Table 2, Entries 13 & 14) and **2i** (Table 2, Entries 15 & 16).

All the diastereoisomers obtained were separated by flash chromatography except compounds **3c** and **3d**, which could not be totally purified, and their stereochemistry was established on the basis of the chemical shifts of the proton at the N,O-acetal carbon atom and the coupling constants of that proton with the angular one.[9] NOESY experiments allowed the assignation of the stereochemistry for diastereoisomers **3g** and *epi*-**3g**[10] (Figure 1). As expected, the substituents at the double bond retained the stereochemistry in the cyclic system, and both diastereoisomers differed in the relative stereochemistry of that substituent with respect to the hydrogen at the N,O-acetal carbon atom, being *cis* for **3a**–**i** and *trans* for *epi*-**3a**–**i**.

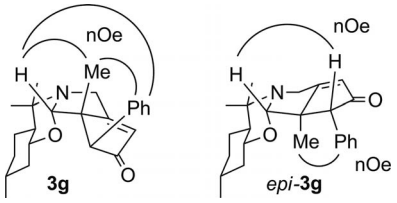
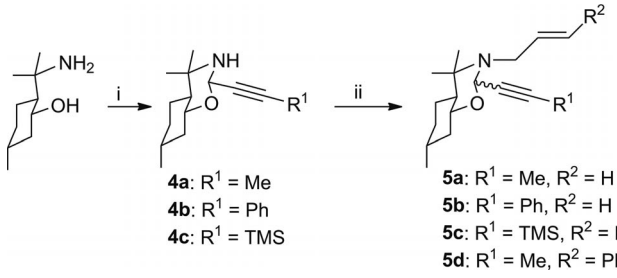


Figure 1. NOE contacts for compounds **3g** and *epi*-**3g**.

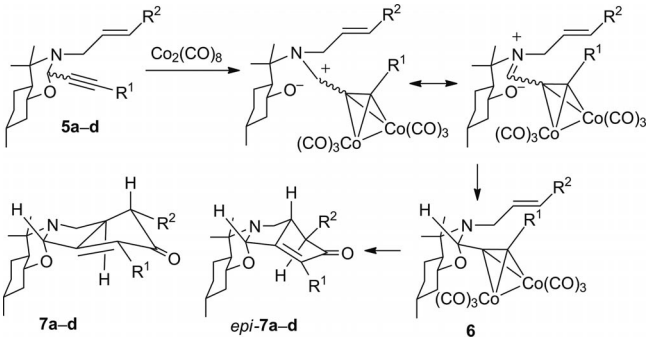
We have previously demonstrated that the diastereoselectivity for radical cyclizations in related systems is highly dependent on the regioisomers of the starting perhydrobenzoxazine derivative.[11] The low selectivity observed for the intramolecular PKR of compounds **2** led us to study the reaction on regioisomeric perhydrobenzoxazines **5** with the acetylenic bond at C-2 and the olefinic component on the nitrogen atom.

The synthesis of compounds **5** was achieved, in two steps, by condensation of (–)-8-aminomenthol with acetylenic aldehydes followed by alkylation of **4** with the corresponding allyl bromides (Scheme 3). The condensation of the aldehydes with aminomenthol is totally diastereoselective, leading to compounds **4a**–**c** as single diastereoisomers with *S* configuration at C-2, but surprisingly the alkylation process led to a mixture (19:1) of epimers of **5a**–**d** after 10 d at room temperature or an equimolar mixture after 72 h in boiling acetonitrile. In addition, the mixtures of epimers could not be separated by flash chromatography because of the stereochemical lability at C-2 of these compounds.



Scheme 3. Reagents and conditions: (i) aldehydes, DCM, r.t.; (ii) allyl bromide, acetonitrile, r.t., 10 d (19:1 *dr*) or allyl bromides, acetonitrile, reflux, 72 h. (1:1 *dr*).

Compounds **5a**–**d** (as a mixture of diastereoisomers) were subjected to intramolecular PKRs under both stoichiometric and catalytic conditions, and the results are summarized in Scheme 4 and Table 3. Three important facts can be generalized from these data. First, the chemical yields for the stoichiometric reactions (conditions A) are much better than those for the catalytic ones (conditions B) but the diastereoselectivities are not affected by the reaction conditions. Second, the diastereoselection for the intramolecular PKR of perhydrobenzoxazines **5a**–**d**, with the acetylenic bond at C-2 and the olefinic bond on the nitrogen atom, is better than that for their regioisomers **2a**–**i**, and reactions of compounds **5a**–**c**, with unsubstituted double bonds, are more diastereoselective than the same reaction performed with a substrate with a substituted double bond (i.e., **5d**; Table 3, Entries 1–8 vs. 9–11). Third, the same mixtures of diastereoisomeric PKR products (**7**/*epi*-**7**) were obtained independent of the stereochemical composition of the starting perhydrobenzoxazines **5a**–**d** (Table 3, Entry 1 vs. Entries 2 & 3, Entry 4 vs. Entries 5 & 6, and Entry 9 vs. Entries 10 & 11). Moreover, cyclization diastereoisomers **7** and *epi*-**7** have the *S* configuration at the N,O-acetal carbon atom. This can be explained by accepting that the transformation of **5a**–**d** into **7a**–**d** and *epi*-**7a**–**d** occurs by a tandem intramolecular Nicholas reaction and PKR.[12] In fact, the coordination of $Co_2(CO)_8$ to compounds **5a**–**d** leads to cobalt complexes derived from a propargylic alcohol, which evolve into cobalt carbonyl stabilized propargylic cations. Those complexes can be intramolecularly captured to form stable intermediate **6** with the *S* configuration at C-2 in a Nicholas-like transformation.[13] Subsequent PKRs on complexes **6** give cyclization adducts **7a**–**d** and *epi*-**7a**–**d** (Scheme 4). Compounds **7** and *epi*-**7** were purified by flash chromatography, and the stereochemistry of **7c** was assigned by X-ray diffraction analysis[10] and extended by analogy to all the diastereoisomers.



Scheme 4. Isomerization and Pauson–Khand reaction of perhydrobenzoxazines **5a**–**d**.

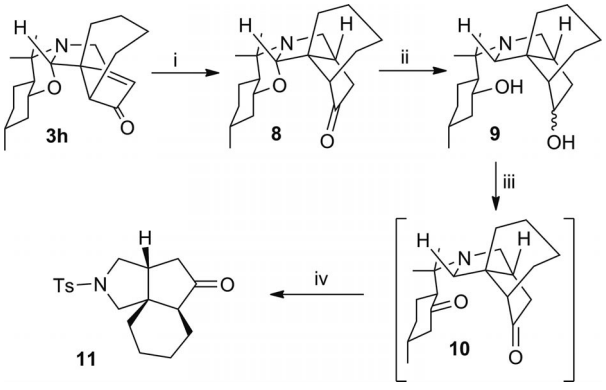
Table 3. Stoichiometric and catalytic Pauson–Khand reactions of perhydrobenzoxazines **5a**–**d**.

Entry	Compd.	Epimers at C-2 (*S*/*R*)	R^1/R^2	Cond.[a]	Yield[b] [%]	*dr* (**7**/*epi*-**7**)[c]
1	**5a**	97:3	Me/H	A	73	75:25
2	**5a**	50:50	Me/H	A	70	75:25
3	**5a**	50:50	Me/H	B	30	75:25
4	**5b**	95:5	Ph/H	A	80	80:20
5	**5b**	50:50	Ph/H	A	85	80:20
6	**5b**	50:50	Ph/H	B	40	80:20
7	**5c**	50:50	TMS/H	A	61	80:20
8	**5c**	50:50	TMS/H	B	20	80:20
9	**5d**	92:8	Me/Ph	A	61	60:40
10	**5d**	50:50	Me/Ph	A	67	60:40
11	**5d**	50:50	Me/Ph	B	40	60:40

[a] Conditions A: Stoichiometric reaction. Conditions B: Catalytic reaction. [b] Isolated yield. [c] Determined by ^{1}H NMR spectroscopic analysis of the reaction mixture.

The elimination of the aminomenthol appendage in the adducts is very well established[5] and allows the synthesis of enantiopure polycyclic keto pirrolidines; we tested this transformation with compound **3h**. The cyclization product was first hydrogenated to saturated compound **8**, and its

absolute stereochemistry was determined by X-ray diffraction analysis,[10] which confirmed that previously assigned for **3h**. Reductive ring opening of **8** with aluminum hydride gave diol **9** as a mixture of diastereoisomers that was converted into diketone **10** by oxidation with PCC. This ketone, without isolation, was subjected to a retro-Michael reaction by treatment with a solution of KOH in ethanol. The tricyclic keto pyrrolidine was isolated as tosylate **11** by reaction with tosyl chloride (Scheme 5).



Scheme 5. Reagents and conditions: (i) H_2, 1 atm, 10% Pd/C, EtOH, r.t.. (ii) AlH_3, THF, 0 °C. (iii) PCC, 4 Å MS, DCM, r.t. (iv) 1. KOH, MeOH/THF; 2. TsCl, DIPEA EtOAc, r.t.

Conclusions

Chiral perhydrobenzoxazines derived from (–)-8-aminomenthol with acetylenic and olefinic substituents at the 2- and 3-positions have been shown to be good chiral templates for diastereoselective intramolecular PKRs. The diastereoselectivity of the reaction is dependent on both the substitution pattern of the double bond and the nature of the starting regioisomer.

For 2-vinyl-3-propargyl-substituted substrates, the diastereoselection was very low except when the olefinic component had two substituents at the *endo* and *exo* positions. Much better stereochemical discrimination was observed for regioisomers bearing the acetylenic bond at C-2 and the allyl substituent at the nitrogen atom. In that case, the diastereoselection improved with the size of the substituent at the triple bond.

Interestingly, the same stereochemical results were obtained starting from perhydrobenzoxazines **5a**–**d** as an equimolar mixture of epimers at C-2 than from stereochemically pure ones, indicating that a Nicholas-like reaction occurred on these compounds prior to the intramolecular PKR.

Experimental Section

General Methods: ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded with a Bruker AC–300 spectrometer in $CDCl_3$. Chemical shifts for protons are reported in ppm from tetramethylsilane with the residual $CHCl_3$ resonance as internal reference. Chemical shifts for carbon atoms are reported in ppm from tetramethylsilane and are referenced to the carbon resonance of the solvent. Specific rotations were measured with a Perkin–Elmer digital polarimeter by using a 5-mL cell with a 1-dm path length and a sodium lamp. Infrared spectra were recorded with a Perkin–Elmer FTIR spectrometer. Melting points were obtained with open capillary tubes. Flash chromatography was carried out by using silica gel (230–240 mesh). Chemical yields refer to pure isolated substances. TLC analysis was performed on glass-backed plates coated with silica gel 60 and an F_{254} indicator and were visualized by either UV irradiation or by staining with a phosphomolybdic acid solution. Organic compounds were purchased from Aldrich and used as received. Solvents were dried and stored over microwave-activated 4 Å molecular sieves.

General Procedure for the Stoichiometric Pauson–Khand Reactions (Method A): A 25-mL flask was charged with perhydrobenzoxazine (1.3 mmol) in dry DCM (10 mL), 3 Å molecular sieves (8-fold in weight), and $Co_2(CO)_8$ (1.4 mmol) under an argon atmosphere, and the mixture was stirred for 2 h at room temperature. Then, TMANO (10.4 mmol) was added and stirring was continued at room temperature until the reaction was complete (TLC). The reaction mixture was filtered, the solids were washed with DCM (2 or 3×), and the solvent was evaporated under vacuum. The residues were purified by flash chromatography (EtOAc/hexanes).

General Procedure for the Catalytic Pauson–Khand Reactions (Method B): A two-necked flask equipped with septum inlets and a magnetic stirring bar was charged with the corresponding perhydrobenzoxazine (0.8 mmol) in dimethoxyethane (8 mL), and the solution was flushed with carbon monoxide for 2 min. Then, $Co_2(CO)_8$ (0.08 mmol) was added, the solution was flushed with carbon monoxide again, and cyclohexylamine (0.16 mmol) was added. The mixture was heated to 60 °C under a CO atmosphere (CO balloon) until the reaction was complete (TLC). After cooling to room temperature, the mixture was filtered, the solids were washed with dimethoxyethane, and the solvent was evaporated under reduced pressure. The residue was purified by flash chromatography on silica gel (EtOAc/hexanes).

Adduct 3a: Yellowish oil. $[a]_D^{25}$ = –213.30 (c = 1.12, $CHCl_3$). ^{1}H NMR: δ = 0.90 (d, J = 6.6 Hz, 3 H), 0.93–1.12 (m, 2 H), 1.18 (s, 3 H), 1.24 (s, 3 H), 1.29–1.45 (m, 2 H), 1.57–1.79 (m, 4 H), 2.38 (dd, J = 6.3, 17.3 Hz, 1 H), 2.50 (dd, J = 4.1, 17.2 Hz, 1 H), 3.25 (m, 1 H), 3.43 (dt, J = 4.2, 10.5 Hz, 1 H), 3.82 (d, J = 17.1 Hz, 1 H), 3.91 (d, J = 17.1 Hz, 1 H), 4.88 (d, J = 4.0 Hz, 1 H), 5.93 (s, 1 H) ppm. ^{13}C NMR: δ = 22.1 (CH_3), 22.2 (CH_3), 24.6 (CH_2), 26.4 (CH_3), 31.2 (CH), 34.9 (CH_2), 36.8 (CH_2), 41.0 (CH_2), 42.7 (CH), 45.6 (CH_2), 50.9 (CH), 53.5 (C), 74.0 (CH), 83.4 (CH), 124.5 (CH=), 184.7 (C=), 210.5 (C=O) ppm. IR (thin layer): $\tilde{\nu}$ = 3078, 2924, 1710, 1643 cm^{-1}.

Adduct *epi*-3a: White solid, m.p. 87.7–88.9 °C (hexane). $[a]_D^{25}$ = +57.90 (c = 0.92, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.91 (s, 3 H), 0.94 (d, J = 6.5 Hz, 3 H), 0.98–1.13 (m, 2 H), 1.18 (s, 3 H), 1.26–1.73 (m, 5 H), 1.98 (m, 1 H), 2.27 (dd, J = 3.5, 17.9 Hz, 1 H), 2.66 (dd, J = 6.3, 17.9 Hz, 1 H), 3.21 (m, 1 H), 3.39 (dt, J = 4.1, 10.6 Hz, 1 H), 3.60 (d, J = 16.9 Hz, 1 H), 4.05–4.11 (m, 2 H), 5.97–5.99 (m, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 11.1 (CH_3), 22.0 (CH_3), 24.6 (CH_2), 26.5 (CH_3), 31.3 (CH), 34.5 (CH_2), 39.3 (CH_2), 41.1 (CH_2), 44.5 (CH_2), 50.2 (CH), 50.7 (CH), 54.7 (C), 76.2 (CH), 90.2 (CH), 126.0 (CH=), 180.7 (C=), 209.0 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3078, 2931, 1706, 1606 cm^{-1}.

Adduct 3b: White solid, m.p. 113.6–115.0 °C (hexane). $[a]_D^{25}$ = –167.25 (c = 0.8, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.89 (d, J = 6.5 Hz, 3 H), 0.94–1.06 (m, 2 H), 1.18 (s, 3 H), 1.20 (d, J = 7.3 Hz, 3 H), 1.25 (s, 3 H), 1.27–1.45 (m, 2 H), 1.58–1.80 (m, 5 H), 2.54 (dq, J = 4.0,J_2 = 7.2 Hz, 1 H), 2.87 (m, 1 H), 3.44 (dt, J = 4.1, 10.5 Hz, 1 H), 3.78–3.92 (m, 2 H), 4.93 (d, J = 4.0 Hz, 1 H), 5.9

(d, J = 1.8 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 13.1 (CH_3), 22.2 (CH_3), 22.3 (CH_3), 24.7 (CH_2), 26.5 (CH_3), 31.2 (CH), 35.0 (CH_2), 41.0 (CH_2), 42.6 (CH), 42.7 (CH), 45.6 (CH_2), 53.6 (C), 59.2 (CH), 74.1 (CH), 83.0 (CH), 123.5 (CH=), 182.1 (C=), 212.4 (C=O) ppm. IR (Nujol): $\tilde{\nu}$ = 3072, 2920, 1706, 1643 cm^{-1}. $C_{18}H_{27}NO_2$ (289.41): calcd. C 74.70, H 9.40, N 4.84; found C 74.59, H 8.17, N 4.20.

Adduct *epi*-3b: Colorless oil. $[\alpha]_D^{25}$ = +130.77 (c = 0.52, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.92 (s, 3 H), 0.94 (d, J = 6.5 Hz, 3 H), 0.97–1.14 (m, 2 H), 1.17 (s, 3 H), 1.25 (d, J = 7.3 Hz, 3 H), 1.28–1.58 (m, 3 H), 1.70–1.73 (m, 2 H), 1.98 (m, 1 H), 2.31 (dq, J = 3.6, 7.2 Hz, 1 H), 2.85 (m, 1 H), 3.38 (dt, J = 4.1, 10.6 Hz, 1 H), 3.58 (d, J = 17.0 Hz, 1 H), 4.05 (dt, J = 1.9, 17.0 Hz, 1 H), 4.12 (d, J = 7.6 Hz, 1 H), 5.96 (dd, J = 1.9, 3.7 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 11.3 (CH_3), 13.6 (CH_3), 22.1 (CH_3), 24.6 (CH_2), 26.6 (CH_3), 31.4 (CH), 34.6 (CH_2), 41.2 (CH_2), 44.4 (CH_2), 46.5 (CH), 50.0 (CH), 54.7 (C), 58.7 (CH), 58.3 (CH), 76.1 (CH), 90.2 (CH), 124.9 (CH=), 178.5 (C=), 211.2 (C=O) ppm. IR (thin layer): $\tilde{\nu}$ = 3076, 2926, 1709, 1642 cm^{-1}.

Adduct *epi*-3c: White solid. m.p. 175.6–177.1 °C (hexane). $[\alpha]_D^{25}$ = +114.05 (c = 1.11, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.91 (d, J = 6.5 Hz, 3 H), 0.96 (s, 3 H), 0.98–1.12 (m, 2 H), 1.19 (s, 3 H), 1.21–1.43 (m, 3 H), 1.69–1.71 (m, 2 H), 1.92 (m, 1 H), 3.34–3.50 (m, 3 H), 3.66 (d, J = 16.8 Hz, 1 H), 4.12 (dt, J = 1.8, 16.9 Hz, 1 H), 4.28 (d, J = 7.1 Hz, 1 H), 6.06 (m, 1 H), 7.22–7.33 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 11.6 (CH_3), 22.0 (CH_3), 24.6 (CH_2), 26.6 (CH_3), 31.3 (CH), 34.6 (CH_2), 41.1 (CH_2), 44.5 (CH_2), 49.8 (CH), 54.8 (C), 56.9 (CH), 58.3 (CH), 76.1 (CH), 90.2 (CH), 124.7 (CH=), 126.9 (CH=), 128.3 (2 CH=), 128.5 (2 CH=), 137.3 (C=), 178.7 (C=), 208.0 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3028, 2934, 1705, 1646 cm^{-1}. $C_{23}H_{29}NO_2$ (351.58): calcd. C 78.59, H 8.32, N 3.99; found C 79.17, H 8.35, N 4.19.

Adduct *epi*-3d: Yellowish oil. $[\alpha]_D^{25}$ = +121.33 (c = 0.30, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.11 (s, 9 H), 0.87 (s, 3 H), 0.80–1.11 (m, 3 H), 0.92 (d, J = 6.5 Hz, 3 H), 1.16 (s, 3 H), 1.19–1.43 (m, 2 H), 1.67–1.70 (m, 2 H), 1.92 (m, 1 H), 2.01 (d, J = 2.1 Hz, 1 H), 3.06 (m, 1 H), 3.31 (dt, J = 4.0, 10.6 Hz, 1 H), 3.54 (dd, J = 0.9, 16.4 Hz, 1 H), 3.96 (d, J = 7.9 Hz, 1 H), 4.05 (dt, J = 1.8, 16.4 Hz, 1 H), 5.90 (s,1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = –2.6 (3CH_3), 11.0 (CH_3), 22.1 (CH_3), 24.6 (CH_2), 26.6 (CH_3), 31.3 (CH), 34.6 (CH_2), 41.1 (CH_2), 42.9 (CH), 44.4 (CH_2), 50.5 (CH), 53.8 (CH), 54.9 (C), 76.2 (CH), 90.6 (CH), 127.0 (CH=), 179.1 (C=), 210.8 (C=O) ppm. IR (thin layer): $\tilde{\nu}$ = 2925, 1690, 1647 cm^{-1}. $C_{20}H_{32}NO_2Si$ (347.57): calcd. C 69.11, H 9.57, N 4.03; found C 67.55, H 9.62, N 3.99.

Adduct 3e: Colorless oil. $[\alpha]_D^{25}$ = –306.06 (c = 1.04, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.24 (s, 9 H), 0.85–1.17 (m, 3 H), 0.93 (d, J = 6.5 Hz, 3 H), 1.22 (s, 3 H), 1.24 (s, 3 H), 1.27–1.43 (m, 2 H), 1.62 (m, 1 H), 1.73 (m, 1 H), 1.85 (m, 1 H), 3.41–3.48 (m, 2 H), 3.72 (d, J = 5.1 Hz, 1 H), 3.87 (dd, J = 2.6, 17.4 Hz, 1 H), 3.97 (dd, J = 2.0, 17.4 Hz, 1 H), 4.94 (d, J = 4.1 Hz, 1 H), 7.18–7.27 (m, 3 H), 7.32–7.37 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = –1.4 (3 CH_3), 22.2 (CH_3), 22.3 (CH_3), 24.7 (CH_2), 26.5 (CH_3), 31.2 (CH), 35.0 (CH_2), 41.1 (CH_2), 46.7 (CH_2), 53.6 (C), 54.6 (CH), 60.0 (CH), 74.3 (CH), 82.9 (CH), 126.6 (CH=), 128.4 (2 CH=), 128.5 (2 CH=), 133.8 (C=), 138.3 (C=), 189.3 (C=), 212.1 (C=O) ppm. IR (thin layer): $\tilde{\nu}$ = 3023, 2926, 1698, 1623 cm^{-1}. $C_{26}H_{37}NO_2Si$ (423.66): calcd. C 73.71, H 8.80, N 3.31; found C 77.3, H 8.24, N 3.17.

Adduct *epi*-3e: Colorless oil. $[\alpha]_D^{25}$ = +181.52 (c = 0.66, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.23 (s, 9 H), 0.84–1.17 (m, 3 H), 0.92 (d, J = 6.5 Hz, 3 H), 0.96 (s, 3 H), 1.21 (s, 3 H), 1.26–1.44 (m, 2 H), 1.70–1.73 (m, 2 H), 1.94 (m, 1 H), 3.38 (dt, J = 4.2, 10.5 Hz, 1 H), 3.45–3.54 (m, 2 H), 3.62 (dd, J = 2.2, 17.2 Hz, 1 H), 4.13 (dd, J = 1.5, 17.2 Hz, 1 H), 4.23 (d, J = 7.2 Hz, 1 H), 7.20–7.41 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = –1.4 (3 CH_3), 11.2 (CH_3), 22.1 (CH_3), 24.6 (CH_2), 26.7 (CH_3), 31.3 (CH), 34.6 (CH_2), 41.2 (CH_2), 45.6 (CH_2), 50.0 (CH), 54.7 (C), 57.5 (CH), 58.9 (CH), 76.0 (CH), 90.1 (CH), 126.6 (CH=), 128.3 (2 CH=), 128.4 (2 CH=), 135.8 (C=), 137.4 (C=), 185.3 (C=), 210.8 (C=O) ppm. IR (thin layer): $\tilde{\nu}$ = 3017, 2930, 1700, 1620 cm^{-1}.

Adduct 3f: Colorless oil. $[\alpha]_D^{25}$ = –185.96 (c = 1.14, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.81–1.11 (m, 4 H), 0.89 (d, J = 6.5 Hz, 3 H), 1.16 (s, 3 H), 1.21 (s, 3 H), 1.28 (s, 3 H), 1.57–1.79 (m, 3 H), 2.07 (d, J = 16.6 Hz, 1 H), 2.79 (d, J = 16.6 Hz, 1 H), 3.41 (dt, J = 4.1, 10.4 Hz, 1 H), 3.80 (d, J = 17.5 Hz, 1 H), 3.89 (d, J = 17.5 Hz, 1 H), 4.57 (s, 1 H), 5.80 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 22.2 (CH_3), 22.3 (CH_3), 24.7 (CH_2), 24.9 (CH_3), 26.4 (CH_3), 31.2 (CH), 35.0 (CH_2), 41.1 (CH_2), 42.9 (CH), 44.7 (CH_2), 45.2 (CH_2), 53.2 (C), 55.0 (C), 74.1 (CH), 88.1 (CH), 123.0 (CH=), 189.0 (C=), 210.7 (C=O) ppm. IR (thin layer): $\tilde{\nu}$ = 3072, 2926, 1708, 1640 cm^{-1}.

Adduct *epi*-3f: Colorless oil. $[\alpha]_D^{25}$ = +72.50 (c = 0.40, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.88–1.32 (m, 4 H), 0.88 (s, 3 H), 0.94 (d, J = 6.5 Hz, 3 H), 1.14 (s, 3 H), 1.27 (s, 3 H), 1.44 (m, 1 H), 1.69 (d, J = 7.1 Hz, 2 H), 1.97 (m, 1 H), 2.34 (d, J = 2.6 Hz, 1 H), 3.37 (dt, J = 4.1, 10.5 Hz, 1 H), 3.57 (d, J = 17.1 Hz, 1 H), 4.01 (dd, J = 1.7, 17.5 Hz, 1 H), 4.09 (s, 1 H), 5.85 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 10.7 (CH_3), 20.5 (CH_3), 22.1 (CH_3), 24.5 (CH_2), 26.7 (CH_3), 31.3 (CH), 34.5 (CH_2), 41.1 (CH_2), 43.3 (CH_2), 48.3 (CH_2), 50.4 (CH), 52.5 (C), 54.3 (C), 75.8 (CH), 91.3 (CH), 124.5 (CH=), 186.0 (C=), 209.3 (C=O) ppm. IR (thin layer): $\tilde{\nu}$ = 3078, 2933, 1708, 1642 cm^{-1}.

Adduct 3g: White solid, m.p. 192.9–194.7 °C (hexane). $[\alpha]_D^{25}$ = –108.15 (c = 0.92, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.89 (s, 3 H), 0.93 (d, J = 6.5 Hz, 3 H), 0.82–1.13 (m, 3 H), 1.17 (s, 3 H), 1.19 (s, 3 H), 1.34 (m, 1 H), 1.47 (m, 1 H), 1.61 (m, 1 H), 1.71 (m, 1 H), 1.89 (m, 1 H), 3.51 (dt, J = 4.1, 10.4 Hz, 1 H), 3.91 (s, 2 H), 4.32 (s, 1 H), 4.54 (s, 1 H), 5.96 (s, 1 H), 7.18–7.35 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 22.2 (CH_3), 22.3 (CH_3), 23.0 (CH_3), 24.8 (CH_2), 26.4 (CH_3), 31.3 (CH), 35.0 (CH_2), 41.2 (CH_2), 43.1 (CH), 45.2 (CH_2), 53.3 (C), 58.5 (CH), 60.0 (C), 74.4 (CH), 87.7 (CH), 122.7 (CH=), 126.6 (CH=), 128.2 (2 CH=), 129.9 (2 CH=), 136.6 (C=), 186.3 (C=), 209.0 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3051, 2908, 1702, 1639 cm^{-1}. $C_{24}H_{31}NO_2$ (365.51): calcd. C 78.87, H 8.55, N 3.83; found C 77.56, H 8.28, N 3.94.

Adduct *epi*-3g: White solid, m.p. 185.8–187.1 °C (hexane). $[\alpha]_D^{25}$ = –46.82 (c = 0.44, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.88–1.09 (m, 3 H), 0.88 (s, 3 H), 0.94 (s, 3 H), 0.95 (d, J = 6.5 Hz, 3 H), 1.15 (s, 3 H), 1.23 (m, 1 H), 1.48 (m, 1 H), 1.70 (d, J = 8.3 Hz, 2 H), 1.96 (m, 1 H), 3.44 (dt, J = 4.2, 10.5 Hz, 1 H), 3.63 (d, J = 18.8 Hz, 1 H), 3.66 (s, 1 H), 4.03 (d, J = 18.8 Hz, 1 H), 4.31 (s, 1 H), 6.03 (s, 1 H), 7.24–7.35 (m, 5 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 10.8 (CH_3), 18.7 (CH_3), 22.1 (CH_3), 24.6 (CH_2), 26.7 (CH_3), 31.3 (CH), 34.6 (CH_2), 41.3 (CH_2), 43.3 (CH_2), 50.3 (CH), 54.4 (C), 56.9 (C), 63.6 (CH), 75.8 (CH), 92.8 (CH), 124.3 (CH=), 126.7 (CH=), 128.0 (2 CH=), 130.0 (2 CH=), 135.8 (CH=), 184.1 (C=), 208.2 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3030, 2920, 1699, 1641 cm^{-1}.

Adduct 3h: Colorless oil. $[\alpha]_D^{25}$ = –162.31 (c = 0.32, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.89 (d, J = 6.6 Hz, 3 H), 0.91–1.15 (m, 4 H), 1.17 (s, 3 H), 1.23 (s, 3 H), 1.25–1.48 (m, 4 H), 1.52–1.63 (m, 4 H), 1.70 (m, 1 H), 1.78 (m, 1 H), 2.13–2.27 (m, 2 H), 2.74 (d, J = 6.7 Hz, 1 H), 3.44 (dt, J = 4.1, 10.5 Hz, 1 H), 3.84 (s, 2 H), 4.63 (s, 1 H), 5.82 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 21.6 (CH_2), 22.2 (CH_3), 22.4 (CH_3), 22.5 (CH_2), 22.7 (CH_2), 24.8 (CH_2), 26.5 (CH_3), 31.2 (CH), 35.0 (CH_2), 35.5 (CH_2), 41.1 (CH_2), 42.9 (CH), 45.2 (CH_2), 48.9 (CH), 53.2 (C), 58.3 (C), 74.3 (CH), 86.3 (CH), 121.1 (CH=), 188.3 (C=), 211.2 (C=O) ppm. IR (thin layer): $\tilde{\nu}$ = 3051,

2928, 1708, 1642 cm^{-1}. $C_{21}H_{31}NO_2$ (329.24): calcd. C 76.55, H 9.48, N 4.25; found C 74.98, H 10.53, N 4.29.

Adduct 3i: Colorless oil. $[\alpha]_D^{25}$ = –151.76 (*c* = 1.48, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.81–1.16 (m, 5 H), 0.88 (d, *J* = 6.6 Hz, 3 H), 1.18 (s, 3 H), 1.23 (s, 3 H), 1.25–1.62 (m, 6 H), 1.69 (s, 3 H), 1.72–2.04 (m, 3 H), 2.11 (d, *J* = 18.3 Hz, 1 H), 2.25 (d, *J* = 15.6 Hz, 1 H), 2.66 (d, *J* = 6.7 Hz, 1 H), 3.43 (dt, *J* = 4.1, 10.4 Hz, 1 H), 3.76 (s, 2 H), 4.61 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 8.9 (CH_3), 21.8 (CH_2), 22.2 (CH_3), 22.4 (CH_2, CH_3), 22.7 (CH_2), 24.8 (CH_2), 26.5 (CH_3), 31.2 (CH), 35.0 (CH_2), 35.4 (CH_2), 41.2 (CH_2), 42.9 (CH), 44.3 (CH_2), 48.2 (CH), 53.2 (C), 56.3 (C), 74.2 (CH), 86.6 (CH), 128.4 (C=), 180.2 (C=), 211.2 (C=O) ppm. IR (thin layer): $\tilde{\nu}$ = 2922, 1708, 1680 cm^{-1}.

Adduct 7a: Yellowish oil. $[\alpha]_D^{25}$ = –171.50 (*c* = 0.92, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.93 (d, *J* = 6.7 Hz, 3 H), 0.98–1.13 (m, 2 H), 1.16 (s, 3 H), 1.22 (s, 3 H), 1.49–1.57 (m, 2 H), 1.65 (m, 1 H), 1.72–1.76 (m, 2 H), 1.79 (d, *J* = 2.4 Hz, 3 H), 1.91 (m, 1 H), 2.20 (dd, *J* = 3.4, 17.5 Hz, 1 H), 2.69–2.77 (m, 2 H), 3.42–3.52 (m, 2 H), 3.62 (dt, *J* = 4.2, 10.4 Hz, 1 H), 5.45 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 9.0 (CH_3), 20.8 (CH_3), 22.2 (CH_3), 24.7 (CH_2), 25.8 (CH_3), 31.2 (CH), 34.9 (CH_2), 38.7 (CH), 41.3 (CH_2), 42.9 (CH_2), 44.3 (CH), 48.8 (CH_2), 53.7 (C), 74.6 (CH), 81.0 (CH), 131.7 (C=), 173.3 (C=), 210.6 (C=O) ppm. IR (thin layer): $\tilde{\nu}$ = 2923, 1714, 1691 cm^{-1}. $C_{18}H_{27}NO_2$ (289.41): calcd. C 74.70, H 9.40, N 4.84; found C 73.62, H 8.08, N 4.10.

Adduct *epi*-7a: White solid, m.p. 131.7–133.7 °C (hexane). $[\alpha]_D^{25}$ = +68.20 (*c* = 0.78, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.85–1.13 (m, 3 H), 0.90 (d, *J* = 6.5 Hz, 3 H), 1.17 (s, 3 H), 1.20 (s, 3 H), 1.30 (m, 1 H), 1.42 (m, 1 H), 1.60–1.71 (m, 2 H), 1.79 (d, *J* = 2.5 Hz, 1 H), 1.84 (m, 1 H), 2.21 (dd, *J* = 3.6, 7.4 Hz, 1 H), 2.58 (dd, *J* = 6.2, 17.4 Hz, 1 H), 2.73 (dd, *J* = 7.4, 9.2 Hz, 1 H), 2.96 (m, 1 H), 3.24 (t, *J* = 7.2 Hz, 1 H), 3.56 (dt, *J* = 4.3, 10.4 Hz, 1 H), 5.62 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 8.7 (CH_3), 20.2 (CH_3), 22.2 (CH_3), 24.9 (CH_2), 26.6 (CH_3), 31.2 (CH), 34.9 (CH_2), 40.3 (CH_2), 41.4 (CH_2), 42.3 (CH), 45.6 (CH), 48.7 (CH_2), 53.6 (C), 74.6 (CH), 82.2 (CH), 134.5 (C=), 177.6 (C=), 210.6 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 2924, 1709, 1678 cm^{-1}.

Adduct 7b: Yellowish solid, m.p. 148.4–150.2 °C (hexane). $[\alpha]_D^{25}$ = –122.21 (*c* = 1.04, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.83–1.08 (m, 3 H), 0.96 (d, *J* = 6.5 Hz, 3 H), 1.13 (s, 3 H), 1.17 (s, 3 H), 1.53–1.77 (m, 4 H), 2.02 (m, 1 H), 2.42 (dd, *J* = 10.3, 14.0 Hz, 1 H), 2.92 (dd, *J* = 6.3, 17.3 Hz, 1 H), 3.49–3.58 (m, 2 H), 3.66 (dt, *J* = 4.0, 10.0 Hz, 1 H), 5.43 (s, 1 H), 7.31–7.59 (m, 3 H), 7.60–7.63 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.4 (CH_3), 22.2 (CH_3), 24.8 (CH_2), 26.0 (CH_3), 31.4 (CH), 35.0 (CH_2), 39.2 (CH), 41.5 (CH_2), 44.5 (CH_2), 44.7 (CH), 48.3 (CH_2), 53.8 (C), 75.0 (CH), 82.6 (CH), 128.4 (3 CH=), 128.8 (2 CH=), 130.8 (C=), 175.0 (C=), 208.3 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3022, 2922, 1707, 1668 cm^{-1}. $C_{23}H_{29}NO_2$ (351.48): calcd. C 78.59, H 8.32, N 3.99; found C 77.09, H 8.13, N 4.06.

Adduct 7c: Yellowish solid. m.p. 99.5–101.5 °C (hexane). $[\alpha]_D^{25}$ = –173.30 (*c* = 0.94, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.21 (s, 9 H), 0.86–1.12 (m, 3 H), 0.92 (d, *J* = 6.5 Hz, 3 H), 1.15 (s, 3 H), 1.18 (s, 3 H), 1.45–1.55 (m, 2 H), 1.62 (m, 1 H), 1.70 (m, 1 H), 1.91 (m, 1 H), 2.17 (dd, *J* = 3.6, 17.2 Hz, 1 H), 2.62–2.75 (m, 2 H), 3.39–3.49 (m, 2 H), 3.57 (dt, *J* = 4.1, 10.6 Hz, 1 H), 5.39 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = –1.4 (3 CH_3), 20.4 (CH_3), 22.2 (CH_3), 24.7 (CH_2), 25.8 (CH_3), 31.3 (CH), 34.9 (CH_2), 41.4 (CH_2), 42.4 (CH), 44.3 (CH_2), 44.5 (CH), 48.3 (CH_2), 53.7 (C), 74.9 (CH), 82.3 (CH), 136.0 (C=), 187.9 (C=), 214.1 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 2921, 1698, 1643 cm^{-1}. $C_{20}H_{33}NO_2Si$ (347.57): calcd. C 69.11, H 9.57, N 4.03; found C 66.04, H 10.01, N 3.93.

Adduct *epi*-7c: Colorless oil. $[\alpha]_D^{25}$ = +82.14 (*c* = 0.56, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.20 (s, 9 H), 0.83–1.05 (m, 3 H), 0.91 (d, *J* = 6.5 Hz, 3 H), 1.18 (s, 3 H), 1.23 (s, 3 H), 1.30 (m, 1 H), 1.45 (m, 1 H), 1.59–1.72 (m, 2 H), 1.82 (m, 1 H), 2.21 (dd, *J* = 4.3, 17.2 Hz, 1 H), 2.54 (dd, *J* = 6.5, 17.1 Hz, 1 H), 2.70 (dd, *J* = 7.2, 9.5 Hz, 1 H), 3.02 (m, 1 H), 3.24 (t, *J* = 7.2 Hz, 1 H), 3.56 (dt, *J* = 4.3, 10.4 Hz, 1 H), 5.54 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = –1.5 (3 CH_3), 21.2 (CH_3), 22.2 (CH_3), 24.9 (CH_2), 26.7 (CH_3), 31.2 (CH), 34.9 (CH_2), 41.3 (CH_2), 41.7 (CH_2), 44.6 (CH), 46.4 (CH), 48.4 (CH_2), 53.5 (C), 74.6 (CH), 82.2 (CH), 138.9 (C=), 193.9 (C=), 213.7 (C=O) ppm. IR (thin layer): $\tilde{\nu}$ = 2929, 1702, 1628 cm^{-1}.

Adduct 7d: Yellow oil. $[\alpha]_D^{25}$ = –160.00 (*c* = 1.10, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.93 (d, *J* = 6.5 Hz, 3 H), 0.97–1.11 (m, 2 H), 1.16 (s, 3 H), 1.25 (s, 3 H), 1.48–1.56 (m, 3 H), 1.63 (m, 1 H), 1.74 (m, 1 H), 1.87 (d, *J* = 2.3 Hz, 3 H), 1.92 (m, 1 H), 2.95 (dd, *J* = 3.8, 8.0 Hz, 1 H), 3.39 (d, *J* = 3.9 Hz, 2 H), 3.48–3.55 (m, 2 H), 3.64 (dt, *J* = 4.2, 10.4 Hz, 1 H), 5.53 (s, 1 H), 7.16–7.19 (m, 2 H), 7.23–7.36 (m, 3 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 9.1 (CH_3), 20.2 (CH_3), 22.2 (CH_3), 25.0 (CH_2), 26.7 (CH_3), 31.3 (CH), 35.0 (CH_2), 41.5 (CH_2), 45.6 (CH), 48.3 (CH_2), 51.3 (CH), 53.7 (C), 58.5 (CH), 74.8 (CH), 82.3 (CH), 126.9 (CH=), 128.3 (2 CH=), 128.6 (2 CH=), 133.3 (C=), 138.4 (C=), 174.7 (C=), 209.3 (C=O) ppm. IR (thin layer): $\tilde{\nu}$ = 3027, 2922, 1719, 1690 cm^{-1}. $C_{24}H_{31}NO_2$ (365.51): calcd. C 78.87, H 8.55, N 3.83; found C 77.68, H 8.30, N 3.94.

Adduct *epi*-7d: White solid, m.p. 135.3–137.2 °C (hexane). $[\alpha]_D^{25}$ = +211.50 (*c* = 1.06, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.93 (d, *J* = 6.5 Hz, 3 H), 0.95–1.14 (m, 2 H), 1.16 (s, 3 H), 1.20 (s, 3 H), 1.27–1.49 (m, 2 H), 1.61–1.73 (m, 3 H), 1.87 (m, 1 H), 1.92 (m, 1 H), 2.94 (dd, *J* = 8.8, 7.2 Hz, 1 H), 3.14–3.22 (m, 1 H), 3.31 (dd, *J* = 7.1, 7.1 Hz, 1 H), 3.43 (d, *J* = 4.0 Hz, 1 H), 3.56–3.65 (td, *J* = 4.3, 10.5 Hz, 1 H), 5.67 (s, 1 H), 7.16–7.20 (m, 2 H), 7.25 (m, 1 H), 7.30–7.36 (m, 2 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 9.1 (CH_3), 20.2 (CH_3), 22.2 (CH_3), 24.9 (CH_2), 26.6 (CH_3), 31.3 (CH), 35.0 (CH_2), 41.4 (CH_2), 45.5 (CH), 48.3 (CH_2), 51.3 (CH), 53.7 (C), 58.5 (CH), 74.7 (CH), 82.2 (CH), 126.9 (CH=), 128.3 (2 CH=), 128.6 (2 CH=), 133.2 (C=), 138.4 (C=), 174.7 (C=), 209.3 (C=O) ppm. IR (KBr): $\tilde{\nu}$ = 3018, 2936, 1719, 1682 cm^{-1}.

Adduct 8: White solid, m.p. 64.7–66.3 °C (hexane). $[\alpha]_D^{25}$ = +11.46 (*c* = 0.89, $CHCl_3$). ^{1}H NMR ($CDCl_3$): δ = 0.90 (d, *J* = 6.5 Hz, 3 H), 0.94–1.04 (m, 2 H), 1.07 (s, 3 H), 1.08 (s, 3 H), 1.14–1.48 (m, 8 H), 1.56–1.61 (m, 3 H), 1.64–1.69 (m, 2 H), 1.84 (m, 1 H), 2.12–2.25 (m, 2 H), 2.48 (m, 1 H), 2.74–2.78 (m, 2 H), 3.13 (t, *J* = 8.4 Hz, 1 H), 3.36 (dt, *J* = 4.2, 10.4 Hz, 1 H), 4.35 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 18.0 (CH_3), 22.2 (CH_3), 22.6 (CH_2), 22.9 (CH_2), 23.1 (CH_2), 24.7 (CH_2), 26.8 (CH_3), 31.2 (CH), 34.2 (CH_2), 35.0 (CH_2), 39.3 (CH), 41.3 (CH_2), 41.7 (CH_2), 45.7 (CH), 48.5 (CH), 50.5 (CH_2), 51.4 (C), 53.3 (C), 74.7 (CH), 92.2 (CH), 219.7 (C=O) ppm. IR (Nujol): $\tilde{\nu}$ = 2928, 1741 cm^{-1}. $C_{21}H_{33}NO_2$ (331.49): calcd. C 76.09, H 10.03, N 4.23; found C 76.86, H 9.71, N 4.36.

(3a*R*,5a*S*)-2-{2-[(1*S*,2*R*,4*R*)-2-Hydroxy-4-methylcyclohexyl]propan-2-yl}decahydro-1*H*-indeno[1-*c*]pyrrol-5-ol (9): Colorless oil. $[\alpha]_D^{25}$ = –8.42 (*c* = 1.52, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 333 K): δ = 0.86 (d, *J* = 6.5 Hz, 3 H), 0.89 (s, 3 H), 0.79–1.09 (m, 4 H), 1.12 (s, 3 H), 1.18–1.64 (m, 12 H), 1.77 (m, 1 H), 1.81–1.88 (m, 3 H), 2.23–2.37 (m, 2 H), 2.60–2.74 (m, 3 H), 3.58 (dt, *J* = 4.0, 10.2 Hz, 1 H), 3.91 (dd, *J* = 9.2, 17.0 Hz, 1 H), 8.28 (s, 1 H) ppm. ^{13}C NMR ($CDCl_3$, 333 K): δ = 17.1 (CH_3), 21.5 (CH_2), 21.9 (2 CH_3), 22.6 (CH_2), 24.0 (CH_2), 25.6 (CH_2), 30.9 (CH), 35.1 (CH_2), 36.1 (CH_2), 39.7 (CH_2), 44.4 (CH_2), 45.3 (CH), 47.5 (C), 48.0 (CH), 50.7 (CH), 52.1 (CH_2), 57.3 (CH_2), 58.7 (C), 72.9 (CH), 73.7 (CH) ppm. IR (thin layer): $\tilde{\nu}$ = 3372, 2921 cm^{-1}.

(3a*R*,5a*S*,9[1]*R*)-2-Tosyloctahydro-1*H*-indeno[1-*c*]pyrrol-5(5a*H*)-one (11): Yellowish oil. $[\alpha]_D^{25}$ = +64.17 (*c* = 0.60, $CHCl_3$). ^1H NMR ($CDCl_3$): δ = 1.19–1.50 (m, 3 H), 1.58–1.80 (m, 4 H), 1.93 (m, 1 H), 2.05 (m, 1 H), 2.22 (m, 1 H), 2.49–2.55 (m, 2 H), 2.56 (s, 3 H), 3.12 (dd, *J* = 7.5, 10.4 Hz, 1 H), 3.20 (d, *J* = 10.1 Hz, 1 H), 3.71 (d, *J* = 10.1 Hz, 1 H), 3.77 (dd, *J* = 8.7, 10.4 Hz, 1 H), 7.46 (d, *J* = 8.0 Hz, 1 H), 7.84 (d, *J* = 8.3 Hz, 1 H) ppm. ^{13}C NMR ($CDCl_3$): δ = 20.9 (CH_2), 21.5 (CH_3), 22.6 (CH_2), 23.0 (CH_2), 32.7 (CH_2), 39.3 (CH_2), 41.6 (CH), 49.4 (C), 50.5 (CH), 52.6 (CH_2), 57.2 (CH_2), 127.3 (2 CH=), 129.7 (2 CH=), 133.2 (CH=), 143.8 (C=), 216.1 (C=O) ppm. IR (thin layer): $\tilde{\nu}$ = 3017, 2937, 1740 cm^{-1}.

Supporting Information (see footnote on the first page of this article): Synthesis and characterization of compounds **1a**, **1d**, **1g**, **2a**–**i**, **4a**–**c**, and **5a**–**d**; copies of the ^1H NMR and ^{13}C NMR spectra for all new compounds; ORTEP representation of the X-ray structures for compounds **7c** and **8**.

Acknowledgments

We acknowledge the financial support of the Spanish Ministerio de Ciencia e Innovacion (MICINN) (Projects CTQ2005-01191/BQU and CTQ2008-03960/BQU) and Junta de Castilla y León (Project GR 168). J. J. P.-R. also thanks the Ministerio de Educación y Ciencia (MEC) for a predoctoral fellowship (FPU program).

[1] For recent reviews, see: a) H.-W. Lee, F.-Y. Kwong, *Eur. J. Org. Chem.* **2010**, 789; b) T. Shibata, *Adv. Synth. Catal.* **2006**, *348*, 2328; c) D. Strübing, M. Beller, *Top. Organomet. Chem.* **2006**, *18*, 165; d) S. Laschat, A. Becheanu, T. Bell, A. Baro, *Synlett* **2005**, 2547; e) M. R. Rivero, J. Adrio, J. C. Carretero, *J. Synlett* **2005**, 26; f) S. E. Gibson, N. Mainolfi, *Angew. Chem.* **2005**, *117*, 3082; *Angew. Chem. Int. Ed.* **2005**, *44*, 3022; g) J. Blanco-Urgoiti, L. Añorbe, L. Pérez-Serrano, G. Domínguez, J. Pérez-Castells, *Chem. Soc. Rev.* **2004**, *33*, 32; h) S. E. Gibson (née Thomas), A. Stevenazzi, *Angew. Chem.* **2003**, *115*, 1844; *Angew. Chem. Int. Ed.* **2003**, *42*, 1800; i) K. M. Brummond, J. L. Kent, *Tetrahedron* **2000**, *53*, 3263.

[2] For Rh derivatives, see: a) J. H. Park, Y. Cho, Y. K. Chung, *Angew. Chem. Int. Ed.* **2010**, *49*, 5138; b) K. M. Brummond, M. M. Davies, C. Huang, *J. Org. Chem.* **2009**, *74*, 8314; c) D. E. Kim, I. S. Kim, V. Ratovelomanana-Vidal, J. P. Genêt, N. Jeong, *J. Org. Chem.* **2008**, *73*, 7985; for Pd derivatives, see: d) Y. Lan, L. Deng, J. Liu, C. Wang, O. Wiest, Z. Yang, Y.-D. Wu, *J. Org. Chem.* **2009**, *74*, 5049; e) L. Deng, J. Liu, J. Huang, Y. Hu, M. Chen, Y. Lan, J. Chen, A. Lei, Z. Yang, *Synthesis* **2007**, 2565; for Mo derivatives, see: f) D. Moradov, A. A. A. Al Quntar, M. Youssef, R. Smoum, A. Rubinstein, M. Srebnik, *J. Org. Chem.* **2009**, *74*, 1029; g) J. Adrio, J. C. Carretero, *J. Am. Chem. Soc.* **2007**, *129*, 778; for Ru derivatives, see: h) T. Kondo, M. Nomura, Y. Uru, K. Wada, T.-A. Mitsudo, *J. Am. Chem. Soc.* **2006**, *128*, 14816; for Ti derivatives, see: i) S. J. Sturla, S. L. Buchwald, *Organometallics* **2002**, *21*, 739; j) F. A. Hicks, S. L. Buchwald, *J. Am. Chem. Soc.* **1999**, *121*, 7026; for Ir derivatives, see: k) H. Cao, S. R. Mundla, J. M. Cook, *Tetrahedron Lett.* **2003**, *44*, 6165; l) T. Shibata, S. Kadowaki, M. Hirase, K. Takagi, *Synlett* **2003**, 573; m) T. Shibata, K. Takagi, *J. Am. Chem. Soc.* **2000**, *122*, 9852.

[3] a) M. Revés, T. Achard, J. Solá, A. Riera, X. Verdaguer, *J. Org. Chem.* **2008**, *73*, 7080; b) J. Solà, M. Revés, A. Riera, X. Verdaguer, *Angew. Chem.* **2007**, *119*, 5108; *Angew. Chem. Int. Ed.* **2007**, *46*, 5020; c) J. Solá, A. Riera, M. A. Pericàs, X. Verdaguer, M. A. Maestro, *Tetrahedron Lett.* **2004**, *45*, 5387; d) M. R. Rivero, I. Alonso, J. C. Carretero, *Chem. Eur. J.* **2004**, *10*, 5443; e) M. R. Rivero, J. C. de la Rosa, J. C. Carretero, *J. Am. Chem. Soc.* **2003**, *125*, 14992; f) L. Shen, R. P. Hsung, *Tetrahedron Lett.* **2003**, *44*, 9353; g) I. Marchueta, E. Montenegro, D. Panov, M. Poch, X. Verdaguer, A. Moyano, M. A. Pericàs, A. Riera, *J. Org. Chem.* **2001**, *66*, 6400; h) J. Balsells, J. Vázquez, A. Moyano, M. A. Pericàs, A. Riera, *J. Org. Chem.* **2000**, *65*, 7291; i) K. Hiroi, T. Watanabe, *Tetrahedron Lett.* **2000**, *41*, 3935; j) S. Fonquerna, R. Rios, A. Moyano, M. A. Pericàs, A. Riera, *Eur. J. Org. Chem.* **1999**, 3459; k) X. Verdaguer, A. Moyano, M. A. Pericàs, A. Riera, A. E. Greene, J. F. Piniella, A. Alvarez-Larena, *J. Organomet. Chem.* **1992**, *433*, 305; l) J. Castro, H. Sörensen, A. Riera, C. Morin, A. Moyano, M. A. Pericàs, A. E. Greene, *J. Am. Chem. Soc.* **1990**, *112*, 9388.

[4] For some references, see: a) H. Wang, J. R. Sawyer, P. A. Evans, M. H. Baik, *Angew. Chem.* **2008**, *120*, 348; *Angew. Chem. Int. Ed.* **2008**, *47*, 342; b) K. Kaneda, T. Honda, *Tetrahedron* **2008**, *64*, 11589; c) T. Honda, K. Kaneda, *J. Org. Chem.* **2007**, *72*, 6541; d) I. Nomura, C. Mukai, *J. Org. Chem.* **2004**, *69*, 1803; e) C. Mukai, T. Kozuka, Y. Suzuki, I. J. Kim, *Tetrahedron* **2004**, *60*, 2497; f) M. Günter, H.-J. Gais, *J. Org. Chem.* **2003**, *68*, 8037; g) P. A. Evans, J. E. Robinson, *J. Am. Chem. Soc.* **2001**, *123*, 4609; h) P. M. Breczinski, A. Stumpf, H. Hope, M. E. Krafft, J. A. Casalnuovo, N. E. Schore, *Tetrahedron* **1999**, *55*, 6797; i) D. L. J. Clive, D. C. Cole, Y. Tao, *J. Org. Chem.* **1994**, *35*, 4511; j) P. Magnus, C. Exon, P. Albaugh-Robertson, *Tetrahedron* **1985**, *41*, 5869; k) C. Exon, P. Magnus, *J. Am. Chem. Soc.* **1983**, *105*, 2477.

[5] a) C. Andrés, J. P. Duque-Soladana, R. Pedrosa, *J. Org. Chem.* **1999**, *64*, 4273; b) C. Andrés, J. P. Duque-Soladana, R. Pedrosa, *J. Org. Chem.* **1999**, *64*, 4282.

[6] a) C. Andrés, G. Maestro, J. Nieto, R. Pedrosa, S. García-Granda, E. Pérez-Carreño, *Tetrahedron Lett.* **1997**, *38*, 1463; b) C. Andrés, J. Nieto, R. Pedrosa, M. Vicente, *J. Org. Chem.* **1998**, *63*, 8570; c) C. Andrés, M. García, J. Nieto, R. Pedrosa, *J. Org. Chem.* **1999**, *64*, 5230; d) R. Pedrosa, C. Andrés, J. Nieto, *J. Org. Chem.* **2000**, *65*, 831.

[7] R. Pedrosa, C. Andrés, L. de las Heras, J. Nieto, *Org. Lett.* **2002**, *4*, 2513.

[8] a) R. Pedrosa, C. Andrés, J. M. Iglesias, *J. Org. Chem.* **2001**, *66*, 243; b) R. Pedrosa, C. Andrés, J. M. Iglesias, A. Pérez-Encabo, *J. Am. Chem. Soc.* **2001**, *123*, 1817.

[9] a) J. Adrio, M. Rodríguez Rivero, J. C. Carretero, *Angew. Chem.* **2000**, *112*, 3028; *Angew. Chem. Int. Ed.* **2000**, *39*, 2906; b) A. S. Gybin, W. A. Smit, R. Caple, A. L. Veretenov, A. S. Shashkov, L. G. Vorontsova, M. G. Kurella, V. S. Chertkov, A. A. Carapetyan, A. Y. Kosnikov, M. S. Alexanyan, S. V. Lindeman, V. N. Panov, A. V. Maleev, Y. T. Struchkov, S. M. Sharpe, *J. Am. Chem. Soc.* **1992**, *114*, 5555; c) P. Magnus, M. J. Slater, L. M. Principe, *J. Org. Chem.* **1989**, *54*, 5148.

[10] See the Supporting Information. CCDC-858968 and -858969 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[11] a) R. Pedrosa, C. Andrés, J. M. Iglesias, M. A. Obeso, *Tetrahedron* **2001**, *57*, 4005; b) C. Andrés, J. P. Duque-Soladana, J. M. Iglesias, R. Pedrosa, *Synlett* **1997**, 1391.

[12] a) M. M. Quintal, K. D. Closser, K. M. Shea, *Org. Lett.* **2004**, *6*, 4949; b) T. F. Jamison, S. Shambayati, W. E. Crowe, S. L. Schreiber, *J. Am. Chem. Soc.* **1997**, *119*, 4353; c) T. F. Jamison, S. Shambayati, W. E. Crowe, S. L. Schreiber, *J. Am. Chem. Soc.* **1994**, *116*, 5505.

[13] For some reviews on the Nicholas reaction, see: a) I. Omae, *Appl. Organomet. Chem.* **2007**, *21*, 318; b) B. J. Teobald, *Tetrahedron* **2002**, *58*, 4133; c) T. J. J. Müller, *Eur. J. Org. Chem.* **2001**, 2021; d) J. R. Green, *Curr. Org. Chem.* **2001**, *5*, 809; e) K. M. Nicholas, *Acc. Chem. Res.* **1987**, *20*, 207.

Received: October 7, 2011
Published Online: December 27, 2011

