

Synthesis of AE and BE Ring Analogues of the Alkaloid Methyllycaconitine

Holger Guthmann,^[a] Daniel Conole,^[a] Emma Wright,^[a] Karsten Körber,^[b] David Barker,^[a] and Margaret A. Brimble*^[a]

Keywords: Alkaloids / Olefination / Hydrogenation / Nicotinic acetylcholine receptors

The synthesis of AE and BE analogues of the alkaloid methyllycaconitine is reported. The analogues contain two key pharmacophores: a 2-(2-methylmaleimido)benzoate ester and a homocholine motif formed from a tertiary *N*-(3-phenylpropyl)amine incorporated into either a 3-azabicyclo[3.3.1]nonane (AE) or octahydroquinoline (BE) ring system. An additional aromatic group is introduced into the AE bicyclic system using a Horner–Wadsworth–Emmons reaction. The BE analogues are synthesised by a one-pot cyclisation using ethyl α -(bromomethyl)acrylate, a primary amine and

cyclohexanone leading to an efficient assembly of an octahydroquinoline ring system that mimics the BE-rings of methyllycaconitine. In both the AE and BE analogues, the key 2-(2-methylsuccinimido)benzoate ester pharmacophore is introduced by esterification of the alcohol precursors with 2-(2-methylmaleimido)benzoic acid (**10**) under Steglich conditions followed by hydrogenation over palladium on charcoal.

(© Wiley-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, Germany, 2009)

Introduction

Methyllycaconitine (**1**) is the major toxic component in *Delphinium brownii* and was first discovered by Manske in 1938.^[1] Goodson later determined the formula of methyllycaconitine (**1**) to be the 2-[2-(*S*)-methylsuccinimido]benzoate ester of the norditerpenoid alkaloid lycoctonine (**2**).^[2] The methyllycaconitine (**1**) core structure contains a piperidine (E) ring and a cyclohexane (A) ring embedded in an azabicyclo[3.3.1]nonane framework. The primary mode of action of methyllycaconitine (**1**) is via competitive blockade at the nicotinic acetylcholine receptors (nAChRs). Structure–activity studies on methyllycaconitine (**1**) have shown that the *N*-substituted anthranilate ester moiety is essential for potent pharmacological activity.^[3] Comparison of the neuronal activity of methyllycaconitine (**1**) and lycoctonine (**2**), established that lycoctonine (**2**) exhibits 2000 times less affinity for rat neuronal $\alpha 7$ nAChRs than its *N*-substituted anthranilate ester methyllycaconitine (**1**) (Figure 1).^[4,5]

nAChRs are a family of ligand-gated ion channels formed by the association of five subunits, involving homomeric and heteromeric structures, which are widely distributed in the human brain.^[6] The $\alpha 7$ nAChR subtype is amongst the most common in the brain and has been linked to pain, neurodegenerative diseases such as Alzheimer's disease and Parkinson's disease, and psychiatric disorders such as schizophrenia and depression.^[7] Only a few compounds

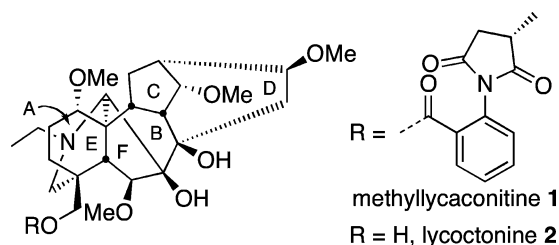


Figure 1. Methyllycaconitine and lycoctonine.

like methyllycaconitine (**1**) such as the poison frog alkaloid 235B^[8] or the peptide toxins α -bungarotoxin and α -conotoxin ImI bind with high affinity and selectivity to the $\alpha 7$ nAChR.^[9] Methyllycaconitine (**1**) is reported to be the most potent non-protein competitive $\alpha 7$ nAChR antagonist presently available.

An essential structural feature of methyllycaconitine (**1**) is the *N*-substituted anthranilate ester which is postulated to be the key pharmacophore of the molecule.^[3,4,10] It has been proposed that at physiological pH the tertiary amine in the AE ring system of methyllycaconitine (**1**) is protonated. Both the ester and the protonated amine form a homocholine motif that mimics acetylcholine. The (*S*)-methylsuccinimido moiety may help to maintain the correct geometry between the tertiary nitrogen atom of the piperidine E ring in the alkaloid with the carbonyl oxygen of the ester bond.^[11] A structure–activity relationship study of simple E ring analogues **3** by Bergmeier et al.^[12,13] demonstrated that the *N*-3-phenylpropyl moiety in comparison to the natural *N*-Et group resulted in a significant increase in binding affinity. Biological evaluation determined that all

[a] Department of Chemistry, The University of Auckland, 23 Symonds Street, Auckland 1142, New Zealand
Fax: +64-9-373-7422
E-mail: m.brimble@auckland.ac.nz

[b] BASF SE, Crop Protection Global Research Insecticides, 67056 Ludwigshafen, Germany

four diastereomers of **3** showed the same potency, indicating that the binding to nAChRs is not stereospecific for these analogues (Figure 2).^[14]

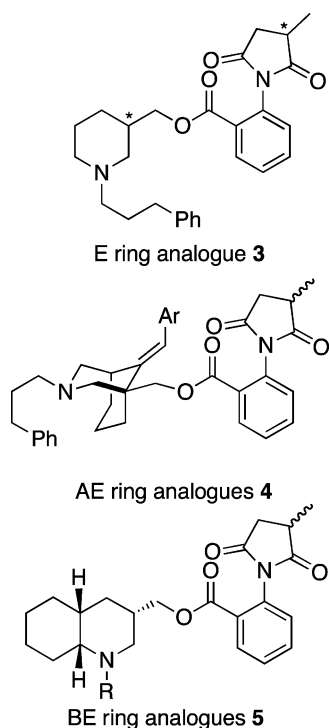


Figure 2. Simple methyllycaconitine analogues.

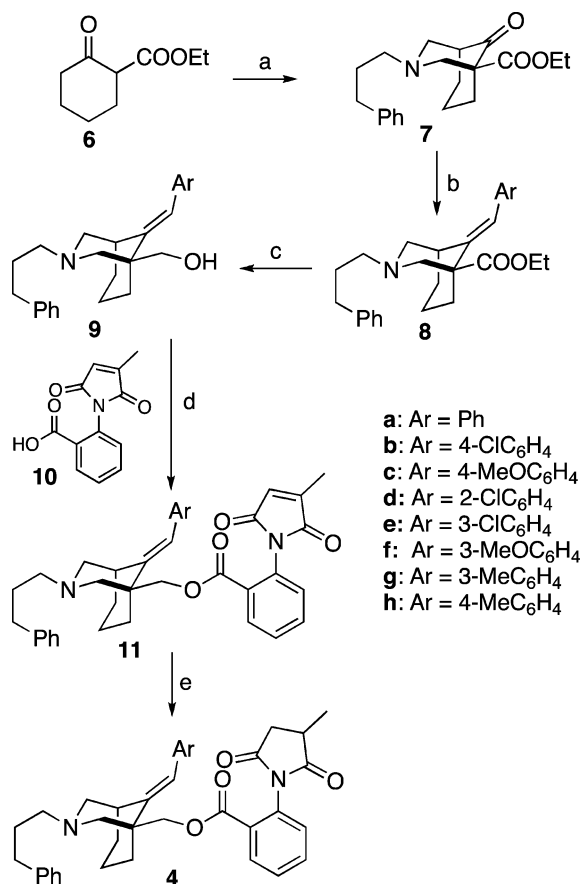
A total synthesis of methyllycaconitine (**1**) has not been reported to date, however, semi-syntheses of methyllycaconitine (**1**) from its parent alkaloid lycoctonine have been reported by Blagborough^[15] and Carrol.^[16] A number of simpler analogues of MLA incorporating the putative pharmacophore have been reported.^[17]

We herein report the full details of the synthesis of several AE and BE analogues (**4** and **5**) of methyllycaconitine (**1**). The AE analogues **4** contain the key 2-(2-methylsuccinimido)benzoate ester, in which an additional styrene (part of the B ring) is appended to the azabicyclo[3.3.1]nonane core structure (AE rings). An additional aryl moiety is included in the AE analogues to raise the binding affinity, due to increased interactions in a reported hydrophobic pocket.^[18] In order to enhance the selectivity and potency of previously reported methyllycaconitine E ring analogues we also synthesized BE ring analogues **5** in which the cyclohexyl E ring was embedded in a more rigid *cis*-fused octahydroquinoline framework (Figure 2). Incorporation of the *N*-substituted anthranilate ester and the *N*-3-phenylpropyl moiety within a conformationally restricted framework was envisaged to enhance the biostability, selectivity and potency of previously reported analogues.

Results and Discussion

The strategy devised for the synthesis of AE bicyclic methyllycaconitine analogues, represented by compound **4**,

is shown in Scheme 1. The initial step was the synthesis of the AE bicyclic framework system using a double Mannich reaction (Scheme 1). Our group has previously reported a high yielding double Mannich reaction using bis(aminol) ethers.^[19] However, in the present work a simpler acid-catalysed double Mannich reaction using formaldehyde and 3-phenylpropylamine proved more reliable on a larger scale. Treatment of 3-phenylpropylamine and β -keto ester **6** with a catalytic quantity of acetic acid under reflux gave the racemic bicycle **7** in 49% yield. This acid-catalysed double Mannich reaction^[20] proceeded in much higher yield than carrying out the reaction using standard Mannich conditions.^[21] Nevertheless, the moderate yield obtained for this reaction is consistent with literature examples of double Mannich reactions using cyclohexanones such as **6** that only contain one α -carboxylate group. Better yields have been reported for analogous reactions using cyclohexanones substituted with electron-withdrawing groups at both the α - and α' -positions.^[22]



Scheme 1. (a) 3-phenylpropylamine, paraformaldehyde, AcOH, EtOH, H₂O (49%); (b) ArCH₂PO(OEt)₂, *n*BuLi, THF, room temp., ovn or, for **8f**, reflux ovn, **8a** (84%), **8b** (99%), **8c** (31%), **8d** (76%), **8e** (68%), **8f** (15%), **8g** (10%), **8h** (42%); (c) LiAlH₄, THF, **9a** (99%), **9b** (98%), **9c** (74%), **9d** (61%), **9e** (95%), **9f** (91%), **9g** (95%), **9h** (79%); (d) **10**, DCC, DMAP, CH₂Cl₂, **11a** (76%), **11b** (57%), **11c** (58%), **11d** (53%), **11e** (60%), **11f** (82%), **11g** (63%), **11h** (63%); (e) H₂, Pd/C, EtOAc, **4a** (88%), **4b** (73%), **4c** (68%), **4d** (47%), **4e** (55%), **4f** (57%), **4g** (71%), **4h** (79%).

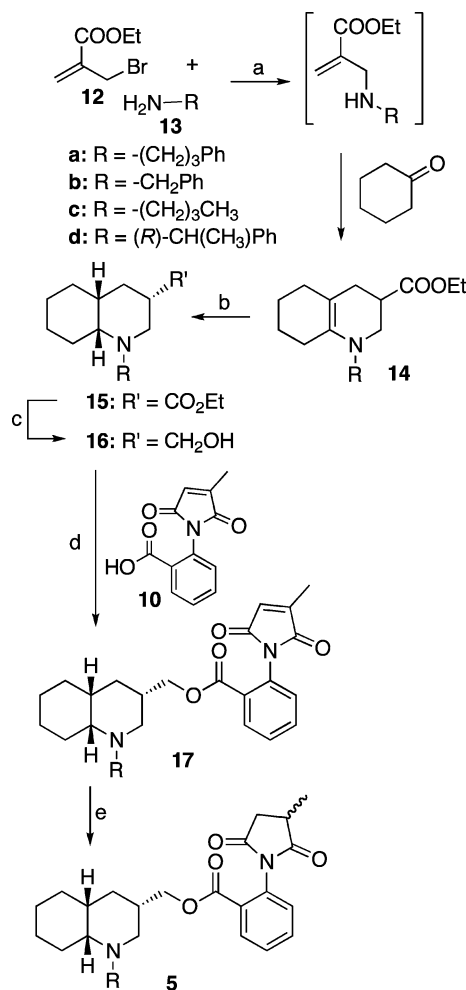
With the synthesis of the azabicyclic **7** in hand, attention focused on the introduction of the styrene group by Wittig olefination. Wittig olefination of azabicyclic ketones similar to **6** has been reported using methyl^[23] and methoxymethyl^[21] phosphonium salts. When Wittig olefination of the azabicyclic **6** was attempted using the benzyl phosphonium salt with *n*BuLi as the base, the reaction did not proceed and only starting material was recovered. However using a Horner–Wadsworth–Emmons modification^[24,25] with benzyl diethyl phosphonate and *n*BuLi as base gave the required styrene **8a** in good yield (84%). Due to the steric hindrance of the ester group only the (*E*)-substituted olefin **8a** was formed. The reaction was also carried out using *para*-methoxybenzyl diethylphosphonate and *para*-chlorobenzyl diethylphosphonate to afford olefins **8b** and **8c** in 31% and 99% yield, respectively. It is postulated that neutral and electron-withdrawing aryl rings, which form stable phosphonate anions, afford higher yields of the Horner–Wadsworth–Emmons products than when using phosphonate anions that bear electron-donating aryl components. Our experimental observations are consistent with these literature reports.^[21,23]

With the styrene unit appended to the key azabicyclic scaffold, attention turned to appendage of the 2-(2-methylsuccinimido)benzoate ester via the neopentyl alcohols **9**. Lithium aluminium hydride reduction of ethyl ester **8a** afforded neopentyl alcohol **9a** in good yield facilitating the use of an efficient two-step procedure to introduce the 2-(2-methylsuccinimido)benzoate ester. Firstly, the key 2-(2-methylsuccinimido)benzoate group was introduced by direct coupling with 2-(2-methylmaleimido)benzoic acid (**10**) under Steglich conditions to afford ester **11a**. The double bond of the maleimide **11a** was then hydrogenated over 10% palladium on charcoal in ethyl acetate. Surprisingly, hydrogenation effected conversion of the maleimido moiety to a succinimido ring leaving the styrene double bond intact. Usually styrene double bonds are hydrogenated under mild conditions however, in the present case the double bond of the styrene is sterically hindered. Overall use of this four-step sequence afforded racemic ester **4a** in 56% overall yield, starting from azabicyclic **7**.

With a reliable synthesis of **4a** in hand, the remaining analogues, **4b–h** were synthesized uneventfully in a similar fashion starting from the appropriate ketone **7**. All reactions proceeded in reliable yields affording the AE analogues **4b–h** of methyllycaconitine.

We next proceeded to synthesize a series of BE analogues of MLA (**1**). The strategy for the synthesis of the BE analogues, represented by compound **5**, is shown in Scheme 2. During the course of this work the first synthesis of a BE-ring analogue of methyllycaconitine was reported^[26] however, no data on this analogue's ability to bind to $\alpha 7$ nAChRs was included. Importantly, this BE analogue did not contain the critical 2-(2'-methylsuccinimido)benzoate pharmacophore.

The aim was to prepare BE-ring analogues of methyllycaconitine (**1**) by efficient one-pot cyclisation of ethyl α -(bromomethyl)acrylate, a primary amine and cyclohexa-



Scheme 2. (a) 0 °C, 15 min, toluene, then add cyclohexanone, reflux, 18 h **14a** (60%), **14b** (47%), **14c** (72%), **14d** (50%); (b) H_2 , PtO_2 , EtOAc, 18 h, **15a** (41%), **15b** (54%), **15c** (54%), **15d** (72%); (c) LiAlH_4 , THF, 1 h, **16a** (100%), **16b** (100%), **16c** (100%), **16d** (100%); (d) **10**, DCC, DMAP, CH_2Cl_2 , **17a** (95%), **17b** (53%), **17c** (53%), **17d** (70%); (e) H_2 , 10% Pd/C, EtOAc, 18 h, **5a** (95%), **5b** (97%), **5c** (99%), **5d** (95%) all as 1:1 mixtures of diastereomers.

none to assemble an octahydroquinoline ring system that mimics the BE-rings of methyllycaconitine. Moreover, the nature of the alkaloid substituent on the E-ring nitrogen is also probed in the present work.

The synthetic strategy hinges on a successful one-pot cyclisation to set up an octahydroquinoline core using ethyl α -(bromomethyl)acrylate (**12**), cyclohexanone and various primary amines **13** to vary the substitution on the alkaloid nitrogen. The strategy is based on a method used by both Horii et al.^[27] and Cassady et al.^[28] who constructed a tetracyclic ergot alkaloid core by reaction of a highly substituted cyclohexanone with ethyl α -(bromomethyl)acrylate (**12**) and methylamine. The present work tests the generality of this one-pot cyclisation as a method to afford an octahydroquinoline core by reaction of simple cyclohexanone with a range of primary amines (Scheme 1).

Ethyl α -(bromomethyl)acrylate (**12**) was prepared by bromination of ethyl α -(hydroxymethyl)acrylate using phos-

phorus tribromide, as previously reported by Villieras and Rambaud.^[29] In our case an alternative route to ethyl α -(hydroxymethyl)acrylate was used wherein 1,4-diazabicyclo[2.2.2]octane (DABCO) was an effective catalyst to effect union of formaldehyde with ethyl acrylate.^[30]

With ethyl α -(bromomethyl)acrylate (**12**) in hand, attention turned to the synthesis of the octahydroquinoline ring system. The first amine to be investigated was 3-phenylpropylamine **13a**, as the 3-phenylpropyl substituent had previously been shown to exhibit increased binding affinity to $\alpha_3\beta_4$ nAChRs.^[14] Thus, ethyl α -(bromomethyl)acrylate (**12**) (1.0 equiv.) in dry toluene was added dropwise to 3-phenylpropylamine (**13a**) (2.0 equiv.) at 0 °C, the mixture stirred for 15 min then ice-cold cyclohexanone (1.0 equiv.) in toluene added and the resultant mixture heated at reflux for 18 h. Work-up and purification by flash chromatography gave octahydroquinoline **14a** in 60% yield (Scheme 2). Pleasingly, the literature yields for construction of related octahydroquinolines were similar.^[28,31]

Having successfully synthesized octahydroquinoline **14a**, the next step was to investigate this one-pot reaction varying the nature of the amine thus providing different substituents on the E-ring nitrogen. Using the exact conditions described above, the one-pot reaction was investigated with benzylamine **13b**, butylamine **13c** and (*R*)-1-phenylethylamine (**13d**) affording octahydroquinolines **14b**, **14c** and **14d** in 47%, 72% and 50% yield, respectively. Interestingly, use of ethylamine and isopropylamine as the amine component only afforded low yields of the desired octahydroquinolines, which was attributed to the volatile nature of these amines. In addition, in these cases the crude octahydroquinoline products were unstable decomposing upon attempted purification by flash chromatography.

With the BE framework in hand, attention focused on hydrogenation to establish the *cis* stereochemistry of the bridgehead protons in decahydroquinolines **14** thus retaining the natural stereochemistry of the BE-rings in methyllycaconitine (**1**). Precedent for the use of a similar catalytic hydrogenation to prepare a *cis*-decahydroquinoline was reported by Cassidy et al. using Adam's catalyst (PtO_2).^[28] Octahydroquinoline **14a** was therefore subjected to hydrogenation (1 atm) over Adam's catalyst in ethyl acetate for 18 h to afford *cis*-decahydroquinoline **15a** in 41% yield after flash chromatography. *cis*-Decahydroquinoline **15a** was established to exhibit *cis-syn* stereochemistry as confirmed by the observation of an nOe interaction (Figure 3) between 4a-H and 3-H thus establishing the relative stereochemistry to be (3*S**,4*aR**,8*aR**) which is the same as that found in methyllycaconitine (**1**).

Reduction of octahydroquinolines **14b** and **14c** proceeded in a similar manner affording the desired *cis-syn* decahydroquinolines **15b** and **14c** both in 54% yield. In the case of octahydroquinoline **14d**, which already contained a stereogenic centre of fixed configuration in the amine side chain, only one diastereomer of the decahydroquinoline was obtained from the hydrogenation step, however, the stereochemistry was not determined.

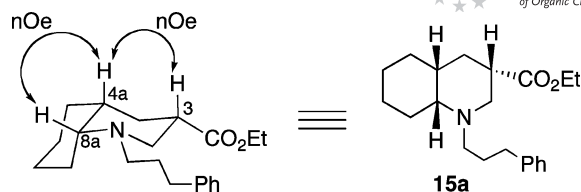


Figure 3. Stereochemistry of decahydroquinoline **15a** determined by nOe interactions between 8a-H and 4a-H and between 4a-H and 3-H.

In a similar fashion to the synthesis of other analogues of methyllycaconitine (**1**), the 2-(2-methylsuccinimido)benzoate ester was next appended to the BE ring system (Scheme 2). Prior to this esterification step the ethyl esters **15a–d** were reduced to a primary alcohol. Reduction of the ethyl esters **15a–d** using lithium aluminium hydride in THF at room temperature for 1.0 h afforded alcohols **16a–d** in quantitative yield in preparation for appendage of the key 2-(2-methylsuccinimido)benzoate pharmacophore.

Having synthesised decahydroquinoline alcohols **16a–d** the final step was to install the anthranilate ester pharmacophore of methyllycaconitine (**1**). The direct coupling of 2-(3-methyl-2,5-dioxo-2,5-dihydro-1*H*-pyrrol-1-yl)benzoic acid (**10**, 2.0 equiv.) with neopentyl-type alcohols in dry acetonitrile using 10 mol-% of DMAP and 2 equiv. of DCC for 6 h has been reported.^[32] In the present work however, these conditions failed to effect conversion of alcohol **16a** to anthranilate ester **17a**. The use of DIC/HOBt and EDCI were also ineffective. Fortunately, simply changing the solvent to dichloromethane using DCC and DMAP (cat.) effected smooth conversion of alcohol **16a** to anthranilate ester **17a** in 95% yield after 18 h. Similar conversion of alcohols **16b**, **16c** and **16d** to anthranilates **17b**, **17c** and **17d** proceeded uneventfully in moderate yield.

Finally the maleimide unit in anthranilates **17a–d** underwent smooth hydrogenation over 10% palladium on charcoal (1 atm H_2) for 18 h to yield the desired succinimide anthranilates **5a–d** as 1:1 mixtures of diastereomers in 95–99% yield.

Conclusions

In summary, the successful syntheses of eight AE bicyclic analogues **4a–h** and four BE-ring analogues **5a–d** of methyllycaconitine (**1**) have been achieved. Both AE and BE analogues contain the key structural features that contribute to the observed bioactivity, namely the presence of a homocholine motif derived from a tertiary *N*-3-phenylpropylamine embedded in either a 3-azabicyclo[3.3.1]nonane (AE) or piperidine (BE) ring system together with a 2-(2-methylsuccinimido)benzoate ester side chain.

The key steps in the synthesis of AE analogues **4a–h** involved a double Mannich cyclisation to assemble the 3-azabicyclo[3.3.1]nonane AE ring system in combination with use of a Horner–Wadsworth–Emmons reaction to further functionalize the B ring.

The BE analogues **5a–d** were constructed using an efficient one pot annelation of ethyl α -(bromomethyl)acrylate with a primary amine and cyclohexanone followed by *cis*-hydrogenation of the resultant octahydroquinoline ring system. Appendage of the key 2-(2-methylsuccinimido)benzoate pharmacophore required the use of dichloromethane as the solvent to effect coupling of benzoic acid **9** with alcohols **16a–d**.

The synthesis of AE **4a–h** and BE **5a–d** ring analogues of methyllycaconitine (**1**) may provide access to more effective inhibitors of the $\alpha 7$ nAChR sub-type.

Experimental Section

General Methods: Analytical thin layer chromatography (TLC) was performed using 0.2 mm thick precoated silica gel plates (Merck Kieselgel 60 F254). Compounds were visualized by ultraviolet fluorescence or by staining with potassium permanganate in aqueous sodium hydroxide. Flash chromatography was performed using Riedel-de Haën silica gel (0.032–0.063 mm) with the indicated solvents. ^1H NMR spectra were recorded with a Bruker DRX 300 (300 MHz) or a Bruker DRX 400 (400 MHz) spectrometer at ambient temperature using CDCl_3 as a solvent. Chemical shifts are given in parts per million (ppm) downfield shift from tetramethylsilane as an internal standard, and reported as position (δ), multiplicity (*s* = singlet, *d* = doublet, *dd* = double doublet, *t* = triplet, *dt* = double triplet, *q* = quartet, *m* = multiplet), relative integral, assignment and coupling constant (*J* in Hz). ^{13}C NMR spectra were recorded with a Bruker DRX 300 (75 MHz) or a Bruker DRX 400 (100 MHz) spectrometer at ambient temperature with complete proton decoupling. Chemical shifts are expressed in parts per million referenced to the residual chloroform peak (δ = 77.0 ppm), and reported as position (δ) and assignment, aided by DEPT 135 experiments ppm. In addition, ^1H - ^1H -COSY and ^1H - ^{13}C -HSQC correlation spectra were used for the complete assignment of the proton and carbon resonances. ^1H - ^1H -NOESY NMR spectra were recorded in special cases. The NMR spectroscopic data for the bicyclic analogues of methyllycaconitine were assigned using the following descriptors: bicyclic ring system (no primes), anthranilate ester (one prime ') and methylsuccinimide (two primes ''). High resolution mass spectra were recorded with a VG-70SE mass spectrometer. Ionisation method employed was electron impact (EI). Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. 2-(3-methyl-2,5-dioxo-2,5-dihydropyrrol-1-yl)-benzoic acid (**10**)^[33] and the diethylphosphonates^[25] were prepared as reported.

Ethyl 9-Oxo-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonane-1-carboxylate (6): AcOH (1 mL) was added to a solution of 3-phenylpropylamine (13.3 mL, 12.6 g, 74.1 mmol), ethyl-2-oxocyclohexanecarboxylate **5** (9.40 mL, 10.0 g, 74.1 mmol) and paraformaldehyde (4.44 g, 148 mmol) in EtOH/H₂O (60 mL, *v/v* = 1:1). The mixture was stirred under reflux overnight and then concentrated under reduced pressure. To crude residue was added water (100 mL) and the aqueous mixture was extracted with EtOAc (3 $\times$ 75 mL). The combined organic layers were dried (Na_2SO_4) and solvent removed in vacuo to give the crude product, which was purified by flash chromatography (5% ethyl acetate in hexane) to give **6** as a pale yellow oil (12.0 g, 49%). R_f = 0.26 (hexane/EtOAc, 9:1). ^1H NMR (300 MHz, CDCl_3): δ = 1.28 (t, 3J = 7.1 Hz, 3 H, OCH_2CH_3), 1.52–1.63 (m, 1 H, 7-H), 1.83 (quintet, 3J = 7.2 Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.06–2.19 (m, 2 H, 6-H), 2.21–2.29 (m, 1 H, 8-

H), 2.36 (t, 3J = 7.2 Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.44–2.49 (m, 1 H, 5-H), 2.49–2.61 (m, 2 H, 4-H and 8-H), 2.69 (t, 3J = 7.2 Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.81–2.99 (m, 1 H, 7-H), 2.94 (dd, 2J = 11.4, 4J = 1.7 Hz, 1 H, 2-H), 3.14 (dt, 2J = 11.0, 3J = 2.0 Hz, 1 H, 4-H), 3.21 (dd, 2J = 11.4, 4J = 2.0 Hz, 1 H, 2-H), 4.21 (q, 3J = 7.1 Hz, 2 H, OCH_2CH_3), 7.16–7.32 (m, 5 H, ArH) ppm. ^{13}C NMR (75.5 MHz, CDCl_3): δ = 14.1 (OCH_2CH_3), 20.6 (C-7), 29.0 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.5 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 34.2 (C-6), 36.8 (C-8), 47.2 (C-5), 56.4 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 58.8 (C-1), 60.4 (C-4), 61.1 (OCH_2CH_3), 62.0 (C-2), 125.8, 128.4 ($\times$ 2), 142.0 (Ph), 171.1 (COOEt), 212.5 (C-9) ppm. This data was in agreement with that reported in the literature.^[19]

General Procedure for the Synthesis of Styrenes 7: *n*-Butyllithium in hexane (1.4 equiv.) was added to a solution of benzyl diethylphosphonates (1.4 equiv.) in THF (0.9 M) at -78°C and the mixture stirred for 30 min. The mixture was warmed to room temperature, left to stand for 30 min, recooled to -78°C , and a solution of ethyl 9-oxo-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonane-1-carboxylate (**6**, 1.0 equiv.) in THF (0.6 M) was added. The resulting mixture was stirred overnight at room temperature. The reaction mixture was diluted with brine and extracted with EtOAc. The combined organic layers were dried (MgSO_4) and solvent was evaporated in vacuo to give the crude product which was purified by flash chromatography to yield desired styrenes **7a–h**.

Ethyl (E)-9-Benzylidene-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonane-1-carboxylate (7a): Using benzyl diethylphosphonate (970 mg, 4.26 mmol) and ketone **6** (1.00 g, 3.04 mmol); purified by column chromatography (hexane/EtOAc, 95:5), to give the olefin **7a** as a pale yellow oil (1.03 g, 84%). R_f = 0.44 (hexane/EtOAc, 9:1). ^1H NMR (300 MHz, CDCl_3): δ = 1.33 (t, 3J = 7.1 Hz, 3 H, OCH_2CH_3), 1.56–1.68 (m, 1 H, 7-H), 1.81 (t, 3J = 7.6 Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 1.85–1.92 (m, 2 H, 6-H), 2.05 (ddd, 2J = 13.3, 3J = 6.5, 4J = 1.8 Hz, 1 H, 8-H), 2.21–2.32 (m, 3 H, 4-H and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.39 (ddt, 2J = 13.3, 3J = 6.5, 4J = 1.8 Hz, 1 H, 8-H), 2.65–2.76 (m, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.72 (dd, 2J = 10.5, 4J = 1.8 Hz, 1 H, 2-H), 2.80–2.98 (m, 2 H, 4-H and 7-H), 3.04–3.09 (m, 1 H, 5-H), 3.12 (dd, 2J = 10.5, 4J = 0.9 Hz, 1 H, 2-H), 4.25 (qd, 3J = 7.1, J = 1.8 Hz, 2 H, OCH_2CH_3), 6.08 (s, 1 H, CHAr), 7.15–7.15 (m, 10 H, ArH) ppm. ^{13}C NMR (75.5 MHz, CDCl_3): δ = 14.3 (OCH_2CH_3), 21.4 (C-7), 28.9 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.1 (C-6), 33.5 (C-5 and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 36.2 (C-8), 51.3 (C-1), 57.4 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{CPh}$), 60.5 (C-4), 60.6 (OCH_2CH_3), 62.7 (C-2), 119.1 (CHAr), 125.7, 126.3, 128.1, 128.3, 128.5, 128.7 ($\text{CH}_{\text{arom.}}$), 137.6, 142.5 ($\text{C}_{\text{arom.}}$), 145.7 (C-9), 174.6 (COOEt) ppm. IR (film): $\tilde{\nu}$ = 3024 (w), 2936 (s), 1724 (vs), 1650 (w), 1599 (w), 1494 (w), 1453 (s), 1260 (s), 1244 (s), 1112 (s), 1052 (s), 746 (w), 699 (s) cm^{-1} . MS (EI, 70 eV): m/z (%) = 403 (16) [^{35}Cl , M^+] 298 (100) [$\text{M}^+ - \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2$], 148 (14), 91 (25) [$\text{C}_6\text{H}_5\text{CH}_2$]; found (M^+ , 403.25186); $\text{C}_{27}\text{H}_{33}\text{NO}_2$ calcd. 403.25113.

Ethyl (E)-9-(4-Chlorobenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonane-1-carboxylate (7b): Using 4-chlorobenzyl diethylphosphonate (1.04 g, 3.95 mmol) and ketone **6** (1.00 g, 3.04 mmol); purified by column chromatography (hexane/EtOAc, 95:5), to give the olefin **7b** as an oil (1.33 g, 100%). R_f = 0.43 (hexane/EtOAc, 9:1). ^1H NMR (300 MHz, CDCl_3): δ = 1.31 (t, 3J = 7.2 Hz, 3 H, OCH_2CH_3), 1.54–1.66 (m, 1 H, 7-H_A), 1.72–1.94 (m, 4 H, 6-H and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.04 (dd, 2J = 13.3, 3J = 5.3 Hz, 1 H, 8-H_A), 2.20 (dd, 2J = 10.0, 4J = 1.8 Hz, 1 H, 4-H_A), 2.27 (td, 3J = 7.0, J = 2.2 Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.36 (ddt, 2J = 13.3, 3J = 6.5, J = 2.0 Hz, 1 H, 8-H_B), 2.63–2.73 (m, 3 H, 2-H_A and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.79–3.01 (m, 3 H, 4-H_B, 5-H and 7-H_B), 3.10 (d, 2J = 11.0 Hz, 1 H, 2-H_B), 4.23 (td, 3J = 7.2, J = 1.7 Hz, 2 H,

OCH₂CH₃), 6.00 (s, 1 H, CHAr), 7.07–7.31 (m, 9 H, ArH) ppm. ¹³C NMR (75.5 MHz, CDCl₃): δ = 14.3 (OCH₂CH₃), 21.3 (C-7), 28.9 (NCH₂CH₂CH₂Ph), 33.1 (C-6), 33.5 (C-5), 33.6 (NCH₂CH₂CH₂Ph), 36.2 (C-8), 51.3 (C-1), 57.3 (NCH₂CH₂H₂CPh), 60.4 (C-4), 60.6 (OCH₂CH₃), 62.6 (C-2), 117.9 (CHAr), 125.7, 128.3 (×2), 128.4, 130.0 (CH_{arom.}), 132.0, 135.9, 142.4 (C_{arom.}), 146.5 (C-9), 174.4 (COOEt) ppm. IR (film): ν̄ = 3025 (w), 2937 (s), 1724 (vs, C=O), 1489 (s), 1372 (w), 1259 (s), 1244 (s), 1111 (s), 1091 (s), 854 (m), 747 (m), 699 (m) cm⁻¹. MS (EI, 70 eV): *m/z* (%) = 439 (7) [³⁷Cl, M⁺], 437 (15) [³⁵Cl, M⁺], 332 (100) [M⁺ – C₆H₅CH₂CH₂], 148 (21), 91 (25) [C₆H₅CH₂]. found (M⁺, 437.21248), C₂₇H₃₂³⁵ClNO calcd. 437.21216; found (M⁺, 439.20744), C₂₇H₃₂³⁷ClNO calcd. 439.20921.

Ethyl (E)-9-(4-Methoxybenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonane-1-carboxylate (7c): Using 4-methoxybenzyl diethylphosphonate (1.10 g, 4.26 mmol) and ketone **6** (1.00 g, 3.04 mmol); purified by column chromatography (hexane/EtOAc, 95:5), to give the olefin **7c** as a pale yellow oil (402 mg, 31%). *R*_f = 0.50 (hexane/EtOAc, 9:1). ¹H NMR (300 MHz, CDCl₃): δ = 1.31 (t, ³*J* = 7.2 Hz, 3 H, OCH₂CH₃), 1.54–1.65 (m, 1 H, 7-H_A), 1.81 (t, ³*J* = 7.6 Hz, 2 H, NCH₂CH₂CH₂Ph), 1.83–1.93 (m, 2 H, 6-H), 1.89–2.07 (m, 1 H, 8-H_A), 2.18–2.30 (m, 3 H, 4-H_A and NCH₂CH₂CH₂Ph), 2.36 (ddt, ²*J* = 13.0, ³*J* = 6.2, ⁴*J* = 1.9 Hz, 1 H, 8-H_B), 2.63–2.72 (m, 3 H, 2-H_A and NCH₂CH₂CH₂Ph), 2.79–2.96 (m, 2 H, 4-H_B and 7-H_B), 3.03–3.06 (m, 1 H, 5-H), 3.09 (d, ²*J* = 11.0 Hz, 1 H, 2-H_B), 3.08 (s, 3 H, OCH₃), 4.23 (td, ³*J* = 7.2, *J* = 1.8 Hz, 2 H, OCH₂CH₃), 6.00 (s, 1 H, CHAr), 6.84 (dt, ³*J* = 8.6, ³*J* = 2.0 Hz, 2 H, *m*-ArH), 6.84 (dt, ³*J* = 8.6, ³*J* = 2.0 Hz, 2 H, *o*-ArH), 7.16–7.31 (m, 5 H, ArH) ppm. ¹³C NMR (75.5 MHz, CDCl₃): δ = 14.3 (OCH₂CH₃), 21.4 (C-7), 28.9 (NCH₂CH₂CH₂Ph), 33.1 (C-6), 33.4 (C-5), 33.5 (NCH₂CH₂CH₂Ph), 36.2 (C-8), 51.3 (C-1), 55.2 (OCH₃), 57.4 (NCH₂CH₂CH₂Ph), 60.5 (C-4), 60.6 (OCH₂CH₃), 62.7 (C-2), 113.5 (*m*-ArC), 118.5 (CHAr), 125.7, 128.3, 128.5 (CH_{arom.}), 129.8 (*o*-ArC), 129.9, 142.5 (C_{arom.}), 144.6 (C-9), 158.0 (ArC-OMe) 174.7 (COOEt) ppm. IR (film): ν̄ = 3026 (w), 2933 (br), 1723 (vs, C=O), 1607 (s), 1510 (vs), 1454 (s), 1247 (vs), 1175 (s), 1111 (s), 1037 (s), 851 (w), 819 (w), 746 (w), 699 (s) cm⁻¹. MS (EI, 70 eV): *m/z* (%) = 433 (33) [M⁺], 328 (100) [M⁺ – C₆H₅CH₂CH₂], 148 (48), 121 (27), 91 (23) [C₆H₅CH₂], 44 (16); found (M⁺, 433.2614), C₂₈H₃₅NO₃ calcd. 433.2617.

Ethyl (E)-9-(2-Chlorobenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonane-1-carboxylate (7d): Using 2-chlorobenzyl diethylphosphonate (1.12 g, 4.25 mmol) and ketone **6** (1.00 g, 3.04 mmol); purified by column chromatography (hexane/EtOAc, 95:5), to give the olefin **7d** as an oil (1.01 g, 76%). *R*_f = 0.72 (hexane/EtOAc, 9:1). ¹H NMR (300 MHz, CDCl₃): δ = 1.29 (t, ³*J* = 6.2 Hz, 3 H, OCH₂CH₃), 1.58–1.64 (m, 1 H, 7-H_A), 1.75–1.92 (m, 4 H, 6-H and NCH₂CH₂CH₂Ph), 2.04 (dd, ²*J* = 8.7, ³*J* = 6.0 Hz, 1 H, 8-H_A), 2.20 (dd, ²*J* = 10.0, ⁴*J* = 1.8 Hz, 1 H, 4-H_A), 2.28 (td, ³*J* = 6.9, *J* = 2.4 Hz, 2 H, NCH₂CH₂CH₂Ph), 2.33 (ddt, ²*J* = 13.1, ³*J* = 6.2, *J* = 2.2 Hz, 1 H, 8-H_B), 2.64–2.71 (m, 3 H, 2-H_A and NCH₂CH₂CH₂Ph), 2.79–3.02 (m, 3 H, 4-H_B, 5-H and 7-H_B), 3.10 (d, ²*J* = 11.7 Hz, 1 H, 2-H_B), 4.23 (td, ³*J* = 6.4, *J* = 1.5 Hz, 2 H, OCH₂CH₃), 6.01 (s, 1 H, CHAr), 7.03–7.31 (m, 9 H, ArH) ppm. ¹³C NMR (75.5 MHz, CDCl₃): δ = 14.2 (OCH₂CH₃), 21.2 (C-7), 28.7 (NCH₂CH₂CH₂Ph), 33.0 (C-6), 33.4 (C-5), 33.5 (NCH₂CH₂CH₂Ph), 36.2 (C-8), 51.2 (C-1), 57.4 (NCH₂CH₂H₂CPh), 60.3 (C-4), 60.7 (OCH₂CH₃), 62.5 (C-2), 118.1 (CHAr), 125.7, 126.4, 126.8, 128.3 (2 ×), 128.4 (2 ×, CH_{arom.}), 128.5 (C_{arom.}), 128.6, 129.4 (CH_{arom.}), 134.0, 139.3, 142.3 (C_{arom.}), 146.6 (C-9), 174.2 (COOEt) ppm. IR (film): ν̄ = 2978 (s), 1722 (vs, C=O), 1651 (s), 1495 (s), 1245 (s), 1111 (s), 1050 (s), 740 (m), 699 (m) cm⁻¹. MS (EI, 70 eV): *m/z* (%) = 439 (7) [³⁷Cl, M⁺], 437 (15) [³⁵Cl, M⁺], 332 (100) [³⁵Cl,

M⁺ – C₆H₅CH₂CH₂], 91 (25) [C₆H₅CH₂]; found (M⁺, 437.21325), C₂₇H₃₂³⁵ClNO calcd. 437.21216; found (M⁺, 439.20863), C₂₇H₃₂³⁷ClNO calcd. 439.20921.

Ethyl (E)-9-(3-Chlorobenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonane-1-carboxylate (7e): Using 3-chlorobenzyl diethylphosphonate (1.12 g, 4.25 mmol) and ketone **6** (1.00 g, 3.04 mmol); purified by column chromatography (hexane/EtOAc, 95:5), to give the olefin **7e** as an oil (906 mg, 68%). *R*_f = 0.71 (hexane/EtOAc, 9:1). ¹H NMR (300 MHz, CDCl₃): δ = 1.33 (t, ³*J* = 7.2 Hz, 3 H, OCH₂CH₃), 1.59–1.64 (m, 1 H, 7-H_A), 1.79–1.85 (m, 4 H, 6-H and NCH₂CH₂CH₂Ph), 2.06 (dd, ²*J* = 13.6, ³*J* = 4.4 Hz, 1 H, 8-H_A), 2.24 (dd, ²*J* = 11.2, ⁴*J* = 2.0 Hz, 1 H, 4-H_A), 2.28 (td, ³*J* = 6.8, *J* = 2.5 Hz, 2 H, NCH₂CH₂CH₂Ph), 2.39 (ddt, ²*J* = 11.5, ³*J* = 5.7, *J* = 2.8 Hz, 1 H, 8-H_B), 2.65–2.69 (m, 3 H, 2-H_A and NCH₂CH₂CH₂Ph), 2.75–2.94 (m, 3 H, 4-H_B, 5-H and 7-H_B), 3.14 (d, ²*J* = 10.4 Hz, 1 H, 2-H_B), 4.24 (td, ³*J* = 4.0, *J* = 2.0 Hz, 2 H, OCH₂CH₃), 6.08 (s, 1 H, CHAr), 7.13–7.37 (m, 9 H, ArH) ppm. ¹³C NMR (75.5 MHz, CDCl₃): δ = 14.2 (OCH₂CH₃), 21.3 (C-7), 28.8 (NCH₂CH₂CH₂Ph), 32.9 (C-6), 33.4 (C-5), 33.9 (NCH₂CH₂CH₂Ph), 36.1 (C-8), 51.2 (C-1), 57.2 (NCH₂CH₂H₂CPh), 60.4 (C-4), 60.6 (OCH₂CH₃), 62.6 (C-2), 116.9 (CHAr), 125.6, 126.2, 127.8, 128.2, 128.4, 129.2, 130.3 (CH_{arom.}), 134.0, 135.8, 142.3 (C_{arom.}), 146.5 (C-9), 174.3 (COOEt) ppm. IR (film): ν̄ = 2978 (s), 1722 (vs, C=O), 1651 (s), 1467 (s), 1245 (s), 1111 (s), 1091 (s), 740 (m), 698 (m) cm⁻¹. MS (EI, 70 eV): *m/z* (%) = 439 (7) [³⁷Cl, M⁺], 437 (15) [³⁵Cl, M⁺], 332 (100) [³⁵Cl, M⁺ – C₆H₅CH₂CH₂], and 91 (25) [C₆H₅CH₂]; found (M⁺, 437.21216), C₂₇H₃₂³⁵ClNO calcd. 437.21216; found (M⁺, 439.20876), C₂₇H₃₂³⁷ClNO calcd. 439.20921.

Ethyl (E)-9-(3-Methoxybenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonane-1-carboxylate (7f): Using 3-methoxybenzyl diethylphosphonate (1.03 g, 4.25 mmol) and ketone **6** (1.00 g, 3.04 mmol); purified by column chromatography (hexane/EtOAc, 95:5), to give the olefin **7f** as a pale yellow oil (197 mg, 15%). *R*_f = 0.48 (hexane/EtOAc, 95:5). ¹H NMR (300 MHz, CDCl₃): δ = 1.30 (t, ³*J* = 7.0 Hz, 3 H, OCH₂CH₃), 1.58–1.63 (m, 1 H, 7-H_A), 1.75–1.88 (m, 4 H, 6-H, NCH₂CH₂CH₂Ph), 2.04 (dd, *J* = 13.2, ²*J* = 5.0 Hz, 1 H, 8-H_A), 2.21–2.30 (m, 3 H, 4-H_A and NCH₂CH₂CH₂Ph), 2.38 (td, ²*J* = 9.8, *J* = 5.6 Hz, 1 H, 8-H_B), 2.64–2.73 (m, 3 H, 2-H_A and NCH₂CH₂CH₂Ph), 2.85–2.94 (m, 2 H, 4-H_B and 7-H_B), 3.07–3.12 (m, 2 H, 5-H and 2-H_B), 3.77 (s, 3 H, OCH₃), 4.22 (dd, ²*J* = 6.8, *J* = 1.8 Hz, 2 H, OCH₂CH₃), 6.06 (s, 1 H, CHAr), 6.73–6.82 (m, 3 H, ArH), 7.04–7.29 (m, 6 H, ArH) ppm. ¹³C NMR (75.5 MHz, CDCl₃): δ = 14.2 (OCH₂CH₃), 21.3 (C-7), 28.8 (NCH₂CH₂CH₂Ph), 33.0 (C-6), 33.4 (C-5), 33.6 (NCH₂CH₂CH₂Ph), 36.2 (C-8), 51.2 (C-1), 55.1 (OCH₃), 57.3 (NCH₂CH₂CH₂Ph), 60.4 (C-4), 60.5 (OCH₂CH₃), 62.6 (C-2), 111.7, 114.2 (CH_{arom.}), 118.9 (CHAr), 121.6, 125.6, 128.2 (2 ×), 128.4 (2 ×), 129.0 (CH_{arom.}), 138.9, 142.5 (C_{arom.}), 145.8 (C-9), 159.3 (ArC-OMe) 174.5 (COOEt) ppm. IR (film): ν̄ = 2921 (br), 1721 (vs, C=O), 1598 (s), 1452 (s), 1257 (vs), 1110 (s), 1047 (s), 735 (w), 694 (s) cm⁻¹. MS (EI, 70 eV): *m/z* (%) = 433 (30) [M⁺], 328 (100) [M⁺ – C₆H₅CH₂CH₂], 148 (21), (91) [C₆H₅CH₂]; found (M⁺, 433.26169), C₂₈H₃₅NO₃ calcd. 433.26152.

Ethyl (E)-9-(3-Methylbenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonane-1-carboxylate (7g): Using 3-methylbenzyl diethylphosphonate (1.03 g, 4.25 mmol) and ketone **6** (1.00 g, 3.04 mmol); purified by column chromatography (hexane/EtOAc, 95:5), to give the olefin **7g** as a pale yellow oil (123 mg, 10%). *R*_f = 0.35 (hexane/EtOAc, 95:5). ¹H NMR (300 MHz, CDCl₃): δ = 1.30 (t, ³*J* = 7.0 Hz, 3 H, OCH₂CH₃), 1.59–1.63 (m, 1 H, 7-H_A), 1.76–1.87 (m, 4 H, 6-H, NCH₂CH₂CH₂Ph), 2.03 (dd, *J* = 13.6, ²*J* = 5.2 Hz, 1 H,

8- H_A), 2.21–2.42 (m, 4 H, 4- H_A , 8- H_B and $NCH_2CH_2CH_2Ph$), 2.32 (s, 3 H, $ArCH_3$), 2.65–2.72 (m, 3 H, 2- H_A and $NCH_2CH_2CH_2Ph$), 2.83–2.94 (m, 2 H, 4- H_B and 7- H_B), 3.06–3.12 (m, 2 H, 5- H and 2- H_B), 4.22 (dd, $^2J = 6.8$, $J = 1.7$ Hz, 2 H, OCH_2CH_3), 6.05 (s, 1 H, $CHAr$), 6.97–7.32 (m, 9 H, ArH) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 14.2$ (OCH_2CH_3), 21.4 ($ArCH_3$), 21.4 (C-7), 28.9 ($NCH_2CH_2CH_2Ph$), 33.1 (C-6), 33.5 (C-5), 33.5 ($NCH_2CH_2CH_2Ph$), 36.2 (C-8), 51.3 (C-1), 57.3 ($NCH_2CH_2CH_2Ph$), 60.5 (C-4), 60.5 (OCH_2CH_3), 62.7 (C-2), 119.1 ($CHAr$), 123.6, 125.6, 127.0, 127.9, 128.2 (2 $\times$), 128.4 (2 $\times$), 129.4 ($CH_{arom.}$), 137.4, 137.6, 142.4 ($C_{arom.}$), 145.4 (C-9), 174.5 ($COOEt$) ppm. IR (film): $\tilde{\nu} = 2921$ (br), 1722 (vs, C=O), 1602 (s), 1453 (s), 1241 (vs), 1111 (s), 784 (w), 744 (w), 696 (s) cm^{-1} . MS (EI, 70 eV): m/z (%) = 417 (30) [M^+], 312 (100) [$M^+ - C_6H_5CH_2CH_2$], 148 (19), 91 (11) [$C_6H_5CH_2$], 44 (8); found (M^+ , 417.26678), $C_{28}H_{35}NO_2$ calcd. 417.26588.

Ethyl (E)-9-(4-Methylbenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonane-1-carboxylate (7h): Using 4-methylbenzyl diethylphosphonate (1.03 g, 5.46 mmol) and ketone **6** (1.00 g, 3.04 mmol); purified by column chromatography (hexane/EtOAc, 9:1), to give the olefin **7h** as a pale yellow oil (538 mg, 42%). $R_f = 0.70$ (hexane/EtOAc, 9:1). 1H NMR (300 MHz, $CDCl_3$): $\delta = 1.30$ (t, $^3J = 7.4$ Hz, 3 H, OCH_2CH_3), 1.58–1.61 (m, 1 H, 7- H_A), 1.75–1.86 (m, 4 H, 6- H , $NCH_2CH_2CH_2Ph$), 2.03 (dd, $J = 13.2$, $^2J = 5.2$ Hz, 1 H, 8- H_A), 2.21–2.41 (m, 4 H, 4- H_A , 8- H_B and $NCH_2CH_2CH_2Ph$), 2.32 (s, 3 H, $ArCH_3$), 2.64–2.71 (m, 3 H, 2- H_A and $NCH_2CH_2CH_2Ph$), 2.83–2.93 (m, 2 H, 4- H_B and 7- H_B), 3.06–3.11 (m, 2 H, 5- H and 2- H_B), 4.22 (dd, $^2J = 6.8$, $J = 1.8$ Hz, 2 H, OCH_2CH_3), 6.04 (s, 1 H, $CHAr$), 7.03–7.29 (m, 9 H, ArH) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 14.2$ (OCH_2CH_3), 21.3 ($ArCH_3$), 21.3 (C-7), 28.9 ($NCH_2CH_2CH_2Ph$), 33.1 (C-6), 33.5 (C-5), 33.5 ($NCH_2CH_2CH_2Ph$), 36.2 (C-8), 51.3 (C-1), 57.4 ($NCH_2CH_2CH_2Ph$), 60.5 (C-4), 60.7 (OCH_2CH_3), 62.7 (C-2), 118.9 ($CHAr$), 125.6, 128.3 (2 $\times$), 128.4 (2 $\times$), 128.6 (2 $\times$), 128.8 (2 $\times$, $CH_{arom.}$), 134.6, 135.8, 142.5 ($C_{arom.}$), 145.6 (C-9), 174.6 ($COOEt$) ppm. IR (film): $\tilde{\nu} = 2920$ (br), 1722 (vs, C=O), 1652 (s), 1453 (s), 1239 (vs), 1110 (s), 1084 (s), 804 (s), 784 (w), 744 (w), 698 (s) cm^{-1} . MS (EI, 70 eV): m/z (%) = 417 (8) [M^+], 312 (90) [$M^+ - C_6H_5CH_2CH_2$], 148 (28), 105 (44), 91 (100) [$C_6H_5CH_2$], 57 (27), 42 (44); found (M^+ , 417.26678), $C_{28}H_{35}NO_2$ calcd. 417.26673.

General Procedure for the Synthesis of Alcohols 8: Lithium aluminium hydride (2.0 equiv.) was added to a solution of the esters **7a–h** (1.0 equiv.) in dry THF (0.2 M), and the mixture was stirred for 30 min at room temperature. Excess $LiAlH_4$ was decomposed by cautiously adding a solution of KOH or NaOH in water (4.0–4.5 M, ca. 6.0 equiv.) until aluminium hydroxide precipitates. After stirring for 15 min the mixture was filtered through Celite and the remaining salts were further washed with EtOAc. The combined organic filtrates were dried ($MgSO_4$) and evaporated in vacuo to give the crude product which was purified by flash chromatography (in all cases using hexane/EtOAc, 8:2) to yield the desired alcohols **8a–h**.

(E)-9-(9-Benzylidene-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl)methanol (8a): According to the general $LiAlH_4$ reduction procedure, ester **7a** (895 mg, 2.22 mmol) gives the desired alcohol **8a** (790 mg, 99%) as a colourless oil. $R_f = 0.64$ (hexane/EtOAc, 8:2). 1H NMR (300 MHz, $CDCl_3$): $\delta = 1.46$ (br. s, 1 H, OH), 1.51–1.65 (m, 2 H, 7- H_A and 8- H_A), 1.70–2.01 (m, 5 H, 6- H , 8- H_B and $NCH_2CH_2CH_2Ph$), 2.12 (dd, $^2J = 10.5$, $^4J = 1.9$ Hz, 1 H, 2- H_A), 2.14–2.20 (m, 1 H, 4- H_A), 2.23 (t, $^3J = 7.0$ Hz, 2 H, $NCH_2CH_2CH_2Ph$), 2.67 (t, $^3J = 7.7$ Hz, 2 H, $NCH_2CH_2CH_2Ph$), 2.79–2.98 (m, 2 H, 4- H_B and 7- H_B), 2.99–3.09 (m, 2 H, 2- H_B and 5- H), 3.63 (d, $^2J = 10.9$ Hz, 1 H, CH_AH_BOH), 3.70 (d, $^2J = 10.9$ Hz, 1 H, CH_AH_BOH), 6.16 (s, 1 H, $CHAr$), 7.13–7.34 (m, 10 H, ArH)

ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 21.5$ (C-7), 28.9 ($NCH_2CH_2CH_2Ph$), 33.5 ($NCH_2CH_2CH_2Ph$), 33.7 (C-6), 34.1 (C-5), 36.7 (C-8), 42.4 (C-1), 57.6 ($NCH_2CH_2CH_2Ph$), 60.7 (C-4), 63.1 (C-2), 69.1 (CH_2OH), 117.0 ($CHAr$), 125.6, 126.1, 128.1, 128.3, 128.5, 128.6 ($CH_{arom.}$), 138.0, 142.6 ($C_{arom.}$), 148.3 (C-9) ppm. IR (film): $\tilde{\nu} = 3368$ (br., O-H), 3023 (w), 2920 (w), 2799 (w), 1648 (s), 1599 (s), 1494 (vs), 1452 (vs), 1372 (s), 1256 (s), 1029 (vs), 915 (w), 841 (w), 759 (s), 698 (m) cm^{-1} . MS (EI, 70 eV): m/z (%) = 361 (20) [M^+], 256 (100) [$M^+ - C_6H_5CH_2CH_2$], 148 (12), 91 (24) [$C_6H_5CH_2$], 44 (24); found (M^+ , 361.2400), $C_{25}H_{31}NO$ calcd. 361.2406.

(E)-9-(4-Chlorobenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl)methanol (8b): According to the general $LiAlH_4$ reduction procedure, ester **7b** (1.18 g, 2.69 mmol) gives the desired alcohol **8b** (1.04 g, 98%) as a colourless oil. $R_f = 0.18$ (hexane/EtOAc, 8:2). 1H NMR (300 MHz, $CDCl_3$): $\delta = 1.50$ –1.65 (m, 3 H, OH, 7- H_A and 8- H_A), 1.66–2.00 (m, 5 H, 6- H , 8- H_B and $NCH_2CH_2CH_2Ph$), 2.07–2.20 (m, 2 H, 2- H_A and 4- H_A), 2.24 (t, $^3J = 6.6$ Hz, 2 H, $NCH_2CH_2CH_2Ph$), 2.67 (t, $^3J = 7.7$ Hz, 2 H, $NCH_2CH_2CH_2Ph$), 2.77–3.07 (m, 4 H, 2- H_B , 4- H_B , 5- H and 7- H_B), 3.62 (d, $^2J = 10.9$ Hz, 1 H, CH_AH_BOH), 3.69 (d, $^2J = 10.9$ Hz, 1 H, CH_AH_BOH), 6.11 (s, 1 H, $CHAr$), 7.11 (d, $^3J = 8.3$ Hz, 2 H, ArH), 7.14–7.32 (m, 7 H, ArH) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 21.4$ (C-7), 28.9 ($NCH_2CH_2CH_2Ph$), 33.5 ($NCH_2CH_2CH_2Ph$), 33.7 (C-6), 34.0 (C-5), 36.6 (C-8), 42.4 (C-1), 57.5 ($NCH_2CH_2CH_2Ph$), 60.5 (C-4), 62.9 (C-2), 68.9 (CH_2OH), 116.0 ($CHAr$), 125.7, 128.2, 128.3, 128.4, 130.0 ($CH_{arom.}$), 131.8, 136.4, 142.5 ($C_{arom.}$), 149.2 (C-9) ppm. IR (film): $\tilde{\nu} = 3368$ (br., O-H), 3025 (s), 2918 (vs), 1646 (m), 1489 (vs), 1453 (s), 1372 (m), 1157 (m), 1089 (s), 1037 (m), 1014 (s), 872 (m), 811 (m), 751 (m), 699 (s) cm^{-1} . MS (EI, 70 eV): m/z (%) = 397 (5) [^{37}Cl , M^+], 395 (7) [^{35}Cl , M^+], 290 (100) [$M^+ - C_6H_5CH_2CH_2$], 148 (16), 91 (24) [$C_6H_5CH_2$]; found (M^+ , 395.20160), $C_{25}H_{30}^{35}ClNO$ calcd. 395.20159; found (M^+ , 397.19763), $C_{25}H_{30}^{37}ClNO$ calcd. 397.19864.

(E)-9-(4-Methoxybenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl)methanol (8c): According to the general $LiAlH_4$ reduction procedure, ester **7c** (280 mg, 647 μ mol) gives the desired alcohol **8c** (186 mg, 74%) as a colourless oil. $R_f = 0.21$ (hexane/EtOAc, 8:2). 1H NMR (400 MHz, $CDCl_3$): $\delta = 1.50$ –1.62 (m, 3 H, OH, 7- H_A and 8- H_A), 1.70–1.85 (m, 3 H, 6- H_A and $NCH_2CH_2CH_2Ph$), 1.86–1.99 (m, 2 H, 6- H_B and 8- H_B), 2.10 (d, $^2J = 10.1$ Hz, 1 H, 2- H_A), 2.17 (d, $^2J = 10.5$ Hz, 1 H, 4- H_A), 2.23 (t, $^3J = 6.3$ Hz, 2 H, $NCH_2CH_2CH_2Ph$), 2.67 (t, $^3J = 7.9$ Hz, 2 H, $NCH_2CH_2CH_2Ph$), 2.79–2.91 (m, 1 H, 7- H_B), 2.93 (d, $^2J = 10.5$ Hz, 1 H, 4- H_B), 3.01 (d, $^2J = 10.1$ Hz, 1 H, 2- H_B), 3.05 (br. s, 1 H, 5- H), 3.61 (d, $^2J = 10.9$ Hz, 1 H, CH_AH_BOH), 3.69 (d, $^2J = 10.9$ Hz, 1 H, CH_AH_BOH), 3.79 (s, 3 H, OCH_3), 6.10 (s, 1 H, $CHAr$), 6.85 (dd, $^3J = 8.7$, $^4J = 2.0$ Hz, 2 H, $m-ArH$), 7.11 (dd, $^3J = 8.7$, $^4J = 2.0$ Hz, 2 H, $o-ArH$), 7.15–7.30 (m, 5 H, ArH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 21.6$ (C-7), 28.9 ($NCH_2CH_2CH_2Ph$), 33.5 ($NCH_2CH_2CH_2Ph$), 33.7 (C-6), 34.0 (C-5), 36.7 (C-8), 42.3 (C-1), 55.2 (OCH_3), 57.6 ($NCH_2CH_2CH_2Ph$), 60.6 (C-4), 63.1 (C-2), 69.1 (CH_2OH), 113.5, 116.4, 125.6, 128.3, 128.5, 129.8 ($CH_{arom.}$), 130.4, 142.6 ($C_{arom.}$), 147.2 (C-9), 159.8 ($ArC-OMe$) ppm. IR (film): $\tilde{\nu} = 3400$ (br., O-H), 3025 (w), 2931 (s), 1606 (s), 1509 (vs), 1453 (s), 1246 (vs), 1176 (s), 1035 (s), 748 (w), 699 (s) cm^{-1} . MS (EI, 70 eV): m/z (%) = 391 (29) [M^+], 286 (100) [$M^+ - C_6H_5CH_2CH_2$], 148 (19), 121 (31) [C_7H_6OMe], 91 (14) [$C_6H_5CH_2$]; found (M^+ , 391.2508), $C_{26}H_{33}NO_2$ calcd. 391.2511.

(E)-9-(2-Chlorobenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl)methanol (8d): According to the general $LiAlH_4$ reduction procedure, ester **7d** (1.40 g, 3.20 mmol) gives the desired alcohol **8d** (1.15 g, 90%) as a colourless oil. $R_f = 0.20$ (hexane/

EtOAc, 8:2). ^1H NMR (300 MHz, CDCl_3): δ = 1.56–1.62 (m, 3 H, OH, 7- H_A and 8- H_A), 1.67–1.99 (m, 5 H, 6-H, 8- H_B and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.04–2.18 (m, 2 H, 2- H_A and 4- H_A), 2.24 (t, 3J = 6.9 Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.67 (t, 3J = 7.7 Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.81–3.05 (m, 4 H, 2- H_B , 4- H_B , 5-H and 7- H_B), 3.70 (d, 2J = 10.8 Hz, 2 H, CH_2OH), 6.13 (s, 1 H, CHAr), 7.14–7.38 (m, 9 H, ArH) ppm. ^{13}C NMR (75.5 MHz, CDCl_3): δ = 21.1 (C-7), 28.6 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.5 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.6 (C-6), 34.3 (C-5), 36.6 (C-8), 42.4 (C-1), 57.6 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 60.3 (C-4), 62.6 (C-2), 68.8 (CH_2OH), 115.2 (CHAr), 125.7, 126.3, 127.8, 128.3 (2 $\times$), 128.4 (2 $\times$), 129.4, 130.4 ($\text{CH}_{\text{arom.}}$), 133.9, 139.9, 142.5 ($\text{C}_{\text{arom.}}$), 148.8 (C-9) ppm. IR (film): $\tilde{\nu}$ = 3387 (br., O-H), 2920 (vs), 1649 (m), 1467 (vs), 1452 (s), 1255 (m), 1052 (m), 1038 (s), 1032 (m), 908 (m), 731 (m), 698 (s) cm^{-1} . MS (EI, 70 eV): m/z (%) = 397 (6) [^{37}Cl , M^+], 395 (15) [^{35}Cl , M^+], 290 (100) [^{35}Cl , $\text{M}^+ - \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2$], 91 (35) [$\text{C}_6\text{H}_5\text{CH}_2$] and 44 (28); found (M^+ , 395.20075), $\text{C}_{25}\text{H}_{30}^{35}\text{ClNO}$ calcd. 395.20159; found (M^+ , 397.19960), $\text{C}_{25}\text{H}_{30}^{37}\text{ClNO}$ calcd. 397.19864.

(E)-{9-(3-Chlorobenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl}methanol (8e): According to the general LiAlH_4 reduction procedure, ester **7e** (500 mg, 1.14 mmol) gives the desired alcohol **8e** (430 mg, 95%) as a colourless oil. R_f = 0.21 (hexane/EtOAc, 8:2). ^1H NMR (300 MHz, CDCl_3): δ = 1.56–1.68 (m, 3 H, OH, 7- H_A and 8- H_A), 1.72–2.04 (m, 5 H, 6-H, 8- H_B and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.04–2.26 (m, 4 H, 2- H_A , 4- H_A and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.67 (t, 3J = 7.7 Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.75–3.08 (m, 4 H, 2- H_B , 4- H_B , 5-H and 7- H_B), 3.65 (d, 2J = 10.8 Hz, 2 H, CH_2OH), 6.11 (s, 1 H, CHAr), 7.11 (d, J = 7.6 Hz, 1 H, ArH), 7.16–7.30 (m, 8 H, ArH) ppm. ^{13}C NMR (75.5 MHz, CDCl_3): δ = 21.5 (C-7), 28.9 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.5 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.7 (C-6), 34.2 (C-5), 36.6 (C-8), 42.4 (C-1), 57.5 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 60.6 (C-4), 63.0 (C-2), 69.0 (CH_2OH), 115.9 (CHAr), 125.7, 126.2, 126.9, 128.3 (2 $\times$), 128.5 (2 $\times$), 128.8, 129.3 ($\text{CH}_{\text{arom.}}$), 133.9, 139.9, 142.5 ($\text{C}_{\text{arom.}}$), 148.9 (C-9) ppm. IR (film): $\tilde{\nu}$ = 3347 (br., O-H), 2977 (vs), 1649 (m), 1471 (vs), 1263 (m), 1157 (m), 1077 (s), 1038 (m), 782 (m), 736 (m), 697 (s) cm^{-1} . MS (EI, 70 eV): m/z (%) = 397 (5) [^{37}Cl , M^+], 395 (15) [^{35}Cl , M^+], 290 (100) [^{35}Cl , $\text{M}^+ - \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2$], 91 (29) [$\text{C}_6\text{H}_5\text{CH}_2$], 44 (33); found (M^+ , 395.20129), $\text{C}_{25}\text{H}_{30}^{35}\text{ClNO}$ calcd. 395.20159; found (M^+ , 397.19849), $\text{C}_{25}\text{H}_{30}^{37}\text{ClNO}$ calcd. 397.19864.

(E)-{9-(3-Methoxybenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl}methanol (8f): According to the general LiAlH_4 reduction procedure, ester **7f** (170 mg, 390 μmol) gives the desired alcohol **8f** (146 mg, 95%) as a colourless oil. R_f = 0.21 (hexane/EtOAc, 8:2). ^1H NMR (400 MHz, CDCl_3): δ = 1.53–1.59 (m, 3 H, OH, 7- H_A and 8- H_A), 1.73–1.81 (m, 3 H, 6- H_A and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 1.87–1.98 (m, 2 H, 6- H_B and 8- H_B), 2.11–2.24 (m, 4 H, 2- H_A , 4- H_A and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.66 (t, 3J = 7.8 Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.83–2.94 (m, 2 H, 7- H_B and 4- H_B), 3.01–3.06 (m, 2 H, 2- H_B and 5-H), 3.62 (d, 2J = 8.9 Hz, 2 H, CH_2OH), 3.77 (s, 3 H, OCH_3), 6.12 (s, 1 H, CHAr), 6.73–6.82 (m, 3 H, ArH), 7.04–7.28 (m, 6 H, ArH) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 21.4 (C-7), 28.8 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.4 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.7 (C-6), 34.1 (C-5), 36.6 (C-8), 42.2 (C-1), 55.1 (OCH_3), 57.5 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 60.6 (C-4), 63.0 (C-2), 68.9 (CH_2OH), 111.7, 114.3 ($\text{CH}_{\text{arom.}}$), 116.9 (CHAr), 121.2, 125.6, 128.3 (2 $\times$), 128.4 (2 $\times$), 129.5 ($\text{CH}_{\text{arom.}}$), 139.4, 142.5 ($\text{C}_{\text{arom.}}$), 148.4 (C-9) 159.3 (ArC-OMe) ppm. IR (film): $\tilde{\nu}$ = 3383 (br., O-H), 2920 (s), 1651 (s), 1597 (vs), 1452 (s), 1259 (vs), 1157 (s), 1040 (s), 779 (w), 746 (w), 694 (s) cm^{-1} . MS (EI, 70 eV): m/z (%) = 392 (16) [MH^+], 307 (18) [$\text{MH}^+ - \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2$], 154 (100), 136 (70), 107 (24), 89 (22), 77 (24); found (MH^+ , 392.25895), $\text{C}_{26}\text{H}_{34}\text{NO}_2$ calcd. 392.25917.

(E)-{9-(3-Methylbenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl}methanol (8g): According to the general LiAlH_4 reduction procedure, ester **7g** (100 mg, 240 μmol) gives the desired alcohol **8g** (82 mg, 91%) as a colourless oil. R_f = 0.19 (hexane/EtOAc, 8:2). ^1H NMR (400 MHz, CDCl_3): δ = 1.55–1.61 (m, 3 H, OH, 7- H_A and 8- H_A), 1.73–1.98 (m, 5 H, 6- H_B , 8- H_B , 6- H_A and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.10–2.25 (m, 4 H, 2- H_A , 4- H_A and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.33 (s, 3 H, ArCH_3), 2.67 (t, 3J = 7.6 Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.84–2.94 (m, 2 H, 7- H_B and 4- H_B), 3.01–3.06 (m, 2 H, 2- H_B and 5-H), 3.66 (d, 2J = 8.9 Hz, 2 H, CH_2OH), 6.12 (s, 1 H, CHAr), 6.98–7.32 (m, 9 H, ArH) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 21.4 (ArCH_3), 21.5 (C-7), 28.9 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.5 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.7 (C-6), 34.0 (C-5), 36.7 (C-8), 42.3 (C-1), 57.6 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 60.6 (C-4), 63.0 (C-2), 69.0 (CH_2OH), 117.0 (CHAr), 125.6, 125.7, 126.8, 128.0, 128.3 (2 $\times$), 128.4 (2 $\times$), 129.5 ($\text{CH}_{\text{arom.}}$), 137.6, 137.9, 142.5 ($\text{C}_{\text{arom.}}$), 148.0 (C-9) ppm. IR (film): $\tilde{\nu}$ = 3383 (br., O-H), 2920 (s), 1651 (s), 1597 (vs), 1452 (s), 1259 (vs), 1157 (s), 1040 (s), 779 (w), 746 (w), 694 (s) cm^{-1} . MS (EI, 70 eV): m/z (%) = 392 (16) [MH^+], 307 (18) [$\text{MH}^+ - \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2$], 154 (100), 136 (70), 107 (24), 89 (22), 77 (24); found (MH^+ , 392.25895), $\text{C}_{26}\text{H}_{34}\text{NO}_2$ calcd. 392.25917.

(E)-{9-(4-Methylbenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl}methanol (8h): According to the general LiAlH_4 reduction procedure, ester **7g** (600 mg, 1.44 mmol) gives the desired alcohol **8h** (407 mg, 75%) as a colourless oil. R_f = 0.20 (hexane/EtOAc, 8:2). ^1H NMR (400 MHz, CDCl_3): δ = 1.52–1.59 (m, 3 H, OH, 7- H_A and 8- H_A), 1.72–1.95 (m, 5 H, 6- H_B , 8- H_B , 6- H_A and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.12–2.29 (m, 4 H, 2- H_A , 4- H_A and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.34 (s, 3 H, ArCH_3), 2.67 (t, 3J = 7.6 Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.77–3.09 (m, 4 H, 7- H_B , 4- H_B , 2- H_B and 5-H), 3.66 (d, 2J = 8.9 Hz, 2 H, CH_2OH), 6.15 (s, 1 H, CHAr), 7.05–7.29 (m, 9 H, ArH) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 21.1 (ArCH_3), 21.3 (C-7), 28.6 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.4 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.4 (C-6), 33.5 (C-5), 36.6 (C-8), 42.2 (C-1), 57.7 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 60.4 (C-4), 62.7 (C-2), 68.8 (CH_2OH), 116.9 (CHAr), 125.7, 128.3 (2 $\times$), 128.4 (2 $\times$), 128.6 (2 $\times$), 128.8 (2 $\times$, $\text{CH}_{\text{arom.}}$), 134.9, 135.8, 142.5 ($\text{C}_{\text{arom.}}$), 149.8 (C-9) ppm. IR (film): $\tilde{\nu}$ = 3336 (br., O-H), 2922 (s), 1646 (s), 1452 (s), 1253 (vs), 1043 (s), 908 (w), 728 (w), 698 (s) cm^{-1} . MS (EI, 70 eV): m/z (%) = 375 (17%) [M^+], 270 (100) [$\text{M}^+ - \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2$], 148 (16), 105 (32), 91 (45) [$\text{C}_6\text{H}_5\text{CH}_2$], 44 (46); found (M^+ , 375.25621), $\text{C}_{28}\text{H}_{33}\text{NO}$ calcd. 375.25593.

General Procedure for the Synthesis of Esters 10: To a solution of alcohols **8a–h** (1.0 equiv.) in dichloromethane (0.1 M) were added benzoic acid **9** (2.0 equiv.) and 4-(dimethylamino)pyridine (0.1 equiv.) and the solution placed under nitrogen. Dicyclohexylcarbodiimide (2.0 equiv.) was added, and the mixture stirred under nitrogen at room temperature overnight. The mixture was filtered through Celite and the solvent removed in vacuo. The residue was dissolved in ethyl acetate, washed with saturated NaHCO_3 and brine, dried (Na_2SO_4), filtered and the solvent removed in vacuo. The crude product was purified by flash chromatography to yield the desired esters **10a–e**.

(E)-{9-Benzylidene-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl}methyl 2-(3-Methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)benzoate (10a): According to the general esterification procedure, alcohol **8a** (361 mg, 1.00 mmol) gives the desired ester **10a** (436 mg, 76%) as an oil. R_f = 0.29 (hexane/EtOAc, 8:2). ^1H NMR (400 MHz, CDCl_3): δ = 1.53–1.69 (m, 2 H, 7- H_A and 8- H_A), 1.74–1.85 (m, 3 H, 6- H_A and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 1.87–1.95 (m, 1 H, 6- H_B), 2.05–2.30 (m, 5 H, 2- H_A , 4- H_A , 8- H_B and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.17 (d,

$^4J = 2.0$ Hz, 3 H, Me), 2.68 (t, $^3J = 7.9$ Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.82–2.98 (m, 1 H, 7- H_B), 2.96 (d, $^2J = 10.6$ Hz, 1 H, 4- H_B), 3.06–3.12 (m, 2 H, 2- H_B and 5-H), 4.28 (s, 2 H, CH_2O), 6.14 (s, 1 H, CHAr), 6.49 (q, $^4J = 2.0$ Hz, 1 H, 4'-H), 7.15–7.36 (m, 11 H, 6'-H and $\text{CH}_{\text{arom.}}$), 7.52 (td, $^3J = 7.5$, $^4J = 1.5$ Hz, 1 H, 5'-H), 7.66 (td, $^3J = 7.5$, $^4J = 1.5$ Hz, 1 H, 4'-H), 8.11 (dd, $^3J = 7.5$, $^4J = 1.5$ Hz, 1 H, 3'-H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 11.2$ (Me), 21.4 (C-7), 28.9 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.5 (C-6 and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.9 (C-5), 36.9 (C-8), 41.2 (C-1), 57.4 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 60.4 (C-4), 63.4 (C-2), 70.9 (CH_2O), 117.4 (CHAr), 125.7, 126.2, 128.0 ($\times 2$), 128.1 ($\text{CH}_{\text{arom.}}$), 128.3 (C-4'), 128.5 ($\text{CH}_{\text{arom.}}$), 128.7 (C-1'), 129.0, 130.5, 131.4 ($\text{CH}_{\text{arom.}}$), 131.9 (C-2'), 133.3 ($\text{CH}_{\text{arom.}}$), 137.8, 142.6 ($\text{C}_{\text{arom.}}$), 146.2 (C-3'), 147.1 (C-9), 164.8 (COO), 169.7 (C-5'), 170.8 (C-2') ppm. IR (film): $\tilde{\nu} = 3024$ (w), 2922 (m), 1713 (vs, C=O), 1644 (w), 1601 (w), 1494 (m), 1454 (m), 1394 (s), 1261 (s), 1108 (s), 1086 (m), 857 (w), 736 (m), 699 (s) cm^{-1} . MS (EI, 70 eV): m/z (%) = 574 (22) [M^+], 469 (100) [$\text{M}^+ - \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2$], 382 (13), 344 (24), 214 (23) [$\text{M}^+ - \text{C}_{12}\text{H}_8\text{NO}_3$], 91 (36) [$\text{C}_6\text{H}_5\text{CH}_2$]; found (M^+ , 574.2832), $\text{C}_{37}\text{H}_{38}\text{N}_2\text{O}_4$ calcd. 574.2832.

(E)-{9-(4-Chlorobenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl}methyl 2-(3-Methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)benzoate (10b): According to the general esterification procedure, alcohol **8b** (913 mg, 2.31 mmol) gives the desired ester **10b** (795 mg, 57%) as a pale yellow oil. $R_f = 0.29$ (hexane/EtOAc, 8:2). ^1H NMR (300 MHz, CDCl_3): $\delta = 1.55$ – 1.75 (m, 2 H, 7- H_A and 8- H_A), 1.75– 1.88 (m, 3 H, 6- H_A and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 1.89– 2.00 (m, 1 H, 6- H_B), 2.05– 2.35 (m, 5 H, 2- H_A , 4- H_A , 8- H_B and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.18 (d, $^4J = 1.8$ Hz, 3 H, Me), 2.70 (t, $^3J = 7.9$ Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.82– 3.07 (m, 2 H, 5-H and 7- H_B), 2.99 (d, $^2J = 11.4$ Hz, 1 H, 4- H_B), 3.11 (d, $^2J = 10.6$ Hz, 1 H, 2- H_B), 4.29 (s, 2 H, CH_2O), 6.11 (s, 1 H, CHAr), 6.51 (q, $^4J = 1.8$ Hz, 1 H, 4'-H), 7.12 (d, $^3J = 8.4$ Hz, 2 H, m -ArH), 7.16– 7.39 (m, 8 H, 6'-H, o -ArH and Ph), 7.53 (td, $^2J = 7.7$, $^4J = 1.7$ Hz, 1 H, 5-H), 7.68 (td, $^2J = 7.7$, $^4J = 1.7$ Hz, 1 H, 4'-H), 8.13 (dd, $^2J = 7.7$, $^4J = 1.7$ Hz, 1 H, 3'-H) ppm. ^{13}C NMR (75.4 MHz, CDCl_3): $\delta = 11.2$ (Me), 21.3 (C-7), 28.8 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.4 (C-6), 33.5 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.9 (C-5), 36.8 (C-8), 41.2 (C-1), 57.3 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 60.3 (C-4), 63.2 (C-2), 70.6 (CH_2O), 116.3 (CHAr), 125.6 (p -Ph), 127.9, 128.3 ($\text{CH}_{\text{arom.}}$), 128.4 (C-4'), 128.9 ($\text{CH}_{\text{arom.}}$), 129.0 (C-1'), 130.0, 130.4, 131.3 ($\text{CH}_{\text{arom.}}$), 131.9 (C-2'), 133.3 ($\text{CH}_{\text{arom.}}$), 136.2, 142.4 ($\text{C}_{\text{arom.}}$), 146.2 (C-3'), 148.0 (C-9), 164.7 (COO), 169.7 (C-5'), 170.7 (C-2') ppm. IR (film): $\tilde{\nu} = 3015$ (w), 2923 (s), 1713 (vs, C=O), 1490 (s), 1452 (s), 1395 (s), 1259 (s), 1108 (s), 909 (s), 732 (vs) cm^{-1} . MS (FAB): m/z (%) = 609 (65) [$\text{M}^+ + \text{H}$], 503 (47) [$\text{M}^+ - \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2$], 378 (29), 214 (64) [$\text{M}^+ - \text{C}_{12}\text{H}_8\text{NO}_3$], 125 (22), 91 (100) [$\text{C}_6\text{H}_5\text{CH}_2$]; found (MH^+ , 609.2519), $\text{C}_{37}\text{H}_{38}^{35}\text{ClN}_2\text{O}_4$ calcd. 609.2520.

(E)-{9-(4-Methoxybenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl}methyl 2-(3-Methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)benzoate (10c): According to the general esterification procedure, alcohol **8c** (174 mg, 445 μmol) gives the desired ester **10c** (157 mg, 58%) as a pale yellow oil. $R_f = 0.23$ (hexane/EtOAc, 8:2). ^1H NMR (400 MHz, CDCl_3): $\delta = 1.52$ – 1.67 (m, 2 H, 7- H_A and 8- H_A), 1.74– 1.84 (m, 3 H, 6- H_A and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 1.87– 1.95 (m, 1 H, 6- H_B), 2.05– 2.13 (m, 2 H, 2- H_A and 8- H_B), 2.16 (d, $^4J = 1.9$ Hz, 3 H, Me), 2.16– 2.30 (m, 3 H, 4- H_A and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.67 (t, $^3J = 7.9$ Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.82– 2.97 (m, 1 H, 7- H_B), 2.96 (d, $^2J = 10.4$ Hz, 1 H, 4- H_B), 3.06– 3.11 (m, 2 H, 2- H_B and 5-H), 3.79 (s, 3 H, OCH_3), 4.27 (s, 2 H, CH_2O), 6.07 (s, 1 H, CHAr), 6.49 (q, $^4J = 1.9$ Hz, 1 H, 4'-H), 6.85 (d, $^3J = 8.8$ Hz, 2 H, m -ArH), 7.10 (d, $^3J = 8.8$ Hz, 2 H, o -ArH), 7.15– 7.30 (m, 5 H, ArH), 7.12 (dd, $^3J = 7.9$, $^4J = 1.5$ Hz, 1 H, 6'-H), 7.51 (td, $^3J =$

7.9 , $^4J = 1.5$ Hz, 1 H, 5'-H), 7.66 (td, $^3J = 7.9$, $^4J = 1.5$ Hz, 1 H, 4'-H), 8.11 (dd, $^3J = 7.9$, $^4J = 1.5$ Hz, 1 H, 3'-H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 11.2$ (Me), 21.4 (C-7), 28.9 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.4 (C-6), 33.5 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.8 (C-5), 36.8 (C-8), 41.1 (C-1), 55.2 (OCH_3), 57.4 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 60.3 (C-4), 63.3 (C-2), 70.9 (CH_2O), 113.5 (m -Ar), 116.8 (CHAr), 125.6 (p -Ph), 127.9 (C-4'), 128.0 (C-1'), 128.2, 128.4, 129.0, 129.8 ($\text{CH}_{\text{arom.}}$), 130.2 ($\text{C}_{\text{arom.}}$), 130.4, 131.4 ($\text{CH}_{\text{arom.}}$), 131.9 (C-2'), 133.3 ($\text{CH}_{\text{arom.}}$), 142.5 ($\text{C}_{\text{arom.}}$), 146.0 (C-3'), 146.2 (C-9), 157.9 (ArC-OMe), 164.8 (COO), 169.7 (C-5'), 170.7 (C-2') ppm. IR (film): $\tilde{\nu} = 3026$ (w), 2933 (s), 1713 (vs, C=O), 1605 (w), 1509 (s), 1453 (w), 1395 (s), 1249 (s), 1108 (s), 1034 (w), 910 (s), 732 (s) cm^{-1} . MS (FAB): m/z (%) = 605 (21) [MH^+], 499 (5) [$\text{M}^+ - \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2$], 307 (23), 154 (100), 136 (67), 107 (21) [$\text{C}_6\text{H}_7\text{OMe}$], 77 (22) [C_6H_5]; found (MH^+ , 605.3023), $\text{C}_{38}\text{H}_{41}\text{N}_2\text{O}_5$ calcd. 605.3016.

(E)-{9-(2-Chlorobenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl}methyl 2-(3-Methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)benzoate (10d): According to the general esterification procedure, alcohol **8d** (1.1 g, 2.778 mmol) gives the desired ester **10d** (901 mg, 53%) as a pale yellow oil. $R_f = 0.29$ (hexane/EtOAc, 8:2). ^1H NMR (300 MHz, CDCl_3): $\delta = 1.57$ – 1.62 (m, 2 H, 7- H_A and 8- H_A), 1.67– 1.83 (m, 3 H, 6- H_A and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 1.86– 1.91 (m, 1 H, 6- H_B), 2.04– 2.30 (m, 5 H, 2- H_A , 4- H_A , 8- H_B and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.17 (d, $^4J = 1.9$ Hz, 3 H, Me), 2.69 (t, $^3J = 7.7$ Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.84– 2.93 (m, 2 H, 5-H and 7- H_B), 2.94 (d, $^2J = 10.8$ Hz, 1 H, 4- H_B), 3.08 (d, $^2J = 10.5$ Hz, 1 H, 2- H_B), 4.31 (s, 2 H, CH_2O), 6.14 (s, 1 H, CHAr), 6.50 (q, $^4J = 1.8$ Hz, 1 H, 4'-H), 7.13– 7.39 (m, 10 H, 6'-H and ArH), 7.50 (td, $^2J = 7.5$, $^4J = 1.2$ Hz, 1 H, 5'-H), 7.66 (td, $^2J = 7.5$, $^4J = 1.5$ Hz, 1 H, 4'-H), 8.19 (dd, $^2J = 8.4$, $^4J = 1.5$ Hz, 1 H, 3'-H) ppm. ^{13}C NMR (75.4 MHz, CDCl_3): $\delta = 11.2$ (Me), 21.3 (C-7), 28.8 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.3 (C-6), 33.4 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 34.4 (C-5), 36.7 (C-8), 41.4 (C-1), 57.5 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 60.3 (C-4), 63.1 (C-2), 70.3 (CH_2O), 114.4 (CHAr), 125.7, 126.3 ($\text{CH}_{\text{arom.}}$), 127.7 (C-1'), 127.8, 127.9, 128.3 ($\times 2$), 128.4 ($\times 2$, $\text{CH}_{\text{arom.}}$), 128.4 (C-4'), 128.9, 129.3, 130.4, 131.6 ($\text{CH}_{\text{arom.}}$), 131.9 (C-2'), 133.3 ($\text{CH}_{\text{arom.}}$), 134.0, 136.3, 142.4 ($\text{C}_{\text{arom.}}$), 146.2 (C-3'), 148.0 (C-9), 164.6 (COO), 169.7 (C-5'), 170.8 (C-2') ppm. IR (film): $\tilde{\nu} = 2978$ (w), 2921 (s), 1709 (s), 1494 (s), 1452 (s), 1393 (s), 1255 (s), 1106 (s), 1083 (s), 755 (s), 735 (s), 698 (vs) cm^{-1} . MS (EI, 70 eV): m/z (%) = 610 (8) [^{37}Cl , M^+], 608 (16) [^{35}Cl , M^+], 503 (82) [^{35}Cl , $\text{M}^+ - \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2$], 378 (25), 214 (100) [$\text{M}^+ - \text{C}_{12}\text{H}_8\text{NO}_3$], 91 (74) [$\text{C}_6\text{H}_5\text{CH}_2$]; found (M^+ , 608.24204), $\text{C}_{37}\text{H}_{37}^{35}\text{ClN}_2\text{O}_4$ calcd. 608.24419; found (M^+ , 610.23934), $\text{C}_{37}\text{H}_{37}^{37}\text{ClN}_2\text{O}_4$ 610.24124.

(E)-{9-(3-Chlorobenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl}methyl 2-(3-Methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)benzoate (10e): According to the general esterification procedure, alcohol **8d** (169 mg, 430 μmol) gives the desired ester **10e** (156 mg, 60%) as a pale yellow oil. $R_f = 0.40$ (hexane/EtOAc, 8:2). ^1H NMR (300 MHz, CDCl_3): $\delta = 1.56$ – 1.66 (m, 2 H, 7- H_A and 8- H_A), 1.75– 1.82 (m, 3 H, 6- H_A and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 1.90– 1.95 (m, 1 H, 6- H_B), 2.03– 2.30 (m, 5 H, 2- H_A , 4- H_A , 8- H_B and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.16 (d, $^4J = 1.8$ Hz, 3 H, Me), 2.67 (t, $^3J = 7.6$ Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.83– 2.96 (m, 2 H, 4- H_B and 7- H_B), 3.08 (d, $^2J = 8.4$ Hz, 2 H, 5-H and 2- H_B), 4.25 (s, 2 H, CH_2O), 6.08 (s, 1 H, CHAr), 6.49 (q, $^4J = 1.8$ Hz, 1 H, 4'-H), 7.04 (d, $^4J = 7.6$ Hz, 1 H, ArH), 7.16– 7.36 (m, 9 H, 6'-H and ArH), 7.51 (td, $^2J = 5.6$, $^4J = 1.0$ Hz, 1 H, 5-H), 7.65 (td, $^2J = 7.6$, $^4J = 1.6$ Hz, 1 H, 4'-H), 8.19 (dd, $^2J = 8.0$, $^4J = 1.2$ Hz, 1 H, 3'-H) ppm. ^{13}C NMR (75.4 MHz, CDCl_3): $\delta = 11.1$ (Me), 20.9 (C-7), 28.8 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.4 (C-6), 33.4 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.9 (C-5), 36.8 (C-8), 41.2 (C-1), 57.3 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 60.3 (C-4), 63.2

(C-2), 70.6 (CH₂O), 116.2 (CHAr), 125.6, 126.2 (CH_{arom.}), 126.9 (C-1'), 127.9, 128.3 (2×), 128.4 (2×, CH_{arom.}), 128.5 (C-4''), 128.9, 129.3, 130.4, 131.2 (CH_{arom.}), 131.9 (C-2'), 133.3 (CH_{arom.}), 133.9, 139.6, 142.4 (C_{arom.}), 146.2 (C-3''), 148.6 (C-9), 164.7 (COO), 169.6 (C-5''), 171.0 (C-2'') ppm. IR (film): $\tilde{\nu}$ = 2921 (s), 1709 (s), 1391 (s), 1254 (s), 1105 (s), 754 (s), 697 (vs) cm⁻¹. MS (FAB): *m/z* (%) = 611 (3) [³⁷Cl, MH⁺], 609 (5) [³⁵Cl, MH⁺], 307 (21), 154 (100), 136 (70), 107 (25), 89 (22), 77 (22); found (MH⁺, 609.25201), C₃₇H₃₇³⁵ClN₂O₄ calcd. 609.25197; found (MH⁺, 611.25089), C₃₇H₃₇³⁷ClN₂O₄ requires 611.25004.

(E)-{9-(3-Methoxybenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl}methyl 2-(3-Methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)benzoate (10f): According to the general esterification procedure, alcohol **8f** (130 mg, 330 μmol) gives the desired ester **10f** (165 mg, 82%) as a white foam. *R*_f = 0.25 (hexane/EtOAc, 8:2). ¹H NMR (300 MHz, CDCl₃): δ = 1.53–1.67 (m, 2 H, 7-H_A and 8-H_A), 1.75–1.82 (m, 3 H, 6-H_A and NCH₂CH₂CH₂Ph), 1.89–1.92 (m, 1 H, 6-H_B), 2.07–2.28 (m, 5 H, 2-H_A, 4-H_A, 8-H_B and NCH₂CH₂CH₂Ph), 2.16 (d, ⁴*J* = 1.6 Hz, 3 H, Me), 2.67 (t, ³*J* = 7.8 Hz, 2 H, NCH₂CH₂CH₂Ph), 2.86–2.97 (m, 2 H, 4-H_B and 7-H_B), 3.09 (d, ²*J* = 10.4 Hz, 2 H, 5-H and 2-H_B), 3.78 (s, 3 H, OCH₃), 4.32 (s, 2 H, CH₂O), 6.11 (s, 1 H, CHAr), 6.48 (q, ⁴*J* = 1.6 Hz, 1 H, 4'-H), 6.72–6.78 (m, 3 H, ArH), 7.15–7.33 (m, 7 H, 6'-H and ArH), 7.51 (td, ²*J* = 7.6, ⁴*J* = 0.4 Hz, 1 H, 5-H), 7.65 (td, ²*J* = 7.6, ⁴*J* = 1.6 Hz, 1 H, 4'-H), 8.11 (dd, ²*J* = 8.8, ⁴*J* = 1.2 Hz, 1 H, 3'-H) ppm. ¹³C NMR (75.4 MHz, CDCl₃): δ = 11.2 (Me), 21.4 (C-7), 28.8 (NCH₂CH₂CH₂Ph), 33.4 (C-6), 33.4 (NCH₂CH₂CH₂Ph), 33.9 (C-5), 36.8 (C-8), 41.1 (C-1), 55.1 (OCH₃), 57.3 (NCH₂CH₂CH₂Ph), 60.3 (C-4), 63.3 (C-2), 70.8 (CH₂O), 111.7, 114.3 (CH_{arom.}), 117.2 (CHAr), 121.2, 125.6, 127.9 (CH_{arom.}), 127.9 (C-1'), 128.2 (2×), 128.4 (2×), 128.9 (CH_{arom.}), 129.0 (C-4''), 130.4, 131.3 (CH_{arom.}), 131.9 (C-2'), 133.2 (CH_{arom.}), 139.2, 142.5 (C_{arom.}), 146.2 (C-3''), 147.3 (C-9), 159.3 (ArC-OMe), 164.8 (COO), 169.7 (C-5''), 170.7 (C-2'') ppm. IR (film): $\tilde{\nu}$ = 2925 (s), 1708 (s), 1392 (s), 1254 (s), 1105 (s), 1083 (s), 754 (s), 728 (s), 695 (vs) cm⁻¹. MS (FAB): *m/z* (%) = 605 (15) [MH⁺], 307 (20), 154 (100), 136 (70), 107 (22), 91 (21) [C₆H₅CH₂], 77 (22); found (MH⁺, 605.30155), C₃₈H₄₁N₂O₅ calcd. 605.30101.

(E)-{9-(3-Methylbenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl}methyl 2-(3-Methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)benzoate (10g): According to the general esterification procedure, alcohol **8g** (80 mg, 200 μmol) gives the desired ester **10g** (76 mg, 63%) as a pale yellow oil. *R*_f = 0.28 (hexane/EtOAc, 8:2). ¹H NMR (300 MHz, CDCl₃): δ = 1.56–1.66 (m, 2 H, 7-H_A and 8-H_A), 1.75–1.82 (m, 3 H, 6-H_A and NCH₂CH₂CH₂Ph), 1.89–1.92 (m, 1 H, 6-H_B), 2.07–2.31 (m, 5 H, 2-H_A, 4-H_A, 8-H_B and NCH₂CH₂CH₂Ph), 2.16 (d, ⁴*J* = 1.6 Hz, 3 H, Me), 2.33 (s, 3 H, ArCH₃), 2.68 (t, ³*J* = 7.6 Hz, 2 H, NCH₂CH₂CH₂Ph), 2.85–2.97 (m, 2 H, 4-H_B and 7-H_B), 3.08–3.10 (m, 2 H, 5-H and 2-H_B), 4.27 (s, 2 H, CH₂O), 6.11 (s, 1 H, CHAr), 6.47 (q, ⁴*J* = 1.6 Hz, 1 H, 4'-H), 6.97–7.02 (m, 3 H, ArH), 7.14–7.35 (m, 7 H, 6'-H and ArH), 7.51 (td, ²*J* = 7.6, ⁴*J* = 1.0 Hz, 1 H, 5-H), 7.66 (td, ²*J* = 7.6, ⁴*J* = 1.2 Hz, 1 H, 4'-H), 8.12 (dd, ²*J* = 7.6, ⁴*J* = 1.4 Hz, 1 H, 3'-H) ppm. ¹³C NMR (75.4 MHz, CDCl₃): δ = 11.2 (Me), 21.4 (C-7), 21.4 (ArCH₃), 28.9 (NCH₂CH₂CH₂Ph), 33.5 (C-6), 33.5 (NCH₂CH₂CH₂Ph), 33.9 (C-5), 36.9 (C-8), 41.1 (C-1), 57.4 (NCH₂CH₂CH₂Ph), 60.4 (C-4), 63.3 (C-2), 70.9 (CH₂O), 117.4 (CHAr), 125.6, 125.7 (CH_{arom.}), 126.9 (C-1'), 127.9, 128.0, 128.3 (2×), 128.4 (2×), 129.0 (CH_{arom.}), 129.0 (C-4''), 129.4, 130.4, 131.4 (CH_{arom.}), 131.9 (C-2'), 133.3 (CH_{arom.}), 136.7, 137.7, 142.5 (C_{arom.}), 146.2 (C-3''), 146.9 (C-9), 164.8 (COO), 169.7 (C-5''), 170.8 (C-2'') ppm. IR (film): $\tilde{\nu}$ = 2920 (s), 1709 (s), 1392 (s), 1253 (s), 1105 (s), 1083 (s), 725 (s), 696 (vs) cm⁻¹. MS (EI, 70 eV): *m/z*

(%) = 588 (3) [M⁺], 483 (15) [M⁺ – C₆H₅CH₂CH₂], 214 (85), 158 (29), 146 (32), 105 (30), 91 (100) [C₆H₅CH₂], 77 (23), 39 (44); found (M⁺, 588.29881), C₃₈H₄₀N₂O₄ calcd. 588.29826.

(E)-{9-(4-Methylbenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl}methyl 2-(3-Methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)benzoate (10h): According to the general esterification procedure, alcohol **8g** (350 mg, 930 μmol) gives the desired ester **10h** (344 mg, 63%) as a white foam. *R*_f = 0.31 (hexane/EtOAc, 8:2). ¹H NMR (300 MHz, CDCl₃): δ = 1.56–1.64 (m, 2 H, 7-H_A and 8-H_A), 1.77–1.82 (m, 3 H, 6-H_A and NCH₂CH₂CH₂Ph), 1.89–1.91 (m, 1 H, 6-H_B), 2.08–2.29 (m, 5 H, 2-H_A, 4-H_A, 8-H_B and NCH₂CH₂CH₂Ph), 2.16 (d, ⁴*J* = 1.6 Hz, 3 H, Me), 2.32 (s, 3 H, ArCH₃), 2.67 (t, ³*J* = 7.0 Hz, 2 H, NCH₂CH₂CH₂Ph), 2.83–2.96 (m, 2 H, 4-H_B and 7-H_B), 3.08 (d, ²*J* = 10.4 Hz, 2 H, 5-H and 2-H_B), 4.27 (s, 2 H, CH₂O), 6.10 (s, 1 H, CHAr), 6.47 (q, ⁴*J* = 1.8 Hz, 1 H, 4'-H), 7.06–7.34 (m, 10 H, 6'-H and ArH), 7.49 (td, ²*J* = 6.8, ⁴*J* = 1.2 Hz, 1 H, 5-H), 7.65 (td, ²*J* = 7.6, ⁴*J* = 1.6 Hz, 1 H, 4'-H), 8.11 (dd, ²*J* = 7.6, ⁴*J* = 0.4 Hz, 1 H, 3'-H) ppm. ¹³C NMR (75.4 MHz, CDCl₃): δ = 11.1 (Me), 21.1 (C-7), 21.4 (ArCH₃), 28.9 (NCH₂CH₂CH₂Ph), 33.4 (C-6), 33.5 (NCH₂CH₂CH₂Ph), 33.8 (C-5), 36.8 (C-8), 41.1 (C-1), 57.4 (NCH₂CH₂CH₂Ph), 60.3 (C-4), 63.3 (C-2), 70.9 (CH₂O), 117.2 (CHAr), 125.6, 127.6, 128.2 (2×), 128.4 (2×), 128.6 (2×), 128.8 (2×, CH_{arom.}), 129.0 (C-4''), 129.0 (C-1'), 130.4, 131.2 (CH_{arom.}), 131.9 (C-2'), 133.2 (CH_{arom.}), 134.8, 135.7, 142.5 (C_{arom.}), 146.2 (C-3''), 146.5 (C-9), 164.8 (COO), 169.7 (C-5''), 170.7 (C-2'') ppm. IR (film): $\tilde{\nu}$ = 2920 (s), 1709 (s), 1391 (s), 1254 (s), 1105 (s), 1084 (s), 725 (s), 697 (vs) cm⁻¹. MS (EI, 70 eV): *m/z* (%) = 588 (15) [M⁺], 483 (100) [M⁺ – C₆H₅CH₂CH₂], 358 (23), 214 (45), 105 (34), 91 (46) [C₆H₅CH₂], 44 (21); found (M⁺, 588.29881), C₃₈H₄₀N₂O₄ calcd. 588.29891.

General Hydrogenation Procedure for the Synthesis of Compound 4:

To a solution of the maleimido esters **10a–h** (1.0 equiv.) in ethyl acetate (0.2 M) was added 10% palladium on carbon (10%w/w) and the mixture stirred under hydrogen for 3 h. After this time the mixture was filtered through Celite, washed with EtOAc, and the solvent removed in vacuo. The crude product was purified by flash chromatography to afford the desired succinimide anthranilate esters **4a–h**.

(E)-{9-Benzylidene-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl}methyl 2-(3-Methyl-2,5-dioxopyrrolidin-1-yl)benzoate (4a): According to the general hydrogenation procedure, maleimide **10a** (200 mg, 350 μmol) gives the product **4a** (178 mg, 88%) purified by column chromatography (hexane/EtOAc, 6:4) as a pale yellow oil and as a 1:1 mixture of diastereomers. *R*_f = 0.43 (hexane/EtOAc, 6:4). ¹H NMR (300 MHz, CDCl₃): δ = 1.45 (d, ⁴*J* = 13.3 Hz, 3 H, Me), 1.55–1.71 (m, 2 H, 7-H_A and 8-H_A), 1.74–1.86 (m, 1 H, 6-H_A), 1.79 (t, ³*J* = 7.7 Hz, 2 H, NCH₂CH₂CH₂Ph), 1.88–1.96 (m, 1 H, 6-H_B), 2.08–2.32 (m, 5 H, 2-H_A, 4-H_A, 8-H_B and NCH₂CH₂CH₂Ph), 2.44–2.62 (m, 2 H, 4'-H), 2.68 (t, ³*J* = 7.7 Hz, 2 H, NCH₂CH₂CH₂Ph), 2.84–3.16 (m, 4 H, 2-H_B, 3'-H, 5-H and 7-H_B), 2.96 (d, ²*J* = 11.2 Hz, 1 H, 4-H_B), 4.28 (s, 2 H, CH₂O), 6.16 (s, 1 H, CHAr), 7.12–7.34 (m, 11 H, 6'-H and CH_{arom.}), 7.51 (td, ³*J* = 7.8, ⁴*J* = 1.5 Hz, 1 H, 5'-H), 7.65 (td, ³*J* = 7.8, ⁴*J* = 1.5 Hz, 1 H, 4'-H), 8.14 (d, ³*J* = 7.8 Hz, 1 H, 3'-H) ppm. ¹³C NMR (75.4 MHz, CDCl₃): δ = 16.2 (Me), 16.4 (Me), 21.3 (C-7), 28.8 (NCH₂CH₂CH₂Ph), 33.4 (C-6 and NCH₂CH₂CH₂Ph), 33.8 (C-5), 35.1 (C-3''), 35.3 (C-3''), 36.8 (C-8), 36.9 (C-4''), 41.1 (C-1), 57.3 (NCH₂CH₂CH₂Ph), 60.3 (C-4), 63.2 (C-2), 70.6 (CH₂O), 117.3 (CHAr), 125.6, 125.7, 126.1, 126.3 (CH_{arom.}), 127.2 (C-1'), 128.0, 128.2, 128.4, 128.6, 128.9 (×2), 129.0, 129.3, 129.6, 129.8, 131.3 (CH_{arom.}), 132.9 (C-2'), 133.4 (CH_{arom.}), 137.7, 142.4 (C_{arom.}), 147.1 (C-9), 164.1 (CO), 164.3 (CO), 175.7 (C-5''), 179.8 (C-2'') ppm. IR

(film): $\tilde{\nu}$ = 3024 (m), 2934 (s), 1738 (vs, C=O), 1732 (vs, C=O), 1714 (vs, C=O), 1602 (m), 1494 (s), 1454 (s), 1392 (vs), 1257 (s), 1190 (s), 1083 (m), 1045 (m), 910 (w), 761 (m), 699 (s) cm^{-1} . MS (EI, 70 eV): m/z (%) = 576 (2) [M^+], 471 (13) [$\text{M}^+ - \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2$], 358 (14), 216 (100) [$\text{M}^+ - \text{C}_{12}\text{H}_{10}\text{NO}_3$], 146 (14), 98 (17), 91 (15) [$\text{C}_6\text{H}_5\text{CH}_2$], 41 (17); found (M^+ , 576.2999), $\text{C}_{37}\text{H}_{40}\text{N}_2\text{O}_4$ calcd. 576.2988.

(E)-{9-(4-Chlorobenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl}methyl 2-(3-Methyl-2,5-dioxopyrrolidin-1-yl)benzoate (4b): According to the general hydrogenation procedure, maleimide **10b** (615 mg, 1.01 mmol) gives the product **4b** (445 mg, 73%) purified by column chromatography (hexane/EtOAc, 8:2) as a pale yellow oil and as a 1:1 mixture of diastereomers. R_f = 0.11 (hexane/EtOAc, 8:2). ^1H NMR (400 MHz, CDCl_3): δ = 1.40–1.51 (m, 3 H, Me), 1.55–1.70 (m, 2 H, 7- H_A and 8- H_A), 1.72–1.99 (m, 4 H, 6-H and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.07–2.40 (m, 5 H, 2- H_A , 4- H_A , 8- H_B and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.42–2.62 (m, 1 H, 4'- H_A), 2.67 (t, 3J = 7.7 Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.81–2.92 (m, 1 H, 7- H_B), 2.92–3.21 (m, 5 H, 2- H_B , 3'-H, 4- H_B , 4'- H_A and 5-H), 4.26 (s, 2 H, CH_2O), 6.13 (s, 1 H, CHAr), 7.08–7.30 (m, 9 H, $\text{CH}_{\text{arom.}}$), 7.52 (t, 3J = 7.7 Hz, 1 H, 5'-H), 7.66 (t, 3J = 7.7 Hz, 1 H, 4'-H), 8.12 (d, 3J = 7.7 Hz, 1 H, 6'-H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 16.3 (Me), 21.1 (C-7), 28.4 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.1 (C-5), 33.4 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.6 (C-6), 34.7 (C-3'), 36.6 (C-4'), 36.9 (C-8), 41.1 (C-1), 57.5 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 59.9 (C-4), 62.7 (C-2), 70.2 (CH_2O), 116.6 (CHAr), 125.6, 126.3 ($\text{CH}_{\text{arom.}}$), 127.1 (C-1'), 128.2, 128.3, 129.3, 129.8, 129.9 ($\text{CH}_{\text{arom.}}$), 131.2, 131.9 ($\text{C}_{\text{arom.}}$), 132.8 (C-2'), 133.4 ($\text{CH}_{\text{arom.}}$), 135.9, 142.1 ($\text{C}_{\text{arom.}}$), 147.2 (C-9), 164.0 (CO), 175.8 (C-5'), 179.7 (C-2'') ppm. IR (film): $\tilde{\nu}$ = 3059 (w), 2934 (m), 1714 (vs, C=O), 1602 (w), 1491 (m), 1454 (m), 1392 (m), 1264 (s), 1187 (m), 1086 (m), 736 (s), 700 (w) cm^{-1} . MS (FAB): m/z (%) = 611 (23) [MH^+], 307 (21), 154 (100), 136 (69), 107, (24), 91 (23) [$\text{C}_6\text{H}_5\text{CH}_2$], 77 (24) [C_6H_5]; found (MH^+ , 611.2684), $\text{C}_{37}\text{H}_{40}^{35}\text{ClN}_2\text{O}_4$ calcd. 611.2677.

(E)-{9-(4-Methoxybenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl}methyl 2-(3-Methyl-2,5-dioxopyrrolidin-1-yl)benzoate (4c): According to the general hydrogenation procedure, maleimide **10c** (80 mg, 132 μmol) gives the product **4c** (54 mg, 68%) purified by column chromatography (hexane/EtOAc, 7:3) as an oil and as a 1:1 mixture of diastereomers. R_f = 0.11 (EtOAc/hexane, 2:8). ^1H NMR (300 MHz, CDCl_3): δ = 1.40–1.54 (m, 3 H, Me), 1.55–1.72 (m, 2 H, 7- H_A and 8- H_A), 1.72–1.98 (m, 4 H, 6-H and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.05–2.33 (m, 5 H, 2- H_A , 4- H_A , 8- H_B and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.44–2.65 (m, 1 H, 3'-H), 2.68 (t, 3J = 7.7 Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.82–3.18 (m, 6 H, 2- H_B , 4- H_B , 5-H and 4'-H), 3.79 (s, 3 H, OCH_3), 4.26 (s, 2 H, CH_2O), 6.09 (s, 1 H, CHAr), 6.85 (d, 3J = 8.7 Hz, 2 H, $m\text{-ArH}$), 7.11 (d, 3J = 8.7 Hz, 2 H, $o\text{-ArH}$), 7.16–7.32 (m, 6 H, 6'-H and Ph), 7.53 (td, 3J = 7.6, 4J = 1.3 Hz, 1 H, 5'-H), 7.67 (td, 3J = 7.6, 4J = 1.3 Hz, 1 H, 4'-H), 8.15 (d, 3J = 7.6 Hz, 1 H, 3'-H) ppm. ^{13}C NMR (75.4 MHz, CDCl_3): δ = 16.3 (Me), 16.5 (Me), 21.4 (C-7), 28.9 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.4 (C-6), 33.5 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.7 (C-5), 35.2 (C-3'), 36.8 (C-4'), 36.9 (C-8), 41.1 (C-1), 55.2 (OCH_3), 57.4 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 60.3 (C-4), 63.3 (C-2), 70.8 (CH_2O), 113.5 ($\text{CH}_{\text{arom.}}$), 116.7 (CHAr), 125.6, 128.2, 128.4, 129.4 ($\text{CH}_{\text{arom.}}$), 129.8 (C-1'), 129.9, 131.4 ($\text{CH}_{\text{arom.}}$), 132.9 (C-2'), 133.4 ($\text{CH}_{\text{arom.}}$), 142.5 ($\text{C}_{\text{arom.}}$), 146.0 (C-9), 157.9 (ArC-OMe), 164.3 (CO), 175.9 (C-5'), 179.9 (C-2'') ppm. IR (film): $\tilde{\nu}$ = 3027 (w), 2934 (s), 1714 (vs, C=O), 1604 (m), 1510 (m), 1454 (m), 1250 (s), 1181 (m), 1083 (m), 910 (m), 732 (m) cm^{-1} . MS (FAB): m/z (%) = 607 (6) [MH^+], 307 (24), 154 (100), 136 (67), 107 (20), 89 (20), 77 (19) [C_6H_5]; found (MH^+ , 607.3177), $\text{C}_{38}\text{H}_{43}\text{N}_2\text{O}_5$ calcd. 607.3172.

(E)-{9-(2-Chlorobenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl}methyl 2-(3-Methyl-2,5-dioxopyrrolidin-1-yl)benzoate (4d): According to the general hydrogenation procedure, maleimide **10d** (800 mg, 1.31 mmol) gives the product **4d** (380 mg, 47%) purified by column chromatography (hexane/EtOAc, 7:3) as a pale yellow oil and as a 1:1 mixture of diastereomers. R_f = 0.12 (hexane/EtOAc, 8:2). ^1H NMR (400 MHz, CDCl_3): δ = 1.45–1.49 (m, 3 H, Me), 1.55–1.65 (m, 2 H, 7- H_A and 8- H_A), 1.65–1.93 (m, 4 H, 6-H and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.04–2.32 (m, 5 H, 2- H_A , 4- H_A , 8- H_B and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.42–2.62 (m, 1 H, 4'- H_A), 2.68 (t, 3J = 7.6 Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.81–2.92 (m, 1 H, 7- H_B), 2.92–3.21 (m, 5 H, 2- H_B , 3'-H, 4- H_B , 4'- H_A and 5-H), 4.31 (s, 2 H, CH_2O), 6.16 (s, 1 H, CHAr), 7.12–7.30 (m, 9 H, $\text{CH}_{\text{arom.}}$), 7.37 (t, 3J = 7.6 Hz, 1 H, 3'-H), 7.53 (t, 3J = 7.6 Hz, 1 H, 5'-H), 7.67 (t, 3J = 7.6 Hz, 1 H, 4'-H), 8.22 (d, 3J = 7.6 Hz, 1 H, 6'-H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 16.2 (Me), 21.1 (C-7), 28.5 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.1 (C-5), 33.3 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 34.2 (C-6), 35.0 (C-3'), 36.4 (C-4'), 36.8 (C-8), 41.2 (C-1), 57.3 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 60.0 (C-4), 62.7 (C-2), 70.0 (CH_2O), 115.4 (CHAr), 125.5, 126.1 ($\text{CH}_{\text{arom.}}$), 127.7 (C-1'), 128.1, 128.2, 129.1, 129.7, 130.2, 131.4 ($\text{CH}_{\text{arom.}}$), 132.8 (C-2'), 133.3 ($\text{CH}_{\text{arom.}}$), 133.8, 136.0, 142.1 ($\text{C}_{\text{arom.}}$), 147.8 (C-9), 164.0 (CO), 175.6 (C-5'), 179.7 (C-2'') ppm. IR (film): $\tilde{\nu}$ = 2970 (w), 2941 (m), 1720 (vs, C=O), 1602 (w), 1493 (m), 1453 (m), 1371 (m), 1257 (s), 1229 (m), 1135 (m), 1082 (m), 734 (s), 699 (w) cm^{-1} . MS (EI, 70 eV): m/z (%) = 612 (7) [^{37}Cl , M^+], 610 (17) [^{35}Cl , M^+], 505 (82) [^{35}Cl , $\text{M}^+ - \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2$], 378 (25), 216 (46) [$\text{M}^+ - \text{C}_{12}\text{H}_{10}\text{NO}_3$], 91 (56) [$\text{C}_6\text{H}_5\text{CH}_2$], 40 (82); found (M^+ , 610.25750), $\text{C}_{37}\text{H}_{39}^{35}\text{ClN}_2\text{O}_4$ calcd. 610.25984; found (M^+ , 612.25461), $\text{C}_{39}\text{H}_{37}^{37}\text{ClN}_2\text{O}_4$ calcd. 612.25689.

(E)-{9-(3-Chlorobenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl}methyl 2-(3-Methyl-2,5-dioxopyrrolidin-1-yl)benzoate (4e): According to the general hydrogenation procedure, maleimide **10d** (150 mg, 240 μmol) gives the product **4e** (83 mg, 55%) purified by column chromatography (hexane/EtOAc, 7:3) as a pale yellow oil and as a 1:1 mixture of diastereomers. R_f = 0.15 (hexane/EtOAc, 8:2). ^1H NMR (400 MHz, CDCl_3): δ = 1.43–1.47 (m, 3 H, Me), 1.57–1.70 (m, 2 H, 7- H_A and 8- H_A), 1.74–1.94 (m, 4 H, 6-H and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.09–2.37 (m, 5 H, 2- H_A , 4- H_A , 8- H_B and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.46–2.55 (m, 1 H, 4'- H_A), 2.68 (t, 3J = 7.7 Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.87–3.14 (m, 6 H, 7- H_B , 2- H_B , 3'-H, 4- H_B , 4'- H_A and 5-H), 4.25 (s, 2 H, CH_2O), 6.10 (s, 1 H, CHAr), 7.05 (d, 3J = 7.5 Hz, ArH), 7.15–7.30 (m, 9 H, 3'-H and $\text{CH}_{\text{arom.}}$), 7.53 (td, 2J = 7.8, 4J = 1.5 Hz, 1 H, 5'-H), 7.66 (td, 2J = 7.5, 4J = 1.5 Hz, 1 H, 4'-H), 8.12 (dd, 2J = 7.8, 4J = 1.2 Hz, 1 H, 3'-H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 16.3 (Me), 21.3 (C-7), 28.9 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.5 (C-5), 33.5 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 34.0 (C-6), 35.2 (C-3'), 36.9 (C-4'), 37.0 (C-8), 41.3 (C-1), 57.4 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 60.3 (C-4), 62.3 (C-2), 70.5 (CH_2O), 116.2 (CHAr), 125.7 ($\text{CH}_{\text{arom.}}$), 126.3 (C-1'), 127.2, 128.3 (2 $\times$), 128.4 (2 $\times$), 128.7, 129.1, 129.1, 129.3, 129.4, 129.9, 131.4 ($\text{CH}_{\text{arom.}}$), 133.0 (C-2'), 133.5 ($\text{CH}_{\text{arom.}}$), 133.9, 139.6, 142.5 ($\text{C}_{\text{arom.}}$), 148.6 (C-9), 164.2 (CO), 176.0 (C-5'), 179.9 (C-2'') ppm. IR (film): $\tilde{\nu}$ = 2924 (m), 1711 (vs, C=O), 1602 (w), 1453 (m), 1390 (m), 1258 (s), 1184 (m), 1136 (m), 1079 (m), 908 (m), 728 (s), 698 (w) cm^{-1} . MS (FAB): m/z (%) = 613 (7) [^{37}Cl , MH^+], 611 (20) [^{35}Cl , MH^+], 307 (16), 154 (100), 136 (68), 107 (26), 91 (22) [$\text{C}_6\text{H}_5\text{CH}_2$], 77 (25); found (MH^+ , 611.26766), $\text{C}_{37}\text{H}_{39}^{35}\text{ClN}_2\text{O}_4$ calcd. 611.26732; found (MH^+ , 613.26654), $\text{C}_{39}\text{H}_{37}^{37}\text{ClN}_2\text{O}_4$ calcd. 613.26593.

(E)-{9-(3-Methoxybenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl}methyl 2-(3-Methyl-2,5-dioxopyrrolidin-1-yl)benzoate (4f): According to the general hydrogenation procedure, maleimide **10f** (58 mg, 100 μmol) gives the product **4f** (41 mg, 71%)

purified by column chromatography (hexane/EtOAc, 7:3) as a pale yellow oil and as a 1:1 mixture of diastereomers. R_f = 0.17 (hexane/EtOAc, 8:2). ^1H NMR (400 MHz, CDCl_3): δ = 1.45–1.49 (m, 3 H, Me), 1.55–1.69 (m, 2 H, 7- H_A and 8- H_A), 1.75–1.93 (m, 4 H, 6-H and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.09–2.34 (m, 5 H, 2- H_A , 4- H_A , 8- H_B and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.52–2.62 (m, 1 H, 4'- H_A), 2.68 (t, 3J = 7.6 Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.87–3.12 (m, 6 H, 7- H_B , 2- H_B , 3'- H , 4- H_B , 4'- H_A and 5-H), 3.80 (s, 3 H, OCH_3), 4.25 (s, 2 H, CH_2O), 6.13 (s, 1 H, CHAr), 6.75 (dd, 3J = 10.8, J = 1.2 Hz, 2 H, ArH), 7.16–7.30 (m, 8 H, 3'-H and $\text{CH}_{\text{arom.}}$), 7.53 (td, 2J = 8.0, 4J = 0.8 Hz, 1 H, 5'-H), 7.67 (td, 2J = 7.6, 4J = 1.2 Hz, 1 H, 4'-H), 8.14 (d, 2J = 7.6 Hz, 1 H, 3'-H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 16.4 (Me), 21.4 (C-7), 28.9 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.5 (C-5), 33.5 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 34.0 (C-6), 35.3 (C-3''), 36.9 (C-4''), 37.0 (C-8), 41.2 (C-1), 55.1 (OCH_3), 57.4 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 60.4 (C-4), 63.3 (C-2), 70.8 (CH_2O), 111.7, 114.3 ($\text{CH}_{\text{arom.}}$), 117.3 (CHAr), 121.2, 123.5, 125.6 ($\text{CH}_{\text{arom.}}$), 127.3 (C-1'), 128.3 (2 $\times$), 128.5 (2 $\times$), 129.1, 129.4, 129.9 ($\text{CH}_{\text{arom.}}$), 131.4 (C-2'), 133.0, 133.5 ($\text{CH}_{\text{arom.}}$), 139.2, 142.5 ($\text{C}_{\text{arom.}}$), 147.4 (C-9), 159.4 (ArC-OMe), 164.8 (CO), 175.8 (C-5'), 179.9 (C-2'') ppm. IR (film): $\tilde{\nu}$ = 2934 (m), 1716 (vs, C=O), 1602 (w), 1453 (m), 1390 (m), 1261 (s), 1187 (m), 1135 (m), 910 (m), 731 (s), 698 (w) cm^{-1} . MS (EI, 70 eV): m/z (%) = 606 (5) [M^+], 501 (33) [$\text{M}^+ - \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2$], 216 (73), 188 (31), 146 (53), 91 (100) [$\text{C}_6\text{H}_5\text{CH}_2$], 77 (23), 69 (26), 41 (77); found (M^+ , 606.30937), $\text{C}_{38}\text{H}_{42}\text{N}_2\text{O}_4$ calcd. 606.30838.

(E)-{9-(3-Methylbenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl}methyl 2-(3-Methyl-2,5-dioxopyrrolidin-1-yl)benzoate (4g): According to the general hydrogenation procedure, maleimide **10g** (37 mg, 62 μmol) gives the product **4g** (20 mg, 55%) purified by column chromatography (hexane/EtOAc, 7:3) as a pale yellow oil and as a 1:1 mixture of diastereomers. R_f = 0.14 (hexane/EtOAc, 8:2). ^1H NMR (400 MHz, CDCl_3): δ = 1.43–1.47 (m, 3 H, Me), 1.56–1.70 (m, 2 H, 7- H_A and 8- H_A), 1.74–1.94 (m, 4 H, 6-H and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.07–2.29 (m, 5 H, 2- H_A , 4- H_A , 8- H_B and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.33 (s, 3 H, ArCH_3), 2.48–2.61 (m, 1 H, 4'- H_A), 2.68 (t, 3J = 6.3 Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.86–3.14 (m, 6 H, 7- H_B , 2- H_B , 3'- H , 4- H_B , 4'- H_A and 5-H), 4.27 (s, 2 H, CH_2O), 6.13 (s, 1 H, CHAr), 7.00 (t, 3J = 7.7 Hz, 2 H, ArH), 7.03–7.30 (m, 8 H, 3'-H and $\text{CH}_{\text{arom.}}$), 7.53 (td, 2J = 7.8, 4J = 1.2 Hz, 1 H, 5'-H), 7.67 (td, 2J = 7.5, 4J = 1.5 Hz, 1 H, 4'-H), 8.14 (dd, 2J = 7.8, 3J = 1.2 Hz, 1 H, 3'-H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 16.4 (Me), 21.5 (C-7), 21.5 (ArCH_3), 28.9 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.5 (C-5), 33.5 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.9 (C-6), 35.3 (C-3''), 36.9 (C-4''), 37.0 (C-8), 41.2 (C-1), 57.5 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 60.4 (C-4), 63.4 (C-2), 70.8 (CH_2O), 117.4 (CHAr), 125.7, 126.4, 127.0 ($\text{CH}_{\text{arom.}}$), 127.7 (C-1'), 128.0, 128.3 (2 $\times$), 128.5 (2 $\times$), 129.1, 129.4, 129.9 ($\text{CH}_{\text{arom.}}$), 130.8 (C-2'), 131.4 ($\text{CH}_{\text{arom.}}$), 133.0 ($\text{C}_{\text{arom.}}$), 133.5 ($\text{CH}_{\text{arom.}}$), 137.7, 142.5 ($\text{C}_{\text{arom.}}$), 146.9 (C-9), 164.1 (CO), 175.9 (C-5'), 179.9 (C-2'') ppm. IR (film): $\tilde{\nu}$ = 2924 (m), 1714 (vs, C=O), 1602 (w), 1454 (m), 1392 (m), 1260 (s), 1187 (m), 1137 (m), 1084 (m), 910 (m), 731 (s), 698 (w) cm^{-1} . MS (EI, 70 eV): m/z (%) = 590 (6) [M^+], 485 (48) [$\text{M}^+ - \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2$], 216 (100), 91 (26) [$\text{C}_6\text{H}_5\text{CH}_2$], 41 (23); found (M^+ , 590.31446), $\text{C}_{38}\text{H}_{42}\text{N}_2\text{O}_4$ calcd. 590.31406.

(E)-{9-(4-Methylbenzylidene)-3-(3-phenylpropyl)-3-azabicyclo[3.3.1]nonan-1-yl}methyl 2-(3-Methyl-2,5-dioxopyrrolidin-1-yl)benzoate (4h): According to the general hydrogenation procedure, maleimide **10h** (250 mg, 420 μmol) gives the product **4h** (198 mg, 79%) purified by column chromatography (hexane/EtOAc, 7:3) as a pale yellow oil and as a 1:1 mixture of diastereomers. R_f = 0.21 (hexane/EtOAc, 8:2). ^1H NMR (400 MHz, CDCl_3): δ = 1.43–1.46 (m, 3 H, Me), 1.61–1.63 (m, 2 H, 7- H_A and 8- H_A), 1.77–1.89 (m, 4 H, 6-H and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.12–2.28 (m, 5 H, 2- H_A , 4- H_A , 8- H_B and

$\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.32 (s, 3 H, ArCH_3), 2.46–2.58 (m, 1 H, 4'- H_A), 2.67 (t, 3J = 7.2 Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.89–3.10 (m, 6 H, 7- H_B , 2- H_B , 3'- H , 4- H_B , 4'- H_A and 5-H), 4.27 (s, 2 H, CH_2O), 6.12 (s, 1 H, CHAr), 7.09–7.26 (m, 8 H, 3'-H and $\text{CH}_{\text{arom.}}$), 7.50 (td, 2J = 7.2, 4J = 1.2 Hz, 1 H, 5'-H), 7.64 (td, 2J = 7.2, 4J = 1.2 Hz, 1 H, 4'-H), 8.13 (dd, 2J = 7.2, 3J = 1.2 Hz, 1 H, 3'-H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 16.2 (Me), 21.0 (C-7), 21.4 (ArCH_3), 28.8 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.4 (C-5), 33.4 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 33.7 (C-6), 35.1 (C-3''), 36.8 (C-4''), 36.8 (C-8), 41.1 (C-1), 57.3 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 60.3 (C-4), 62.2 (C-2), 70.7 (CH_2O), 117.1 (CHAr), 125.5 ($\text{CH}_{\text{arom.}}$), 127.2 (C-1'), 128.2 (2 $\times$), 128.3 (2 $\times$), 128.5 (2 $\times$), 128.7 (2 $\times$), 129.3, 129.8 ($\text{CH}_{\text{arom.}}$), 131.9 (C-2'), 132.9, 133.3 ($\text{CH}_{\text{arom.}}$), 134.7, 135.6, 142.4 ($\text{C}_{\text{arom.}}$), 146.5 (C-9), 164.1 (CO), 175.9 (C-5'), 179.8 (C-2'') ppm. IR (film): $\tilde{\nu}$ = 2925 (m), 1710 (vs, C=O), 1602 (w), 1453 (m), 1388 (m), 1257 (s), 1181 (m), 1135 (m), 731 (s), 698 (w) cm^{-1} . MS (EI, 70 eV): m/z (%) = 590 (12) [M^+], 485 (100) [$\text{M}^+ - \text{C}_6\text{H}_5\text{CH}_2\text{CH}_2$], 358 (16), 216 (28), 105 (27), 91 (36) [$\text{C}_6\text{H}_5\text{CH}_2$], 41 (29); found (M^+ , 590.31446), $\text{C}_{38}\text{H}_{42}\text{N}_2\text{O}_4$ calcd. 590.31475.

Ethyl 2-(Hydroxymethyl)acrylate:^[30] Phosphoric acid (1 M, 0.4 mL, 0.4 mmol) was added to a stirred solution of paraformaldehyde (3.3 g, 110 mmol) in water (10 mL) was added. The resulting mixture was heated at 90 °C for 2.5 h then cooled to room temperature. A solution of ethyl acrylate (10.9 mL, 100 mmol) and 1,4-diazobicyclo[2.2.2]octane (DABCO) (1.13 g, 10.1 mmol) in THF (10 mL), was added and the mixture heated at reflux for 20 h. The mixture was cooled to room temperature and sodium chloride (3.0 g) and diethyl ether (10 mL) added. The organic layer was separated and further product was extracted from the aqueous layer with diethyl ether (3 $\times$ 10 mL). The combined organic layers were washed with brine (2 $\times$ 10 mL), dried (MgSO_4) and the solvent removed in vacuo to give the crude product which was distilled under vacuum to give the title compound (5.9 g, 45%); b.p. 65–82 °C/1 Torr. ^1H NMR (300 MHz, CDCl_3): δ = 1.32 (t, J = 4.0 Hz, 3 H, OCH_2CH_3), 2.68 (s, 1 H, OH), 4.25 (q, J = 7.2 Hz, 2 H, OCH_2CH_3), 4.33 (s, 2 H, CH_2OH), 5.38 (m, 1 H, = CH_2), 6.26 (m, 1 H, = CH_2) The ^1H NMR spectroscopic data was in agreement with the literature values.^[34]

Ethyl 2-(Bromomethyl)acrylate (12):^[29] Phosphorus tribromide (1.4 mL, 15.4 mmol) was slowly added to a stirred solution of ethyl 2-(hydroxymethyl)acrylate (5.9 g, 45 mmol) in diethyl ether (45 mL) at –10 °C. The mixture was stirred for 3 h during which time the temperature was warmed to room temperature. The mixture was then cooled to –10 °C and water (3 mL) added. The mixture was extracted with hexanes (3 $\times$ 20 mL). The combined organic layers were washed with brine (2 $\times$ 20 mL), dried (MgSO_4) and the solvent removed in vacuo to give the crude product which was distilled under vacuum to give the title compound **12** (6.82 g, 78%) for which the spectroscopic data was consistent with the literature values.^[29]

Ethyl 1-(3-Phenylpropyl)-1,2,3,4,5,6,7,8-octahydroquinoline-3-carboxylate (14a): To 3-phenylpropylamine **13a** (0.85 mL, 6.0 mmol) in toluene (32 mL) was added dropwise ethyl 2-(bromomethyl)acrylate (**12**, 580 mg, 3.00 mmol) in toluene (5 mL) at 0 °C. After 15 min a solution of cyclohexanone (0.31 mL, 3.00 mmol) in toluene (5 mL) was added and the reaction mixture was heated under reflux under N_2 for 18 h using a Dean–Stark trap containing 5-Å molecular sieves. The mixture was cooled and extracted with 1 M HCl (2 $\times$ 100 mL). The combined aqueous layers were washed with EtOAc (100 mL), basified with solid Na_2CO_3 and then extracted with CH_2Cl_2 (3 $\times$ 75 mL). The extract was dried Na_2SO_4 and concentrated in vacuo. The crude product was purified by column

chromatography on silica gel (hexane/EtOAc, 8:2) to give **14a** (589 mg, 60%) as a pale yellow oil. R_f = 0.22 (hexane/EtOAc, 8:2). ^1H NMR (300 MHz, CDCl_3): δ = 1.25 (t, J = 6.8 Hz, 3 H, OCH_2CH_3), 1.43–1.79 (m, 4 H, 6- CH_2 and 7- CH_2), 1.72–1.79 (m, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 1.82–1.90 (m, 4 H, 5- CH_2 and 8- CH_2), 1.97–2.03 (m, 2 H, 4- CH_2), 2.59 (td, J = 8.3, J = 2.7 Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.71 (tdd, J = 11.8, J = 3.3, J = 5.7 Hz, 1 H, 3-H), 2.86–2.99 (m, 3 H, 2- H_A , $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 3.20 (ddd, J = 11.9, J = 3.3, J = 1.8 Hz, 1 H, 2- H_B), 4.13 (m, 2 H, OCH_2CH_3), 7.12–7.31 (m, 5 H, Ph) ppm. ^{13}C NMR (75.5 MHz, CDCl_3): δ = 14.2 (OCH_2CH_3), 22.9, 23.6, (CH_2), 26.4 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 29.7 (C-8), 29.9 (C-5), 31.2 (C-4), 33.4 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 38.1 (C-3), 50.0 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 50.2 (C-2), 60.3 (OCH_2CH_3), 106.1 (C-4a), 125.7 (*p*-Ph), 128.3 (*o*- and *m*-Ph), 135.8 (C-8a), 142.0 (Ph), 174.6 (COO) ppm. IR (film): $\tilde{\nu}$ = 3025 (w), 2930 (m), 1729 (vs, C=O), 1637 (w), 1453 (w), 1184 (m), 1029 (w) cm^{-1} . MS (EI, 70 eV): m/z (%) = 327 (88) [M^+], 222 (100) [$\text{M}^+ - \text{EtPh}$], 91 (45) [Bn^+]; found [M^+] 327.2195. $\text{C}_{21}\text{H}_{29}\text{NO}_2$ requires 327.2198.

Ethyl 1-Benzyl-1,2,3,4,5,6,7,8-octahydroquinoline-3-carboxylate (14b): Following a similar procedure to that described above for the preparation of **14a**, benzylamine **13b** (0.66 mL, 6.0 mmol) was treated with ethyl 2-(bromomethyl)acrylate **12** (579 mg, 3.0 mmol) and cyclohexanone (0.31 mL, 3.0 mmol). The crude product was purified by column chromatography on silica gel (hexane/EtOAc, 8:2) to give **14b** (440 mg, 47%) as a pale yellow oil. R_f = 0.24 (hexane/EtOAc, 8:2). ^1H NMR (300 MHz, CDCl_3): δ = 1.21 (t, J = 7.0 Hz, 3 H, OCH_2CH_3), 1.55–1.73 (m, 4 H, 6- CH_2 and 7- CH_2), 1.81–2.14 (m, 3 H, 5- CH_2 and 8- H_A), 2.15–2.26 (m, 3 H, 4- CH_2 and 8- H_B), 2.61–2.75 (m, 1 H, 3-H), 2.91 (t, J = 11.3 Hz, 1 H, 2- H_A), 3.14 (ddd, J = 11.4, J = 3.3, J = 1.9 Hz, 1 H, 2- H_B), 3.96–4.06 (m, 2 H, NCH_2Ph), 4.07–4.13 (m, 2 H, OCH_2CH_3), 7.22–7.33 (m, 5 H, Ph) ppm. ^{13}C NMR (75.5 MHz, CDCl_3): δ = 14.1 (OCH_2CH_3), 23.0, 23.6, (CH_2), 26.7 (C-5), 29.9 (C-8), 31.2 (C-4), 37.6 (C-3), 50.2 (C-2), 53.8 (NCH_2Ph), 60.2 (OCH_2CH_3), 106.3 (C-4a), 126.7, 128.3 (Ph), 135.9 (C-8a), 140.1 (Ph), 174.5 (COO) ppm. IR (film): $\tilde{\nu}$ = 3025 (w), 2927 (m), 2836 (w), 1727 (vs, C=O), 1176 (m), 1027 (w) cm^{-1} . MS (EI, 70 eV): m/z (%) = 299 (76) [M^+], 226 (25), 208 (75), 91 (100) [Bn^+]; found [M^+] 299.18853. $\text{C}_{19}\text{H}_{25}\text{NO}_2$ requires 299.18823.

Ethyl 1-Butyl-1,2,3,4,5,6,7,8-octahydroquinoline-3-carboxylate (14c): Following a similar procedure to that described above for the preparation of **14a**, butylamine **13c** (0.51 mL, 5.2 mmol) was treated with ethyl 2-(bromomethyl)acrylate **12** (500 mg, 2.6 mmol) and cyclohexanone (0.27 mL, 2.6 mmol). The crude product was purified by column chromatography on silica gel (hexane/EtOAc, 8:2) to give **14c** (496 mg, 72%) as a dark yellow oil. R_f = 0.29 (hexane/EtOAc, 8:2). ^1H NMR (300 MHz, CDCl_3): δ = 0.88 (t, J = 7.0 Hz, 3 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 1.23 (t, J = 6.3 Hz, 3 H, OCH_2CH_3), 1.20–1.30 (m, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 1.31–1.39 (m, 2 H, 6- CH_2), 1.41–1.54 (m, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 1.55–1.72 (m, 2 H, 7- CH_2), 1.81–2.05 (m, 3 H, 5- CH_2 and 8- H_A), 2.08–2.11 (m, 1 H, 8- H_B), 2.13–2.22 (m, 2 H, 4- CH_2), 2.66 (ddt, J = 3.1, 5.6 and 10.8 Hz, 1 H, 3-H), 2.73–2.86 (m, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 2.91 (t, J = 10.9 Hz, 1 H, 2- H_A), 3.16 (ddd, J = 2.0, 3.2 and 12.0 Hz, 1 H, 2- H_B) and 4.07–4.14 (m, 2 H, OCH_2CH_3) ppm. ^{13}C NMR (75.5 MHz, CDCl_3): δ = 14.1 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 14.2 (OCH_2CH_3), 20.6 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 23.0 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 23.6 (C-7), 26.4 (C-8), 30.0 (C-6), 30.2 (C-5), 31.3 (C-4), 38.1 (C-3), 50.2 (C-2) and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$, 60.3 (OCH_2CH_3), 105.8 (C-4a), 136.0 (C-8a), 174.7 (COO) ppm. IR (film): $\tilde{\nu}$ = 2955 (w), 2927 (m), 2859 (w), 1729 (vs, C=O), 1659 (m), 1176 (m), 1160 (w) cm^{-1} . MS (EI, 70 eV): m/z (%) = 265 (14) [M^+],

222 (36), 86 (100); found [M^+] 265.20370. $\text{C}_{16}\text{H}_{27}\text{NO}_2$ requires 265.20418.

(*R*)-Ethyl 1-[(*R*)-1-Phenylethyl]-1,2,3,4,5,6,7,8-octahydroquinoline-3-carboxylate (14d): Following a similar procedure to that described above for the preparation of **14a**, (*R*)-1-phenylethylamine **13d** (0.73 mL, 6.0 mmol) was treated with ethyl 2-(bromomethyl)acrylate (**12**, 579 mg, 3.0 mmol) and cyclohexanone (0.31 mL, 3.0 mmol). The crude product was purified by column chromatography on silica gel (hexane/EtOAc, 8:2) to give **14d** (472 mg, 50%) as a bright yellow oil. R_f = 0.24 (hexane/EtOAc, 8:2). $[\alpha]_D^{20}$ = +39 (c = 0.89, CHCl_3). ^1H NMR (300 MHz, CDCl_3): δ = 1.94 (t, J = 7.1 Hz, 3 H, OCH_2CH_3), 1.43 [d, J = 7.0 Hz, 3 H, $\text{NCH}(\text{CH}_3)\text{Ph}$], 1.60–1.77 (m, 4 H, 6- CH_2 and 7- CH_2), 1.85–2.08 (m, 3 H, 5- CH_2 and 8- H_A), 2.13–2.36 (m, 3 H, 4- CH_2 and 8- H_B), 2.61–2.70 (m, 2 H, 2- H_A and 3-H), 2.98–3.10 (m, 1 H, 2- H_B), 3.99–4.17 (m, 2 H, OCH_2CH_3), 4.73–4.81 [m, 1 H, $\text{NCH}(\text{CH}_3)\text{Ph}$], 7.23–7.40 (m, 5 H, Ph) ppm. ^{13}C NMR (75.5 MHz, CDCl_3): δ = 14.1 (OCH_2CH_3), 15.5 [$\text{NCH}(\text{CH}_3)\text{Ph}$], 23.1 (C-7), 23.9 (C-6), 26.7 (C-5), 30.1 (C-8), 30.3 (C-4), 38.1 (C-3), 44.9 (C-2), 53.3 [$\text{NCH}(\text{CH}_3)\text{Ph}$], 60.1 (OCH_2CH_3), 105.6 (C-4a), 126.5, 127.2, 128.6 (Ph), 134.5 (C-8a), 143.3 (Ph), 174.7 (COO) ppm. IR (film): $\tilde{\nu}$ = 3021 (w), 2930 (w), 2846 (w), 1727 (vs, C=O), 1446 (m), 1371 (m), 1176 (w), 1026 (m) cm^{-1} . MS (EI, 70 eV): m/z (%) = 313 (56) [M^+], 209 (35), 136 (24), 105 (100), 77 (27); found [M^+] 313.20420. $\text{C}_{20}\text{H}_{27}\text{NO}_2$ requires 313.20418.

Ethyl (3*S,4*aR**,8*aR**)-1-(3-Phenylpropyl)decahydroquinoline-3-carboxylate (15a):** Olefin **14a** (350 mg, 1.07 mmol) and PtO_2 (40 mg, ca. 10 mol-%) in EtOAc (5 mL) were stirred under H_2 for 18 h. The mixture was filtered through a Celite pad. The filtrate was concentrated in vacuo and the crude product was purified by column chromatography on silica (hexane/EtOAc, 8:2) to give **15a** (149 mg, 41%) as a pale yellow oil. R_f = 0.21 (hexane/EtOAc, 8:2). ^1H NMR (300 MHz, CDCl_3): δ = 1.10–1.97 (m, 1 H, 8- H_A), 1.20 (t, J = 7.1 Hz, 3 H, OCH_2CH_3), 1.28–1.41 (m, 2 H, 6- CH_2), 1.43–1.50 (m, 2 H, 7- CH_2), 1.51–1.58 (m, 2 H, 5- CH_2), 1.61–1.73 (m, 2 H, 4- CH_2), 1.74–1.76 (m, 1 H, 8- H_B), 1.79–1.87 (m, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 1.94–2.01 (m, 1 H, 4a-H), 2.45–2.53 (m, 3 H, 2- H_A , and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.65 (t, J = 7.6 Hz, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.55–2.67 (m, 1 H, 3-H), 2.68–2.73 (m, 1 H, 8a-H), 2.78 (dd, J = 11.2, J = 2.7 Hz, 1 H, 2- H_B), 4.11 (q, J = 7.1 Hz, 2 H, OCH_2CH_3), 7.14–7.29 (m, 5 H, Ph) ppm. ^{13}C NMR (75.5 MHz, CDCl_3): δ = 14.0 (OCH_2CH_3), 17.3 (C-7), 20.2 (C-6), 25.3 (C-8), 26.9 (C-4), 29.3 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 31.2 (C-5), 33.4 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 34.5 (C-4a), 42.0 (C-3), 47.2 (C-2), 53.1 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 58.4 (C-8a), 59.9 (OCH_2CH_3), 125.4 (*p*-Ph), 128.0 (*o*-Ph), 128.1 (*m*-Ph), 142.1 (Ph), 174.2 (COO) ppm. IR (film): $\tilde{\nu}$ = 3025 (w), 2931 (vs), 2864 (s), 1730 (vs, C=O), 1602 (w), 1496 (m), 1453 (m), 1370 (m), 1320 (w), 1261 (m), 1248 (m), 1157 (s), 1032 (m), 746 (m), 699 (m) cm^{-1} . MS (EI, 70 eV): m/z (%) = 329 (38) [M^+], 286 (92), 224 (100) [$\text{M}^+ - \text{EtPh}$], 91 (22) [Bn^+]; found [M^+] 329.2360. $\text{C}_{21}\text{H}_{31}\text{NO}_2$ requires 329.2355.

Ethyl (3*S,4*aR**,8*aR**)-1-Benzyldecahydroquinoline-3-carboxylate (15b):** Following a similar procedure to that described above for the preparation of **15a**, olefin **14b** (415 mg, 1.4 mmol) was subjected to hydrogenation over platinum oxide (50 mg) to give **15b** (227 mg, 54%) as a pale yellow oil. ^1H NMR (300 MHz, CDCl_3): δ = 1.08–1.14 (m, 1 H, 8- H_A), 1.21 (t, J = 10.3 Hz, 3 H, OCH_2CH_3), 1.31–1.39 (m, 2 H, 6- CH_2), 1.45–1.71 (m, 5 H, 4- H_A , 5- CH_2 and 7- CH_2), 1.72–1.92 (m, 2 H, 4- H_B and 8- H_B), 1.94–2.10 (m, 1 H, 4a-H), 2.51–2.66 (m, 2 H, 2- H_A and 3-H), 2.67–2.80 (m, 2 H, 2- H_B and 8a-H), 3.57–3.62 (m, 1 H, $\text{NCH}_A\text{CH}_B\text{Ph}$), 3.71–3.76 (m, 1 H, $\text{NCH}_A\text{CH}_B\text{Ph}$), 4.10 (q, J = 7.0 Hz, 2 H, OCH_2CH_3), 7.16–7.31

(m, 5 H, Ph) ppm. ^{13}C NMR (75.5 MHz, CDCl_3): δ = 14.2 (OCH_2CH_3), 18.1 (C-7), 21.0 (C-6), 25.5 (C-8), 27.3 (C-4), 31.4 (C-5), 34.7 (C-4a), 42.3 (C-3), 47.0 (C-2), 58.4 (NCH_2Ph), 58.9 (C-8a), 60.1 (OCH_2CH_3), 126.7, 128.1, 128.4 (Ph), 139.8 (Ph), 174.7 (COO) ppm. IR (film): $\tilde{\nu}$ = 2927 (vs), 2836 (s), 1727 (vs, C=O), 1660 (w), 1176 (s), 1027 (m) cm^{-1} . MS (EI, 70 eV): m/z (%) = 301 (35) [M^+], 258 (100), 149 (27), 91 (73); found [M^+] 301.20339. $\text{C}_{19}\text{H}_{27}\text{NO}_2$ requires 301.20418.

Ethyl (3*S,4*aR**,8*aR**)-1-Butyldecahydroquinoline-3-carboxylate (15c):** Following a similar procedure to that described above for the preparation of **15a**, olefin **14c** (466 mg, 1.8 mmol) was subjected to hydrogenation over platinum oxide (68 mg) to give **15c** (255 mg, 54%) as a pale yellow oil. IR (film): ^1H NMR (400 MHz, CDCl_3): δ = 0.91 (t, J = 7.3 Hz, 3 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 1.12–1.19 (m, 1 H, 8- H_A), 1.26 (t, J = 7.2 Hz, 3 H, OCH_2CH_3), 1.12–1.41 (m, 4 H, 7- CH_2 and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 1.43–1.50 (m, 4 H, 6- CH_2 and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 1.52–1.62 (m, 3 H, 4- H_A and 5- CH_2), 1.76–1.85 (m, 2 H, 4- H_B and 8- H_B), 1.95–1.99 (m, 1 H, 3-H), 2.41–2.54 (m, 3 H, 2- H_A and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 2.58–2.65 (m, 1 H, 4a-H), 2.72–2.75 (m, 1 H, 8a-H), 2.76–2.81 (m, 1 H, 2- H_B), 4.12 (q, J = 7.1 Hz, 2 H, OCH_2CH_3) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 14.0 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 14.1 (OCH_2CH_3), 17.29 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 20.7 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 20.9 (C-7), 25.5 (C-8), 27.1 (C-4), 30.1 (C-6), 31.4 (C-5), 34.6 (C-3), 42.1 (C-4a), 47.5 (C-2), 53.8 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 58.5 (C-8a), 60.1 (OCH_2CH_3), 174.58 (COO) ppm. $\tilde{\nu}$ = 2929 (vs), 2863 (s), 1729 (vs, C=O), 1448 (w), 1260 (m), 1176 (s), 1160 (m) cm^{-1} . MS (EI, 70 eV): m/z (%) = 267 (13) [M^+], 224 (100), 41 (7); found [M^+] 267.22008. $\text{C}_{16}\text{H}_{29}\text{NO}_2$ requires 267.21983.

Ethyl (3*R*,4*aS*,8*aS*)-1-[(*R*)-1-Phenylethyl]decahydroquinoline-3-carboxylate (15d): Following a similar procedure to that described above for the preparation of **15a**, olefin **14d** (323 mg, 1.0 mmol) was subjected to hydrogenation over platinum oxide (60 mg) to give **15d** (235 mg, 72%) as a yellow oil. $[\alpha]_\text{D}^{20}$ = +45 (c = 0.90, CHCl_3). ^1H NMR (400 MHz, CDCl_3): δ = 1.14–1.22 (m, 1 H, 8- H_A), 1.9 (t, J = 7.2 Hz, 3 H, OCH_2CH_3), 1.27–1.30 [m, 3 H, $\text{NCH}(\text{CH}_3)\text{Ph}$], 1.32–1.46 (m, 2 H, 6- CH_2), 1.43–1.77 (m, 6 H, 4- CH_2 , 5- CH_2 and 7- CH_2), 1.79–1.86 (m, 1 H, 4a-H), 2.00–2.08 (m, 1 H, 8- H_B), 2.40–2.53 (m, 2 H, 2- H_A and 3-H), 2.64 (d, J = 5.6 Hz, 1 H, 2- H_B), 3.05 (dt, J = 3.5, 12 Hz, 1 H, 8a-H), 3.66 [q, J = 6.4 Hz, 1 H, $\text{NCH}(\text{CH}_3)\text{Ph}$], 4.01–4.05 (m, 2 H, OCH_2CH_3), 7.21–7.35 (m, 5 H, Ph) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 14.1 (OCH_2CH_3), 18.0 [$\text{NCH}(\text{CH}_3)\text{Ph}$], 21.0 (C-7), 22.2 (C-6), 25.6 (C-8), 27.6 (C-4), 31.6 (C-5), 34.7 (C-4a), 42.3 (C-3), 45.4 (C-2), 55.1 [$\text{NCH}(\text{CH}_3)\text{Ph}$], 60.0 (C-8a), 60.4 (OCH_2CH_3), 126.5, 126.9, 128.3 (Ph), 147.1 (Ph), 174.8 (COO) ppm. IR (film): $\tilde{\nu}$ = 2973 (s), 2930 (vs), 2870 (s), 1720 (vs, C=O), 1449 (w), 1367 (m), 1324 (m), 1186 (m), 1153 (s), 1029 (m) cm^{-1} . MS (EI, 70 eV): m/z (%) = 315 (79) [M^+], 300 (42), 272 (74), 210 (18), 168 (63), 105 (100), 91 (12); found [M^+] 315.21981. $\text{C}_{20}\text{H}_{29}\text{NO}_2$ requires 315.21983.

[(3*S,4*aR**,8*aR**)-1-(3-Phenylpropyl)decahydroquinolin-3-yl]methanol (16a):** A solution of ester **15a** (350 mg, 1.07 mmol) in dry THF (4.5 mL) was added dropwise to a suspension of LiAlH_4 (40 mg, 1.06 mmol) in dry THF (1.5 mL) and the mixture was stirred under nitrogen for 1 h. The reaction was quenched cautiously with 5.2 M aq. KOH (0.7 mL) and the mixture stirred for 15 min. The mixture was filtered through a pad of Celite and washed with EtOAc. The filtrate was concentrated to yield **16a** (130 mg, 100%) as a pale yellow oil that was used without further purification. ^1H NMR (300 MHz, CDCl_3): δ = 1.10–1.20 (m, 1 H, 7- H_A), 1.29–1.37 (m, 2 H, 4- CH_2), 1.39–1.42 (m, 2 H, 6- CH_2), 1.43–1.50 (m, 2 H, 8- CH_2), 1.58–1.62 (m, 2 H, 5- CH_2), 1.78–1.82 (m, 1 H, 7- H_B), 1.85–

1.93 (m, 3 H, 3-H and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 1.94–2.08 (m, 1 H, 4a-H), 2.12–2.19 (m, 1 H, 2- H_A), 2.40–2.54 (m, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.55–2.71 (m, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.74–2.76 (m, 1 H, 2- H_B), 2.79–2.81 (m, 1 H, 8a-H), 3.41–3.55 (m, 2 H, CH_2OH), 7.14–7.30 (m, 5 H, Ph) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 17.0 (C-8), 21.0 (C-6), 25.6 (C-7), 27.2 (C-4), 29.5 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 31.7 (C-5), 33.8 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 35.2 (C-4a), 39.4 (C-3), 49.4 (C-2), 53.7 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 58.9 (C-8a), 66.6 (CH_2OH), 125.6 (p -Ph), 128.2 (o -Ph), 128.4 (m -Ph), 142.3 (Ph) ppm. IR (film): $\tilde{\nu}$ = 3369 (br., O-H), 3025 (m), 2928 (vs), 2860 (s), 1495 (m), 1466 (m), 1452 (s), 1372 (m), 1081 (s), 1039 (s), 738 (s), 699 (s) cm^{-1} . MS (EI, 70 eV): m/z (%) = 287 (28) [M^+], 244 (100), 182 (87), 91 (26) [Bn^+], 44 (26); found [M^+] 287.2246. $\text{C}_{19}\text{H}_{29}\text{NO}$ requires 287.2249.

[(3*S,4*aR**,8*aR**)-1-Benzyldecahydroquinolin-3-yl]methanol (16b):** Following a similar procedure to that described above for the preparation of **16a**, ester **15b** (277 mg, 0.96 mmol) was reduced with lithium aluminium hydride (37 mg, 0.97 mmol) to give **16b** (195 mg, 100%) as a pale yellow oil, which was used without further purification. ^1H NMR (400 MHz, CDCl_3): δ = (CDCl_3) 1.02–1.18 (m, 1 H, 7- H_A), 1.23–1.29 (m, 2 H, 6- CH_2), 1.29–1.39 (m, 2 H, 4- CH_2), 1.48–1.64 (m, 4 H, 5- CH_2 and 8- CH_2), 1.70–1.77 (m, 1 H, 7- H_B), 1.81–1.92 (m, 1 H, 3-H), 2.01–2.08 (m, 1 H, 4a-H), 2.15–2.21 (m, 1 H, 2- H_A), 2.63 (d, J = 11.4 Hz, 1 H, 2- H_B), 2.72–2.82 (m, 1 H, 8a-H), 3.42–3.45 (m, 2 H, CH_2OH), 3.58 (dd, J = 2.6, 13.6 Hz, 1 H, $\text{NCH}_\text{A}\text{CH}_\text{B}\text{Ph}$), 3.73 (dd, J = 2.6, 13.6 Hz, 1 H, $\text{NCH}_\text{A}\text{CH}_\text{B}\text{Ph}$), 7.20–7.34 (m, 5 H, Ph) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 17.5 (C-8), 20.8 (C-6), 25.4 (C-7), 27.0 (C-4), 31.5 (C-5), 34.9 (C-4a), 39.0 (C-3), 48.6 (C-2), 58.4 (NCH_2Ph), 59.1 (C-8a), 66.1 (CH_2OH), 126.5, 128.1, 128.4 (Ph), 139.6 (Ph) ppm. IR (film): $\tilde{\nu}$ = 3352 (br., O-H), 3027 (m), 2920 (vs), 2852 (s), 1494 (m), 1451 (s), 1369 (m), 1069 (s), 1036 (s), 735 (s), 700 (s) cm^{-1} . MS (EI, 70 eV): m/z (%) = 258 (40) [M^+], 214 (95), 153 (100), 91 (31); found [M^+] 258.20298. $\text{C}_{17}\text{H}_{25}\text{NO}$ requires 258.20275.

[(3*S,4*aR**,8*aR**)-1-Butyldecahydroquinolin-3-yl]methanol (16c):** Following a similar procedure to that described above for the preparation of **16a**, ester **15c** (220 mg, 0.82 mmol) was reduced with lithium aluminium hydride (31 mg, 0.82 mmol) to give **16c** (185 mg, 100%) as a pale yellow oil, which was used without further purification. ^1H NMR (400 MHz, CDCl_3): δ = 0.83 (t, J = 7.3 Hz, 3 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 1.02–1.08 (m, 1 H, 7- H_A), 1.14–1.31 (m, 6 H, 4- CH_2 , 8- CH_2 and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 1.32–1.42 (m, 4 H, 6- CH_2 and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 1.43–1.51 (m, 2 H, 5- CH_2), 1.67 (d, J = 12.8 Hz, 1 H, 7- H_B), 1.74–1.80 (m, 1 H, 3-H), 1.89–1.95 (m, 1 H, 4a-H), 1.99 (t, J = 11.5 Hz, 1 H, 2- H_A), 2.26–2.33 (m, 1 H, $\text{NCH}_\text{A}\text{H}_\text{B}\text{CH}_2\text{CH}_2\text{CH}_3$), 2.66 (dd, J = 3.5, 11.7 Hz, 1 H, 2- H_B), 2.69–2.74 (m, 1 H, 8a-H), 3.26–3.30 (m, 1 H, $\text{CH}_\text{A}\text{H}_\text{B}\text{OH}$), 3.37–3.41 (m, 1 H, $\text{CH}_\text{A}\text{H}_\text{B}\text{OH}$) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 13.9 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 16.6 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 20.8 (C-8 and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 25.5 (C-7), 27.1 (C-4), 29.5 (C-6), 31.5 (C-5), 34.9 (C-4a), 39.1 (C-3), 49.7 (C-2), 54.1 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 58.6 (C-8a), 65.8 (CH_2OH) ppm. IR (film): $\tilde{\nu}$ = 3367 (br., O-H), 2927 (vs), 2861 (s), 1448 (m), 1374 (m), 1079 (s), 1037 (s), 735 (s), 702 (s) cm^{-1} . MS (EI, 70 eV): m/z (%) = 225 (60) [M^+], 41 (32); found [M^+] 225.21248. $\text{C}_{14}\text{H}_{27}\text{NO}$ requires 225.21305.

{(3*R*,4*aS*,8*aS*)-1-[(*R*)-1-Phenylethyl]decahydroquinolin-3-yl}methanol (16d): Following a similar procedure to that described above for the preparation of **16a**, ester **15d** (235 mg, 0.74 mmol) was reduced with lithium aluminium hydride (28 mg, 0.74 mmol) to give **16d** (202 mg, 100%) as a pale yellow oil, which was used

without further purification. $[\alpha]_D^{20} = +44$ ($c = 0.75$, CHCl_3). ^1H NMR (300 MHz, CDCl_3): $\delta = 1.11$ – 1.22 (m, 1 H, 7- H_A), 1.27 [t, $J = 7.4$ Hz, 3 H, $\text{NCH}(\text{CH}_3)\text{Ph}$], 1.30– 1.43 (m, 4 H, 4- CH_2 and 6- CH_2), 1.46– 1.63 (m, 4 H, 5- CH_2 and 8- CH_2), 1.65– 1.78 (m, 1 H, 7- H_B), 1.95– 2.08 (m, 3 H, 2- H_A , 3- H and 4a- H), 2.46 (dd, $J = 3.8$, 11.6 Hz, 1 H, 2- H_B), 3.08– 3.12 (m, 1 H, 8a- H), 3.35 (d, $J = 6.0$ Hz, 2 H, CH_2OH), 3.61 [q, $J = 6.5$ Hz, 1 H, $\text{NCH}(\text{CH}_3)\text{Ph}$], 7.17– 7.31 (m, 5 H, Ph) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 17.6$ (C-8), 21.1 [$\text{NCH}(\text{CH}_3)\text{Ph}$], 22.1 (C-6), 25.9 (C-7), 27.5 (C-4), 31.9 (C-5), 35.2 (C-4a), 39.3 (C-3), 47.1 (C-2), 55.6 [$\text{NCH}(\text{CH}_3)\text{Ph}$], 60.7 (C-8a), 66.6 (CH_2OH), 126.5, 127.0, 128.3 (Ph), 147.4 (Ph) ppm. IR (film): $\tilde{\nu} = 3285$ (br., O-H), 3027 (w), 2920 (vs), 2871 (s), 1450 (m), 1368 (m), 1070 (s), 1040 (s), 761 (s), 701 (s) cm^{-1} . MS (EI, 70 eV): m/z (%) = 273 (47) [M^+], 229 (80), 168 (100), 91 (32); found [M] $^+$ 273.21513. $\text{C}_{18}\text{H}_{27}\text{NO}_2$ requires 273.21533.

[(3S*,4aR*,8aR*)-1-(3-Phenylpropyl)decahydroquinolin-3-yl]methyl 2-(3-Methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)benzoate (17a): 2-(3-Methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)benzoic acid **10** [33] (180 mg, 0.78 mmol), DCC (160 mg, 0.78 mmol) and DMAP (4.00 mg, 0.04 mmol) was added to alcohol **16a** (112 mg, 0.39 mmol) in CH_2Cl_2 (7 mL). The reaction was stirred for 18 h at room temperature, then filtered through Celite, washed with EtOAc and the filtrate concentrated in vacuo. The crude product was purified by column chromatography on silica (hexane/EtOAc, 8:2) to give **17a** (180 mg, 95%) as an oil. $R_f = 0.32$ (hexane/EtOAc, 8:2). ^1H NMR (400 MHz, CDCl_3): $\delta = 1.03$ – 1.17 (m, 1 H, 7''- H_A), 1.29– 1.40 (m, 4-H, 4''- CH_2 and 6''- CH_2), 1.41– 1.50 (m, 2 H, 8''- CH_2), 1.54– 1.59 (m, 2 H, 5''- CH_2), 1.68– 1.84 (m, 3 H, 7''- H_B and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 1.98– 2.09 (m, 2 H, 3''- H and 4a''- H), 2.10– 2.20 (m, 4 H, 2''- H_A and 3'- CH_3), 2.44– 2.57 (m, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.61– 2.65 (m, 3 H, 2''- H_B and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.76– 2.80 (m, 1 H, 8a''- H), 4.04– 4.21 (m, 2 H, CH_2O), 6.48 (t, $J = 1.7$ Hz, 1 H, 4'- H), 7.15– 7.30 (m, 6 H, 6- H and Ph), 7.49 (td, $J = 7.8$, $J = 1.2$ Hz, 1 H, 5- H), 7.61 (td, $J = 7.7$, $J = 1.4$ Hz, 1 H, 4- H), 8.07 (dd, $J = 7.8$, $J = 1.5$ Hz, 1 H, 3- H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 11.1$ (Me), 16.9 (C-8''), 20.9 (C-6''), 25.4 (C-7''), 27.3 (C-4''), 29.4 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 31.5 (C-5''), 33.7 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 35.1 (C-4a''), 36.1 (C-3''), 49.0 (C-2''), 53.4 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 58.4 (C-8a''), 68.3 (CH_2O), 125.6 (*p*-Ph), 127.9 (C-4'), 128.0 (C-1), 128.1 (*m*-Ph), 128.3 (*o*-Ph), 128.8 (C-5), 130.2 (C-6), 131.4 (C-3), 131.5 (C-2), 133.1 (C-4), 142.2 (Ph), 146.1 (C-3'), 164.8 (COO), 169.6 (CO), 170.6 (CO) ppm. IR (film): $\tilde{\nu} = 3025$ (w), 2929 (vs), 1727 (vs, C=O), 1714 (vs, C=O), 1602 (m), 1494 (s), 1454 (s), 1393 (s), 1292 (s), 1259 (s), 1108 (s), 910 (m), 855 (m), 756 (m), 732 (s), 699 (s) cm^{-1} . MS (EI, 70 eV): m/z (%) = 500 (45) [M^+], 457 (68), 395 (100), 308 (14), 214 (40), 91 (35) [Bn^+], 41 (15); found [M] $^+$ 500.2670. $\text{C}_{31}\text{H}_{36}\text{N}_2\text{O}_4$ requires 500.2675.

[(3S*,4aR*,8aR*)-1-Benzyldecahydroquinolin-3-yl]methyl 2-(3-Methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)benzoate (17b): Following a similar procedure to that described above for the preparation of **17a**, alcohol **16b** (80 mg, 0.31 mmol) was treated with 2-(3-methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)benzoic acid **10** (143 mg, 0.62 mmol), DMAP (3 mg) and DCC (128 mg, 0.62 mmol). The crude product was purified by flash chromatography (20% hexanes in ethyl acetate) to give **17b** (0.077 g, 53%) as an oil. ^1H NMR (400 MHz, CDCl_3): $\delta = 1.04$ – 1.14 (m, 1 H, 7''- H_A), 1.26– 1.31 (m, 2 H, 6''- CH_2), 1.34– 1.43 (m, 2 H, 4''- CH_2), 1.46– 1.61 (m, 4 H, 5''- CH_2 and 8''- CH_2), 1.69– 1.79 (m, 1 H, 7''- H_B), 1.87– 1.94 (m, 1 H, 3''- H), 1.97– 2.10 (m, 4 H, 4a''- H , 3'- CH_3), 2.22 (t, $J = 11.2$ Hz, 1 H, 2''- H_A), 2.58 (dd, $J = 3.2$, 1 H, 11.2 Hz, 2''- H_B), 2.73– 2.78 (m, 1 H, 8a''- H), 3.58 (d, $J = 13.6$ Hz, 1 H, $\text{NCH}_A\text{H}_B\text{Ph}$), 3.73 (d, $J = 13.6$ Hz, 1 H, $\text{NCH}_A\text{H}_B\text{Ph}$), 4.01– 4.14 (m, 2 H, CH_2O), 6.45 (s, 1 H, 4'- H), 7.21– 7.34 (m, 6 H, 2- H and

Ph), 7.44 (t, $J = 8.0$ Hz, 1 H, 5- H), 7.61 (t, $J = 8.0$ Hz, 1 H, 4- H), 7.95 (d, $J = 8.0$ Hz, 1 H, 3- H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 11.1$ (3'- CH_3), 17.6 (C-8''), 20.94 (C-6''), 25.4 (C-7''), 27.3 (C-4''), 31.5 (C-5''), 35.0 (C-4a''), 36.1 (C-3''), 48.4 (C-2''), 58.4 (NCH_2Ph), 58.9 (C-8a''), 68.3 (CH_2O), 126.6 (Ph), 127.8 (C-4'), 128.0 (C-1), 128.1 (Ph), 128.5 (Ph), 128.8 (C-5), 130.2 (C-6), 131.4 (C-3), 131.6 (C-2), 133.1 (C-4), 139.7 (Ph), 146.1 (C-3'), 164.7 (COO), 169.64 (CO), 170.7 (CO) ppm. IR (film): $\tilde{\nu} = 3025$ (w), 2929 (vs), 1727 (vs, C=O), 1714 (vs, C=O), 1602 (m), 1494 (s), 1454 (s), 1393 (s), 1292 (s), 1259 (s), 1108 (s) cm^{-1} . MS (EI, 70 eV): m/z (%) = 427 (26) [M^+], 429 (46), 224 (26), 91 (87), 56 (100), 41 (65); found [M] $^+$ 427.23547. $\text{C}_{29}\text{H}_{32}\text{N}_2\text{O}_4$ requires 427.23621.

[(3S*,4aR*,8aR*)-1-Butyldecahydroquinolin-3-yl]methyl 2-(3-Methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)benzoate (17c): Following a similar procedure to that described above for the preparation of **17a**, alcohol **16c** (100 mg, 0.39 mmol) was treated with 2-(3-methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)benzoic acid **10** (143 mg, 0.62 mmol), DMAP (5 mg) and DCC (161 mg, 0.78 mmol). The crude product was purified by flash chromatography (20% hexanes in ethyl acetate) to give **17c** (91 mg, 53%) as an oil. ^1H NMR (400 MHz, CDCl_3): $\delta = 0.98$ (t, $J = 14.8$ Hz, 3 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 1.03– 1.19 (m, 1 H, 7''- H_A), 1.21– 1.36 (m, 4 H, 8''- CH_2 and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 1.39– 1.48 (m, 6 H, 4''- CH_2 , 6''- CH_2 and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 1.51– 1.59 (m, 2 H, 5''- CH_2), 1.67– 1.81 (m, 1 H, 7''- H_B), 1.98– 2.10 (m, 4 H, 4a''- H and 3'- CH_3), 2.12– 2.18 (m, 2 H, 2''- H_A and 3''- H), 2.41– 2.60 (m, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 2.62– 2.69 (m, 1 H, 2''- H_B), 2.78– 2.85 (m, 1 H, 8a''- H), 3.96– 4.27 (m, 2 H, CH_2O), 6.50 (t, $J = 1.8$ Hz, 1 H, 4- H), 7.28 (dd, $J = 1.8$, 10 Hz, 1 H, 6- H), 7.49 (dt, $J = 1.9$, 10.2 Hz, 1 H, 5- H), 7.63 (dt, $J = 2.4$, 10 Hz, 1 H, 4- H), 8.07 (dd, $J = 2.0$, 10.4 Hz, 1 H, 3- H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 11.1$ (3'- CH_3), 14.0 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 16.8 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 20.7 (C-8''), 20.8 (CH_2 , $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 25.5 (C-7''), 27.2 (C-4''), 29.6 (C-6''), 31.4 (C-5''), 34.9 (C-4a''), 38.1 (C-3''), 49.1 (C-2''), 53.8 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 58.4 (C-8a''), 65.4 (CH_2O), 127.8 (C-4'), 128.1 (C-1), 128.8 (C-5), 130.2 (C-6), 131.4 (C-3), 131.6 (C-2), 133.1 (C-4), 146.1 (C-3'), 164.8 (COO), 169.6 (CO), 170.6 (CO) ppm. IR (film): $\tilde{\nu} = 2926$ (w), 2849 (vs), 1715 (vs, C=O), 1449 (s), 1390 (s), 1372 (s), 1292 (s), 1241 (s), 1085 (s) cm^{-1} . MS (EI, 70 eV): m/z (%) = 438 (8) [M^+], 395 (48), 224 (26), 143 (20), 99 (33), 56 (100), 41 (20); found [M] $^+$ 438.25122. $\text{C}_{26}\text{H}_{34}\text{N}_2\text{O}_4$ requires 438.25186.

{(3R,4aS,8aS)-1-[(R)-1-Phenylethyl]decahydroquinolin-3-yl}methyl 2-(3-Methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)benzoate (17d): Following a similar procedure to that described above for the preparation of **17a**, alcohol **16d** (100 mg, 0.36 mmol) was treated with 2-(3-methyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-1-yl)benzoic acid **10** (169 mg, 0.73 mmol), DMAP (5 mg) and DCC (151 mg, 0.73 mmol). The crude product was purified by flash chromatography (20% hexanes in ethyl acetate) to give **17d** (121 mg, 70%) as an oil. $[\alpha]_D^{20} = +46$ ($c = 0.84$, CHCl_3). ^1H NMR (400 MHz, CDCl_3): $\delta = 1.01$ – 1.19 (m, 1 H, 7''- H_A), 1.22– 1.26 [m, 3 H, $\text{NCH}(\text{CH}_3)\text{Ph}$], 1.29– 1.44 (m, 4 H, 4''- CH_2 and 6''- CH_2), 1.52– 1.63 (m, 4 H, 5''- CH_2 and 8''- CH_2), 1.71– 1.80 (m, 1 H, 7''- H_B), 1.89– 2.08 (m, 3 H, 2''- H_A , 3''- H and 4a''- H), 2.13 (s, 3 H, 3'- CH_3), 2.52 (d, $J = 9.2$ Hz, 1 H, 2''- H_B), 3.10– 3.17 (m, 1 H, 8a''- H), 3.61 [q, $J = 6.5$ Hz, 1 H, $\text{NCH}(\text{CH}_3)\text{Ph}$], 3.82– 2.87 (m, 1 H, $\text{CH}_A\text{H}_B\text{O}$), 3.96– 4.01 (m, 1 H, $\text{CH}_A\text{H}_B\text{O}$), 6.45– 6.46 (m, 1 H, 4'- H), 7.21– 7.39 (m, 7 H, 5- H , 6- H and Ph), 7.56– 7.65 (m, 2 H, 3- H and 4- H) ppm. ^{13}C NMR (100 MHz, CDCl_3): $\delta = 11.0$ (3'- CH_3), 17.4 (C-8''), 20.9 (C-6''), 21.0 [$\text{NCH}(\text{CH}_3)\text{Ph}$], 25.5 (C-7''), 27.4 (C-4''), 31.7 (C-5''), 35.2 (4a''- H), 36.2 (C-3''), 47.0 (C-2''), 55.3 [$\text{NCH}(\text{CH}_3)\text{Ph}$], 60.5 (C-8a''), 70.0 (CH_2O), 126.5 (Ph), 127.0 (C-4'), 127.8 (C-1), 127.9,

128.2 (Ph), 128.8 (C-5), 130.1 (C-6), 131.2 (C-3), 131.6 (C-2), 132.9 (C-4), 146.0 (C-3' and Ph), 164.44 (COO), 169.4 (CO), 170.7 (CO) ppm. IR (film): $\tilde{\nu}$ = 2931 (w), 2852 (vs), 1710 (vs, C=O), 1602 (s), 1492 (s), 1452 (s), 1394 (s), 1244 (s), 1208 (s), 1109 (s), 1108 (s) cm^{-1} . MS (EI, 70 eV): m/z (%) = 486 (73) [M^+], 471 (31), 443 (56), 339 (63), 214 (43), 105 (100); found [M] $^+$ 486.25221. $\text{C}_{30}\text{H}_{34}\text{N}_2\text{O}_4$ requires 486.25186.

[(3S*,4aR*,8aR*)-1-(3-Phenylpropyl)decahydroquinolin-3-yl]methyl 2-(3-Methyl-2,5-dioxopyrrolidin-1-yl)benzoate (5a): 10% Palladium on carbon (10 mg) was added to a solution of maleimide **17a** (180 mg, 0.36 mmol) in EtOAc (2 mL) and the mixture stirred under hydrogen for 18 h. The mixture was filtered through Celite that was washed with EtOAc. The solvent was removed in vacuo to give **5a** (172 mg, 95%) as an oil and as a 1:1 mixture of diastereomers. R_f = 0.43 ($\text{CH}_2\text{Cl}_2/\text{MeOH}$, 9:1). ^1H NMR (400 MHz, CDCl_3): δ = 1.02–1.98 (m, 1 H, 7''-H_A), 1.23–1.52 (m, 9 H, 4''-H, 6''-H, 8''-H and 3'-CH₃), 1.57–1.62 (m, 2 H, 5''-H), 1.72–1.80 (m, 1 H, 7''-H_B), 1.81–1.92 (m, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.02–2.07 (m, 1 H, 4a''-H), 2.14–2.20 (m, 2 H, 2''-H_A and 3'-H), 2.47–2.59 (m, 3 H, 4'-H_A and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.61–2.65 (m, 2 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 2.71–2.80 (m, 1 H, 2''-H_B), 2.82–2.91 (m, 1 H, 8a''-H), 2.95–3.14 (m, 2 H, 3'-H and 4'-H_B), 4.06–4.13 (m, 2 H, CH_2O), 7.14–7.28 (m, 6 H, 6-H and Ph), 7.50 (td, J = 7.7, J = 1.1 Hz, 1 H, 5-H), 7.64 (dt, J = 7.7, J = 1.4 Hz, 1 H, 4-H), 8.07 (d, J = 7.5 Hz, 1 H, 3-H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 16.1 (Me), 16.4 (Me), 16.4 (C-8), 17.0 (C-8''), 20.9 (C-6''), 25.3 (C-7''), 26.9 (C-4''), 28.7 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 31.3 (C-5''), 33.4 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 34.6 (C-4a''), 35.0 (C-3'), 35.2 (C-3'), 35.7 (C-3''), 36.8 (C-4'), 49.0 (C-2''), 53.2 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 58.4 (C-8a''), 67.8 (CH_2O), 125.6 (*p*-Ph), 127.2 (C-1), 128.1 (*m*-Ph), 128.2 (*o*-Ph), 129.2 (C-5), 129.6 (C-6), 131.3 (C-3), 132.6 (C-2), 133.2 (C-4), 141.8 (Ph), 164.1 (COO), 175.8 (CO), 179.7 (CO) ppm. IR (film): $\tilde{\nu}$ = 3025 (w), 2931 (vs), 1713 (vs, C=O), 1602 (m), 1494 (m), 1454 (m), 1391 (s), 1291 (m), 1261 (s), 1187 (s), 1137 (m), 1084 (m), 910 (m), 745 (m), 700 (m) cm^{-1} . MS (EI, 70 eV): m/z (%) = 502 (46) [M^+], 459 (67), 397 (100), 216 (18), 146 (15), 91 (24) [Bn^+], 41 (16); found [M] $^+$ 502.2833. $\text{C}_{31}\text{H}_{38}\text{N}_2\text{O}_4$ requires 502.2832.

[(3S*,4aR*,8aR*)-1-Benzyldecahydroquinolin-3-yl]methyl 2-(3-Methyl-2,5-dioxopyrrolidin-1-yl)benzoate (5b): Following a similar procedure to that described above for the preparation of **5a**, olefin **17b** (77 mg, 0.16 mmol) was subjected to hydrogenation over 10% palladium on carbon (7 mg) to give **5b** (75 mg, 97%) as an oil and as a 1:1 mixture of diastereomers. ^1H NMR (400 MHz, CDCl_3): δ = 1.05–1.14 (m, 1 H, 7''-H_A), 1.26–1.34 (m, 2 H, 6''-CH₂), 1.36–1.49 (m, 5 H, 4''-CH₂ and 3'-CH₃), 1.50–1.61 (m, 4 H, 5''-CH₂ and 8''-CH₂), 1.69–1.77 (m, 1 H, 7''-H_B), 1.83–1.97 (m, 1 H, 3''-H), 2.00–2.12 (m, 1 H, 4a''-H), 2.24 (t, J = 11.3 Hz, 1 H, 2''-H_A), 2.42–2.60 (m, 2 H, 4'-CH₂), 2.62–2.65 (m, 1 H, 2''-H_B), 2.72–2.81 (m, 1 H, 8a''-H), 2.98–3.13 (m, 1 H, 3'-H), 3.60 (d, J = 13.1 Hz, 1 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 3.74 (d, J = 13.6 Hz, 1 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{Ph}$), 3.98–4.25 (m, 2 H, CH_2O), 7.21–7.36 (m, 6 H, 2-H, Ph), 7.46 (dt, J = 1.1, 7.7 Hz, 1 H, 5-H), 7.63 (dt, J = 1.5, 7.7 Hz, 1 H, 4-H), 7.96 (d, J = 10 Hz, 1 H, 3-H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 16.2 (3'-CH₃), 16.4 (3'-CH₃), 17.7 (C-8''), 20.9 (C-6''), 25.4 (C-7''), 27.3 (C-4''), 31.5 (C-5''), 33.9 (C-4a''), 35.2 (C-3'), 36.1 (C-3''), 36.9 (C-4'), 48.4 (C-2''), 58.4 ($\text{NCH}_2\text{CH}_2\text{Ph}$), 59.0 (C-8a''), 68.1 (CH_2O), 122.7 (Ph), 127.3 (C-1), 128.1, 128.5 (Ph), 129.2 (C-5), 129.7 (C-6), 131.4 (C-3), 132.6 (C-2), 133.2 (C-4), 139.6 (Ph), 164.1 (COO), 171.0 (CO), 179.8 (CO) ppm. IR (film): $\tilde{\nu}$ = 2926 (vs), 2853 (s), 1713 (s), 1493 (m), 1389 (s), 1290 (m), 1259 (s), 1184 (s), 1036 (s), 1082 (s), 1044 (s) cm^{-1} . MS (EI, 70 eV): m/z (%) = 474 (47) [M^+], 431 (100), 258 (24), 149 (22), 91 (87), 71 (22), 57 (33), 43 (22); found [M] $^+$ 474.25225. $\text{C}_{29}\text{H}_{34}\text{N}_2\text{O}_4$ requires 474.25186.

[(3S*,4aR*,8aR*)-1-Butyldecahydroquinolin-3-yl]methyl 2-(3-Methyl-2,5-dioxopyrrolidin-1-yl)benzoate (5c): Following a similar procedure to that described above for the preparation of **5a**, olefin **17c** (91 mg, 0.21 mmol) was subjected to hydrogenation over 10% palladium on carbon (5 mg) to give **5c** (90 mg, 99%) as an oil and as a 1:1 mixture of diastereomers. ^1H NMR (400 MHz, CDCl_3): δ = 0.92 (t, J = 7.4 Hz, 3 H, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 1.16–1.19 (m, 1 H, 7''-H_A), 1.30–1.37 (m, 4 H, 8''-CH₂ and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 1.40–1.50 (m, 9 H, 4''-CH₂, 6''-CH₂, $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$ and 3'-CH₃), 1.52–1.60 (m, 2 H, 5''-CH₂), 1.71–1.82 (m, 1 H, 7''-H_B), 2.04–2.16 (m, 1 H, 4a''-H), 2.21–2.33 (m, 2 H, 3'-H and 2''-H_A), 2.47–2.52 (m, 4 H, 4'-CH₂ and $\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 2.78–2.83 (m, 1 H, 2''-H_B), 2.87–2.91 (m, 1 H, 8a''-H), 2.95–3.05 (m, 1 H, 3'-H), 4.06–4.15 (m, 2 H, CH_2O), 7.26 (d, J = 7.6 Hz, 1 H, 6-H), 7.53 (t, J = 7.6 Hz, 1 H, 5-H), 7.66 (t, J = 7.2 Hz, 1 H, 4-H), 8.10 (d, J = 7.6 Hz, 1 H, 3-H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 14.1 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 16.4 (3'-CH₃), 16.5 (3'-CH₃), 17.0 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 20.7 (C-8''), 20.8 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 25.5 (C-7''), 26.9 (C-4''), 29.6 (C-6''), 31.2 (C-5''), 34.5 (C-4a''), 35.3 (C-3'), 35.5 (C-3'), 36.9 (C-3''), 38.1 (C-4'), 49.0 (C-2''), 53.7 ($\text{NCH}_2\text{CH}_2\text{CH}_2\text{CH}_3$), 58.4 (C-4a''), 67.9 (CH_2O), 127.2 (C-1), 129.2 (C-5), 129.7 (C-6), 131.3 (C-3), 132.6 (C-2), 133.3 (C-4), 167.2 (COO), 175.9 (CO), 179.7 (CO) ppm. IR (film): $\tilde{\nu}$ = 3323 (br), 2926 (vs), 2849 (s), 1715 (s), 1570 (m), 1449 (m), 1389 (s), 1241 (m), 1185 (s), 1135 (s), 1085 (s), 1045 (s), 1045 (s) cm^{-1} . MS (EI, 70 eV): m/z (%) = 440 (16) [M^+], 397 (100), 224 (14), 99 (16), 56 (41), 41 (16); found [M] $^+$ 440.26751. $\text{C}_{26}\text{H}_{36}\text{N}_2\text{O}_4$ requires 440.26751.

{(3R,4aS,8aS)-1-[(R)-1-Phenylethyl]decahydroquinolin-3-yl}methyl 2-(3-Methyl-2,5-dioxopyrrolidin-1-yl)benzoate (5d): Following a similar procedure to that described above for the preparation of **5a**, olefin **17d** (100 mg, 0.20 mmol) was subjected to hydrogenation over 10% palladium on carbon (5 mg) to give **5c** (95 mg, 95%) as a yellow oil and as a 1:1 mixture of diastereomers. $[\alpha]_D^{20}$ = +30 (c = 0.90, CHCl_3). ^1H NMR (300 MHz, CDCl_3): δ = 1.01–1.13 (m, 1 H, 7''-H_A), 1.17–1.33 [m, 5 H, 6''-CH₂ and $\text{NCH}(\text{CH}_3)\text{Ph}$], 1.35–1.46 (m, 5 H, 4''-CH₂ and 3'-CH₃), 1.51–1.71 (m, 4 H, 5''-CH₂ and 8''-CH₂), 1.75–1.83 (m, 1 H, 7''-H_B), 1.89–1.92 (m, 1 H, 3''-H), 1.95–2.10 (m, 2 H, 2''-H_A and 4a''-H), 2.44–2.50 (m, 2 H, 4'-CH₂), 2.55 (d, J = 8.8 Hz, 1 H, 2-H_B), 2.95–3.14 (m, 1 H, 3'-H), 3.18–3.21 (m, 1 H, 8a''-H), 3.57–3.68 [q, J = 6.8 Hz, 1 H, $\text{NCH}(\text{CH}_3)\text{Ph}$], 3.83–3.90 (m, 1 H, $\text{CH}_2\text{H}_2\text{BO}$), 4.00–4.07 (m, 1 H, $\text{CH}_2\text{H}_2\text{BO}$), 7.19–1.40 (m, 7 H, 5-H, 6-H and Ph), 7.58–7.62 (m, 2 H, 3-H and 4-H) ppm. ^{13}C NMR (100 MHz, CDCl_3): δ = 16.2 (3'-CH₃), 16.4 (3'-CH₃), 17.3 (C-8''), 21.0 [$\text{NCH}(\text{CH}_3)\text{Ph}$], 21.1 (C-6''), 25.5 (C-7''), 27.3 (C-4''), 30.8 (C-5''), 35.1 (C-3''), 35.3 (C-4a''), 36.3 (C-3'), 36.9 (C-4'), 48.8 (C-2''), 55.3 [$\text{NCH}(\text{CH}_3)\text{Ph}$], 60.5 (C-8a''), 67.9 (CH_2O), 126.4 (Ph), 127.0 (C-1), 128.2 (Ph), 129.2 (C-5), 129.6 (C-6), 131.3 (C-3), 132.6 (C-2), 133.1 (C-4), 147.0 (Ph), 163.9 (COO), 171.0 (CO), 179.8 (CO) ppm. IR (film): $\tilde{\nu}$ = 2927 (vs), 2840 (s), 1720 (s), 1605 (m), 1494 (m), 1452 (m), 1393 (s), 1245 (m), 1205 (s), 1110 (s), 1108 (s) cm^{-1} . MS (EI, 70 eV): m/z (%) = 488 (48) [M^+], 473 (34), 445 (58), 341 (63), 216 (100), 149 (55), 105 (98), 71 (43), 57 (71), 41 (64); found [M] $^+$ 488.26769. $\text{C}_{30}\text{H}_{36}\text{N}_2\text{O}_4$ requires 488.26751.

Acknowledgments

We would like to acknowledge BASF SE for supporting this research.

- [1] R. H. Manske, *Can. J. Res.* **1938**, *16B*, 57.
- [2] J. A. Goodson, *J. Chem. Soc.* **1943**, 139–141.

- [3] K. R. Jennings, D. G. Brown, D. P. Wright, *Experientia* **1986**, 42, 611–613.
- [4] S. Wonnacott, E. X. Albuquerque, D. Bertrand, *Methods Neurosci.* **1993**, 12, 263–275.
- [5] D. J. Hardick, G. Cooper, T. Scottward, I. S. Blagbrough, B. V. L. Potter, S. Wonnacott, *FEBS Lett.* **1995**, 365, 79–82.
- [6] L. P. Dwoskin, P. A. Crooks, *J. Pharmacol. Exp. Ther.* **2001**, 298, 395–402.
- [7] G. K. Lloyd, M. Williams, *J. Pharmacol. Exp. Ther.* **2000**, 292, 461–467.
- [8] a) H. Tsuneki, Y. You, N. Toyooka, S. Kagawa, S. Kobayashi, T. Sasaoka, H. Nemoto, I. Kimura, J. A. Dani, *Mol. Pharmacol.* **2004**, 66, 1061–1069; b) N. Toyooka, H. Tsuneki, S. Kobayashi, D. Zhou, M. Kawasaki, I. Kimura, T. Sasaoka, H. Nemoto, *Curr. Chem. Biol.* **2007**, 1, 97–114.
- [9] A. A. Jensen, B. Frolund, T. Liljefors, P. Krosgaard-Larsen, *J. Med. Chem.* **2005**, 48, 4705–4745.
- [10] a) C. F. Kukel, K. R. Jennings, *Can. J. Physiol. Pharmacol.* **1994**, 72, 104–107; b) D. R. E. Macallan, G. G. Lunt, S. Wonnacott, K. L. Swanson, H. Rapoport, E. X. Albuquerque, *FEBS Lett.* **1988**, 226, 357–363; c) M. Reina, A. González-Coloma, *Phytochem. Rev.* **2007**, 6, 81–95.
- [11] J. Alexander, D. S. Bindra, J. D. Glass, M. A. Holahan, M. L. Renyer, G. S. Rork, G. R. Sitko, M. T. Stranieri, R. F. Stupieniski, H. Veerapanane, J. J. Cook, *J. Med. Chem.* **1996**, 39, 480–486.
- [12] D. B. McKay, C. Chang, T. F. Gonzalez-Cestari, S. B. McKay, R. A. El-Hajj, D. L. Bryant, M. X. Zhu, P. W. Swaan, K. M. Arason, A. B. Pulipaka, C. M. Orac, S. C. Bergmeier, *Mol. Pharmacol.* **2007**, 71, 1288–1297.
- [13] D. L. Bryant, R. B. Free, S. M. Thomasy, D. J. Lapinsky, K. A. Ismail, S. B. McKay, S. C. Bergmeier, D. B. McKay, *Neurosci. Res.* **2002**, 42, 57–63.
- [14] K. A. Ismail, S. C. Bergmeier, *Eur. J. Med. Chem.* **2002**, 37, 469–474.
- [15] a) P. A. Coates, I. S. Blagbrough, D. J. Hardick, M. G. Rowan, S. Wonnacott, B. V. L. Potter, *Tetrahedron Lett.* **1994**, 35, 8701–8704; b) I. S. Blagbrough, P. A. Coates, D. J. Hardick, T. Lewis, M. G. Rowan, S. Wonnacott, B. V. L. Potter, *Tetrahedron Lett.* **1994**, 35, 8705–8708.
- [16] J. M. Jacyno, J. S. Harwood, N. H. Lin, J. E. Campbell, J. P. Sullivan, M. W. Holladay, *J. Nat. Prod.* **1996**, 59, 707–709.
- [17] a) K. J. Goodall, D. Barker, M. A. Brimble, *Synlett* **2005**, 1809–1827; b) K. J. Goodall, M. A. Brimble, D. Barker, *Magn. Reson. Chem.* **2007**, 45, 695–699; c) A. Lehmann, C. Brocke, D. Barker, M. A. Brimble, *Eur. J. Org. Chem.* **2006**, 3205–3215; d) K. J. Goodall, M. A. Brimble, D. Barker, *Magn. Reson. Chem.* **2006**, 44, 980–983; e) J. Huang, C. M. Orac, S. McKay, D. B. McKay, S. C. Bergmeier, *Bioorg. Med. Chem.* **2008**, 16, 3816–3824.
- [18] F. M. Leonik, R. L. Papke, N. A. Horenstein, *Bioorg. Med. Chem. Lett.* **2007**, 17, 1520–1522.
- [19] M. A. Brimble, C. Brocke, *Eur. J. Org. Chem.* **2005**, 2385–2396.
- [20] P. A. Coates, I. S. Blagbrough, M. G. Rowan, D. P. J. Pearson, T. Lewis, B. V. L. Potter, *J. Pharm. Pharmacol.* **1996**, 48, 210–213.
- [21] P. A. Coates, I. S. Blagbrough, M. G. Rowan, B. V. L. Potter, D. P. J. Pearson, T. Lewis, *Tetrahedron Lett.* **1994**, 35, 8709–8712.
- [22] a) G. A. Kraus, J. M. Shi, *J. Org. Chem.* **1990**, 55, 5423–5424; b) M. Ihara, M. Suzuki, K. Fukumoto, C. Kabuto, *J. Am. Chem. Soc.* **1990**, 112, 1164–1171.
- [23] D. Barker, M. A. Brimble, M. D. McLeod, *Tetrahedron* **2004**, 60, 5953–5963.
- [24] W. Wadsworth, W. D. Emmons, *J. Am. Chem. Soc.* **1961**, 83, 1733–1738.
- [25] A. Franke, F. F. Frickel, R. Schlecker, P. C. Thieme, *Synthesis* **1979**, 712–714.
- [26] J. Huang, S. C. Bergmeier, *Tetrahedron* **2008**, 64, 6434–6439.
- [27] Z. Horii, T. Watanabe, M. Ikeda, T. Kurihara, Y. Tamura, *Yakugaku Zasshi* **1964**, 84, 142–145.
- [28] J. M. Cassady, G. S. Li, E. B. Spitzner, H. G. Floss, J. A. Clemens, *J. Med. Chem.* **1974**, 17, 300–307.
- [29] J. Villieras, M. Rambaudo, *Org. Synth.* **1988**, 66, 220–224.
- [30] H.-S. Byun, K. C. Reddy, R. Bittman, *Tetrahedron Lett.* **1994**, 35, 1371–1374.
- [31] N. J. Bach, E. C. Kornfeld, N. D. Jones, M. O. Chaney, D. E. Dorman, J. W. Paschal, J. A. Clemens, E. B. Smalstig, *J. Med. Chem.* **1980**, 23, 481–491.
- [32] A. Lehmann, C. Brocke, D. Barker, M. A. Brimble, *Eur. J. Org. Chem.* **2006**, 3205–3215.
- [33] D. Barker, M. A. Brimble, M. D. McLeod, *Synthesis* **2003**, 656–658.
- [34] M. E. Hediger, *Bioorg. Med. Chem.* **2004**, 12, 4995–5010.

Received: January 13, 2009

Published Online: February 26, 2009