Indium metal as a reducing agent in organic synthesis

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The low first ionisation potential (5.8 eV) of indium coupled with its stability towards air and water, suggest that this metallic element should be a useful reducing agent for organic substrates. The use of indium metal for the reduction of C=N bonds in imines, the heterocyclic ring in benzo-fused nitrogen heterocycles, of oximes, nitro compounds and conjugated alkenes and the removal of 4-nitrobenzyl protecting groups is described. Thus the heterocyclic ring in quinolines, isoquinolines and quinoxalines is selectively reduced using indium metal in aqueous ethanolic ammonium chloride. Treatment of a range of aromatic nitro compounds under similar conditions results in selective reduction of the nitro groups; ester, nitrile, amide and halide substituents are unaffected. Likewise indium in aqueous ethanolic ammonium chloride is an effective method for the deprotection of 4-nitrobenzyl ethers and esters. Indium is also an effective reducing agent under non-aqueous conditions and α-oximino carbonyl compounds can be selectively reduced to the corresponding *N*-protected amine with indium powder, acetic acid in THF in the presence of acetic anhydride or di-*tert*-butyl dicarbonate. Conjugated alkenes are also reduced by indium in THF–acetic acid.

Introduction

The metallic element indium has a number of useful properties that suggest it should be useful in organic synthesis. It is unreactive towards air and water, is non-toxic, and is readily available in high purity due to the ease with which it zone refines. However it is relatively rare, being the 63rd most abundant element in the Earth's crust, and hence available at prices similar to other rare elements such as silver.

Despite its desirable chemical properties, indium has only recently been exploited in organic synthesis,[1–3] most notably in the generation of synthetically useful allylindium species.[4–12] However, the first ionisation potential of indium (5.8 eV), which is lower than reducing metals such as zinc (9.4 eV) or tin (7.3 eV) and close to that of alkali metals such as sodium (5.1 eV) suggests that the metal ought to participate readily in single electron transfer processes. Hence we initiated a research programme to explore this possibility, and we have reported, in preliminary form, the selective reduction of aromatic nitro groups,[13] the heterocyclic ring in quinolines, isoquinolines and quinoxalines,[14] the deprotection of 4-nitrobenzyl ethers and esters,[15] and the reductive acetylation of oximes[16] using indium metal. The results of these, and related studies, are reported in detail herein.

Subsequent to the publication of our preliminary results, others have shown that indium metal can be used in the reductive elimination of 1,2-dibromides,[17] pinacol couplings,[18] ketone deoxygenation,[19] reductive dehalogenation of α-halocarbonyl compounds, benzyl halides and halomethylcephalosporins,[20,21] reduction of azides,[22,23] and *N*-oxides,[24,25] reductive coupling of acyl cyanides,[26] and in the reduction of nitrostyrenes,[27] and other nitro compounds.[23,28,29] In complementary studies the use of indium hydride reagents for reduction reactions in organic synthesis has also been reported.[30–35]

Results and discussion

Reductive coupling of imines

One of the earliest reports on indium metal as a reducing agent was by Kalyanam and Rao who found that indium was extremely effective in the reductive coupling of imines (the aza-pinacol coupling) to give 1,2-diamines.[36] Subsequent work with nitrones showed that indium mediated both the initial deoxygenation and the coupling of the resulting imine.[25] Although the aza-pinacol coupling can be effected in other ways, for example using samarium diiodide,[37–39] titanium(0),[40] sodium metal,[41] niobium reagents,[42] ytterbium[43] or electrochemistry,[44] the importance of vicinal diamines justified a more detailed investigation of the indium mediated reaction. Thus on treatment with indium powder in ethanolic aqueous ammonium chloride, *N*-benzylideneaniline **1** gave the diamine **2** as a mixture of (+)/(−) and *meso*-isomers in good yield as reported in the literature.[36] The same product could be obtained, albeit in slightly lower yield (52%) simply by heating aniline and benzaldehyde in the presence of indium. Attempted extension of the reaction to the imines **3** and **5** resulted in simple reduction of the C=N bond (Scheme 1). However, the imine coupling reaction could be effected intramolecularly. Thus the bis-imines **7** and **8** derived from *trans*-1,2-diaminocyclohexane were treated with indium in THF in the presence of acetic acid, the addition of the stronger acid being based on related electrochemical coupling of imines reported by Shono *et al.*[44] The resulting decahydroquinoxalines **9** and **10** were formed in good yield as single diastereomers, assigned as the all-equatorial isomers (Scheme 1) on the basis of previous work.[44] Surprisingly, however, attempted intramolecular coupling of a bis-imine derived from biphenyl-2,2′-dicarbaldehyde failed, suggesting that imine coupling using indium metal is very substrate dependent and may not be a general reaction.

Reduction of benzo-fused nitrogen heterocycles

The selective reduction of the heterocyclic ring in benzo-fused heterocyclic compounds such as quinolines and isoquinolines is an important transformation since the resulting tetrahydro derivatives serve as useful synthetic intermediates.[45] A number of methods have been used for this transformation including catalytic hydrogenation or transfer hydrogenation, alkali metals such as sodium or lithium, diborane, sodium borohydride in the presence of nickel(II) chloride, lithium triethylborohydride or sodium cyanoborohydride.[46] Given that indium can replace alkali metals in the reductive coupling of imines (see above), it

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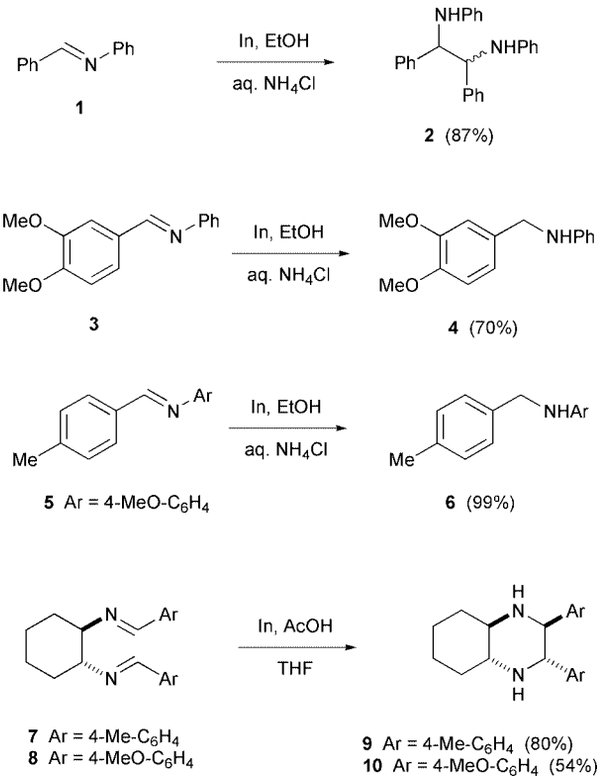
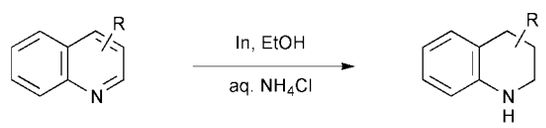


Scheme 1

Table 1 Reduction of quinolines **11** to 1,2,3,4-tetrahydroquinolines **12**



11 **12**

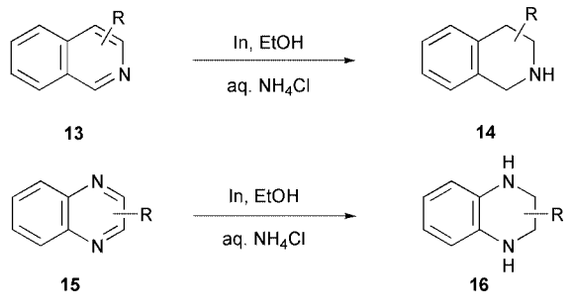
11/12	R	Yield (%)
a	H	52
b	2-Me	46
c	3-Me	76
d	4-Me	73
e	2,4-Me_2	30[a]
f	2-$CH_2CH_2CH_3$	55
g	2-$CH_2CH_2CHMe_2$	49
h	2-$CH_2OCH_2CH{=}CH_2$	39
i	2-Ph	40
j	6-MeO	42
k	6-AcNH	60
l	6-Cl	25
m	3,4-C_6H_4	72[b]

[a] Product is exclusively *cis*. [b] Product is 1,2-dihydrophenanthridine.

was decided to investigate its use in the reduction of a range of heterocyclic compounds.

The reduction of a series of quinolines **11** was carried out by simply heating the substrate with indium powder in aqueous ethanol containing ammonium chloride, and gave, after chromatography, the corresponding 1,2,3,4-tetrahydroquinolines **12** in modest to good yield (Table 1). Attempts to vary the reaction conditions, *e.g.* the use of THF–AcOH in place of aqueous systems, usually resulted in lower yields. A number of functional groups are tolerated including alkyl, aryl, alkoxy, and acetylamino, although the yield from 6-chloroquinoline was low, and 6-aminoquinoline was recovered unchanged. 2-Chloroquinoline, in which the halide is activated was reduced to 1,2,3,4-tetrahydroquinoline in 79% yield. Nitro groups are also reduced (see below); 6-nitroquinoline was cleanly reduced to 6-aminoquinoline (82%).

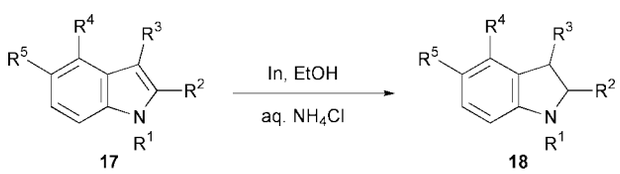
Table 2 Reduction of isoquinolines **13** and quinoxalines **15** to 1,2,3,4-tetrahydro derivatives **14** and **16**



Compounds	R	Yield (%)
13a/14a	H	78
13b/14b	1-Me	74
13c/14c	3-Me	71
13d/14d	3-Me[a]	97[b]
15a/16a	2-Me	92
15b/16b	2,3-Me_2	90[c]

[a] Starting material is methiodide salt. [b] Product is 2,3-dimethyl-1,2,3,4-tetrahydroisoquinoline. [c] Product is formed as a 2 : 1 mixture of *cis* : *trans* isomers.

Table 3 Reduction of indoles **17** to indolines **18**



17/18	R^1	R^2	R^3	R^4	R^5	Yield (%)
a	H	Me	H	H	H	0[a]
b	Me	Me	H	H	H	64
c	Me	–$(CH_2)_4$–		H	H	0[a]
d	Me	Me	H	OBn	OMe	23
e	Me	Me	CO_2Et	H	OMe	0[a]
f	Ac	H	H	H	H	0[a]

[a] No reaction; starting material recovered.

The reduction of isoquinolines **13** was also investigated, the reactions generally proceeding in shorter reaction times and higher yield than the corresponding quinolines (Table 2). The isoquinolinium salt **13d** was rapidly reduced to the *N*-methyltetrahydroisoquinoline **14d** in excellent yield. Again, nitro groups were reduced in preference to the heterocyclic ring, 5-nitroisoquinoline giving the 5-amino derivative in excellent (99%) yield. Carbonyl groups were also reduced under the reaction conditions, isoquinolin-1-yl phenyl ketone giving the corresponding alcohol in 72% yield.

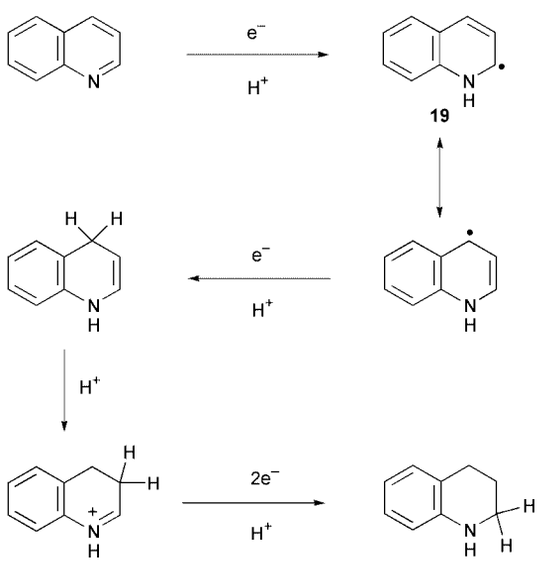
The more electron deficient heterocyclic ring in quinoxalines **15** was rapidly reduced to the tetrahydro derivatives **16** in excellent yield (Table 2). These reductions were much more tolerant of alternative reactions conditions: the use of In–Me_3NHCl–aq EtOH and In–THF–AcOH giving comparable yields to the usual conditions.

The reduction of monocyclic 6-membered heterocyclic system was also briefly investigated, but under the usual indium conditions, both 2-phenylpyridine and 2,6-lutidine were recovered unchanged. An isolated pyridine ring is generally thought to be harder to reduce than the heterocyclic ring of quinoline.[47]

When the indium reduction conditions were applied to indoles **17**, very mixed results were obtained. Whilst some indoles were recovered unchanged, others were reduced to the corresponding indoline **18** (Table 3). However, the reaction is

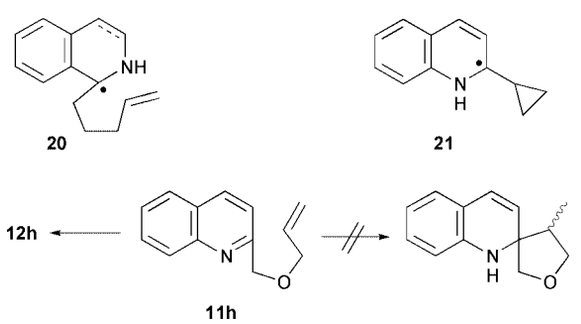
unpredictable, and is not a suitable method. Likewise, a number of pyrroles that have been successfully reduced under Birch reduction conditions by Donohoe and co-workers[48] were inert to metallic indium.

Although there are some limitations, the reduction of the nitrogen heterocyclic ring in benzo-fused heterocycles using indium appears to be a useful reaction. The reaction is assumed to proceed by single electron transfer to the electron deficient ring to give, after protonation, a stabilised radical **19**. A further electron transfer–protonation sequence could then lead to the tetrahydro derivative as outlined for quinoline itself in Scheme 2.



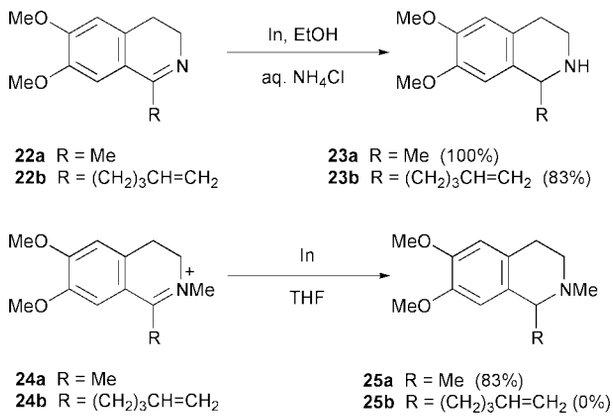
Scheme 2

Attempts were made to intercept the putative radical intermediates derived from quinolines or isoquinolines either in 5-*exo*-*trig* cyclisations or by cyclopropane ring opening as illustrated by the radical structures **20** and **21**, although it had already been shown earlier (Table 1) that 2-(allyloxymethyl)-quinoline **11h** was reduced to the tetrahydro derivative **12h** in modest yield (39%) with no evidence for products derived from the 5-*exo*-*trig* cyclisation process (Scheme 3).



Scheme 3

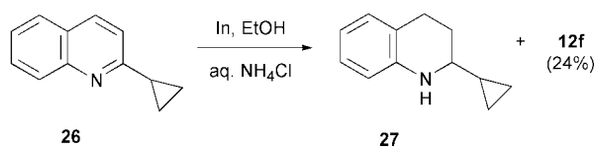
Likewise in the isoquinoline series, no radical intermediates could be intercepted in cyclisation reactions. The 3,4-dihydroisoquinolines **22**, readily prepared using a Bischler–Napieralski reaction, were subjected to the usual indium reducing conditions. In both cases, clean reduction of the C=N bond was observed, with no evidence for cyclised products derived from **22b**. The corresponding methiodide salts **24** were also investigated, and whereas the 1-methyl derivative **24a** was reduced to the tetrahydro compound (carnegine) **25a**, the pentenyl derivative **24b** was recovered unchanged (Scheme 4). It is also noted that in these studies there was no evidence for any dimeric



Scheme 4

products formed by coupling the heterocyclic rings, although such coupling reactions are known to occur on treatment of quinolines or isoquinolines with zinc metal.[49–51]

Finally 2-cyclopropylquinoline **26** was investigated. This was prepared by reaction of 2-chloroquinoline with cyclopropylidenetriphenylphosphorane. Reactions of halo-heterocycles with phosphorus ylides were first developed by Taylor and Martin,[52] and we also used them to prepare the quinolines **11b** and **11f**. When 2-cyclopropylquinoline **26** was treated under the usual indium conditions two products were observed (Scheme 5). One was the corresponding 1,2,3,4-tetrahydroquinoline **27**



Scheme 5

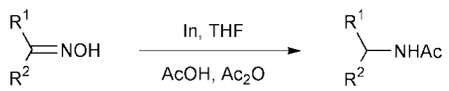
(35%) and the other was identified as 2-propyl-1,2,3,4-tetrahydroquinoline **12f** (24%), identical to the product obtained by reduction of 2-*n*-propylquinoline **11f** (Table 1). The formation of the *n*-propyl compound **12f** suggests that radical intermediates are involved, and the cyclopropane ring opens during the reaction.

Reduction of oximes

Oximes were also thought to be potential substrates for reduction by indium despite the fact that they are generally regarded as more resistant than imines to reduction. Nevertheless the reduction of oximes and oxime ethers to amines is a useful transformation in organic synthesis and has been achieved using a range of reagents. Lithium aluminium hydride is effective,[53] although it is unselective with functionalised oximes since it reacts with carbonyl groups faster and can lead to aziridines with benzyl substituted oximes.[54] Catalytic hydrogenation is also commonly used,[55–57] although the success of reaction is sensitive towards catalyst, solvent and substrate. Again, ketone groups in the substrate are susceptible to competing reduction. Other reagents used include sodium borohydride in the presence of various additives,[58–60] diborane,[61] and zinc and acetic acid, often in the presence of acetic anhydride to effect *in situ* acetylation of the amine.[62–65]

A range of oximes **28** was therefore chosen for reduction by indium metal. The oximes were either commercially available or obtained from the corresponding carbonyl compound by standard methods; in cases where the oxime was obtained as an *E*/*Z*-mixture, no attempt was made to separate such mixtures. The reduction was carried out by simply heating the α-oximino carbonyl compound **28** in THF containing 4 equivalents of acetic acid and 2.5 equivalents of acetic anhydride, and a

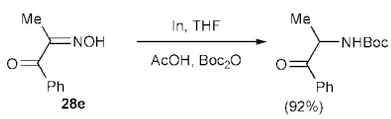
Table 4 Reduction of oximes **28** to *N*-acetyl amines **29**



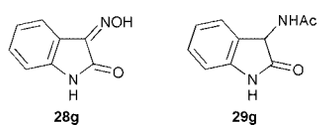
28 **29**

28/29	R^1	R^2	Yield (%)
a	CO_2Me	CO_2Me	65
b	CO^iPr	CO_2Me	95
c	COPh	COMe	69
d	Me	CO_2Et	98
e	Me	COPh	96[a]
f	H	COPh	100
g	[b]	[b]	69
h	[c]	[c]	87

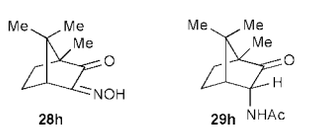
[a] Also carried out in the presence of di-*tert*-butyl dicarbonate to give the *N*-Boc product in 92% yield.



b



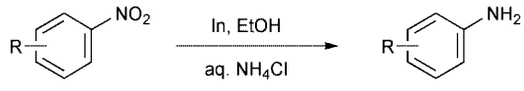
c



suspension of 4 equivalents of indium powder. The reactions were complete in less than 30 minutes for compounds in which the C=N bond was rendered more reactive by the presence of two carbonyl groups, and within 18 hours for monocarbonyl compounds, and gave the *N*-acetyl amines **29** in good to excellent yield (Table 4). Hence the reaction can be used to prepare a range of α-acetamido carbonyl compounds including a diester **29a**, β-ketoester **29b**, β-diketone **29c**, ester **29d**, ketones **29e**, **29f**, **29h**, and amides **29g**; the camphor derived oxime **28h** gave a single *endo*-diastereomer acetamide **29h**. In the case of oxime **28c**, some acetamide derivative **29f** was formed (presumably *via* a retro Claisen reaction) in addition to the expected product **29c** (69%). It is worth noting that the carbonyl group in all cases was unaffected. The reaction is simple to carry out; there is no need for exclusion of air or the use of dry solvents, and the reaction is worked up by simply quenching with bicarbonate and extraction into organic solvent. In most cases further purification by column chromatography was unnecessary. Attempts to reduce simple oximes such as that derived from acetophenone to the corresponding amine under the usual aqueous reducing conditions with indium were unsuccessful. Also attempts to effect reduction and tosylation or trifluoroacetylation were unsuccessful. However, when the reduction of oxime **28e** was carried out in the presence of di-*tert*-butyl dicarbonate, the corresponding *N*-*tert*-butoxycarbonyl amine was formed in excellent yield (92%), thereby extending the reaction to the preparation of other *N*-protected amines.

The use of indium in the presence of acetic acid–anhydride to reduce oximes to the corresponding *N*-acetyl amines closely mirrors the use of zinc metal under similar conditions. For comparison, we conducted the reduction of oximes **28b** and **28e** using both metals; in both cases yields were similar, although in the case of oxime **28b**, the zinc reduction proceeded slowly at room temperature whereas the reaction mixture containing indium required heating to effect the conversion.

Table 5 Reduction of nitrobenzene derivatives **30**



30 **31**

30/31	R	Time/h	Yield (%)
a	4-Cl	3	95
b	2-Me-3-Cl	19	75
c	2-Me-5-Br	72	70
d	2-I	1.5	60
e	2-MeO-5-MsO	18	98
f	4-MeS	0.5	92
g	3-CN	1	95
h	3-CO_2H	18	90
i	4-CO_2Et	1	92
j	4-COMe	48	83
k	4-NHAc	3	95
l	4-$MeOCH_2$	1	84
m	2-Me-3-NO_2	72	90[a]

[a] Reaction carried out in THF–acetic acid and both nitro groups are reduced; product is 2,6-diaminotoluene.

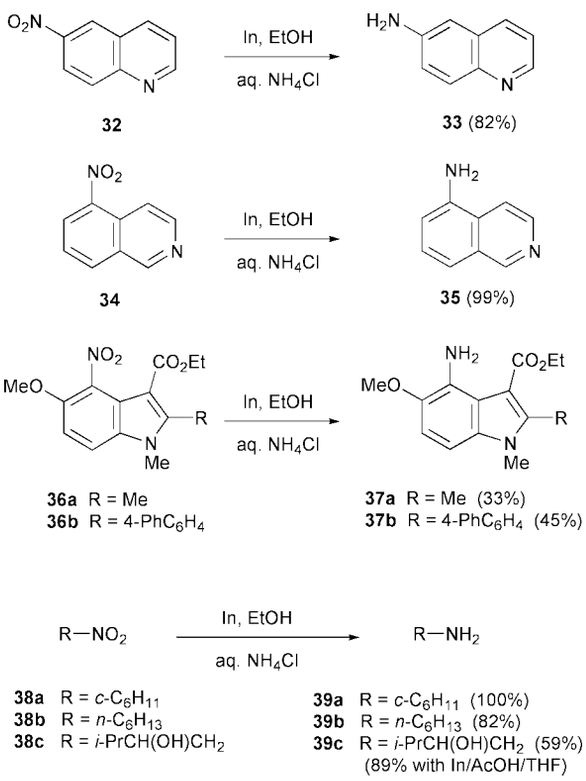
Reduction of nitro compounds

Although a large range of methods for the reduction of aromatic nitro compounds have been developed,[66–68] many of these are incompatible with other functional groups in the molecule. For example, the selective reduction of nitro groups in the presence of carbonyl groups, nitriles, halides and alkenes is often difficult, and in such cases catalytic hydrogenation, which is often the method of choice for nitro reduction, is inappropriate. Thus hydrogenation of 4-chloro-3-nitroacetophenone over palladium-on-carbon results in hydrogenolysis of the halide and reduction of the ketone as well as the nitro group.[68] Consequently new methods for nitro group reduction continue to be developed as a search of the recent literature shows.[69–78] Having already established that nitro-quinolines and -isoquinolines were readily reduced to the corresponding amino compounds without further reduction of the heterocyclic ring (see above), we embarked upon a wider study of nitro group reduction.[79]

As expected, reduction of aromatic nitro compounds **30** proceeded readily on heating the substrate with indium powder in aqueous ethanolic ammonium chloride. The reactions are extremely easy to carry out, are usually complete within 1–3 hours, and give the corresponding aniline **31** in good to excellent yield (Table 5).

A wide range of functional groups remained unaffected by the indium reducing conditions. Thus halogen substituents (Cl, Br, I) are not reduced; a separate study on 3-bromobiphenyl showed only *ca*. 8% cleavage (by GC-MS) of the bromine after heating with indium in aqueous ethanolic ammonium chloride for 96 h. Likewise mesylates survive the reaction conditions, and the reaction is not affected by the presence of sulfur substituents, *e.g.* **30f**. Importantly, other reduction sensitive groups were also unaffected; nitrile, acid, ester, ketone, and amide groups all withstood the reaction conditions. However, one functionality did appear incompatible. Although 4-methoxymethylnitrobenzene **30l** gave the corresponding aniline **31l** in high yield after a reaction time of 1 hour, prolonged heating resulted in the formation of 4-toluidine. This facile cleavage of benzylic C–O bonds using indium forms the basis of a new method of removal of 4-nitrobenzyl protecting groups (see below). Use of the alternative reducing conditions (In, AcOH, THF) was also briefly investigated. The conversion of 4-nitroacetanilide **30k** to 4-aminoacetanilide **31k** was achieved in quantitative yield under these conditions, and with 2,6-dinitrotoluene **30m** as substrate reduction of both nitro groups occurred.

Other nitro compounds were also investigated. The reduction of 6-nitroquinoline **32** and 5-nitroisoquinoline **34** in 82 and 99% yield respectively was discussed above. The 4-nitroindoles **36** were readily reduced to the corresponding 4-aminoindoles **37** in (unoptimised) 30–45% yield. Aliphatic nitro compounds were also readily reduced: nitrocyclohexane **38a** and 1-nitrohexane **38b** were reduced in high yield. 3-Methyl-1-nitrobutan-2-ol **38c** was only slowly reduced under the aqueous conditions; with indium–AcOH–THF, however, the reaction was faster and higher yielding. The reduction of these other nitro compounds is summarised in Scheme 6.

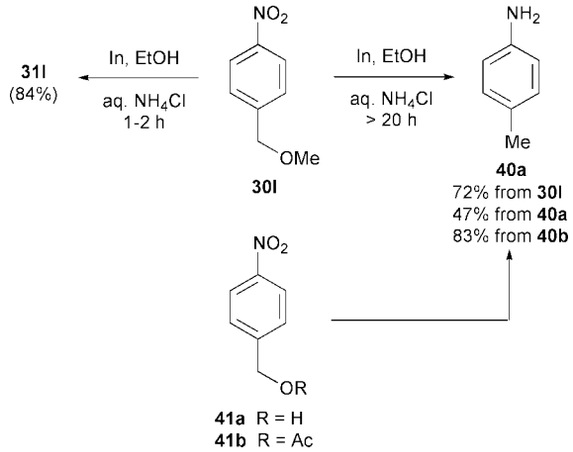


Scheme 6

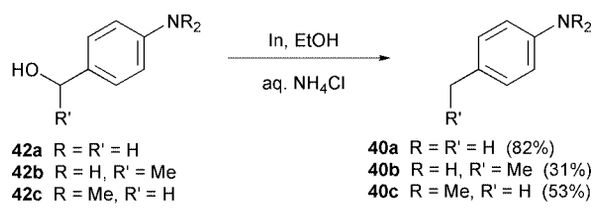
Since the publication of our preliminary communication, others have also reported the use of indium metal for the reduction of nitro groups.[23,28,29]

Deprotection of 4-nitrobenzyl ethers and esters

As outlined above, under the usual aqueous conditions prolonged treatment of 4-methoxymethylnitrobenzene **30l** resulted in formation of 4-toluidine **40a** in 72% yield. Likewise, 4-toluidine was also formed from 4-nitrobenzyl alcohol **41a** and 4-nitrobenzyl acetate **41b** (Scheme 7). Presumably nitro group reduction occurs first, and this is followed by reductive cleavage of the benzylic C–O bond to give a benzylic radical (stabilised by the 4-amino group) which is further reduced and protonated. In accord with this mechanism, 4-aminobenzyl alcohol **42a** was converted into 4-toluidine **40a** (82%) under identical conditions. Likewise 4-aminophenethyl alcohol **42b** and 4-dimethylaminobenzyl alcohol **42c** both underwent reductive C–O bond cleavage to give the corresponding 4-alkylamines **40b** and **40c** (Scheme 8). 3-Aminobenzyl alcohol was, unsurprisingly, inert to the reaction conditions. Evidence for the involvement of benzylic radicals in such processes came from the indium reduction of 4-nitrobenzyl chloride which gave in addition to 4-toluidine (46%), the 'dimer' 1,2-bis(4-aminophenyl)ethane (32%). Therefore on the basis of the foregoing discussion it seemed reasonable that our indium reducing conditions might be useful for the removal of the 4-nitrobenzyl protecting group from a range of substrates.



Scheme 7



Scheme 8

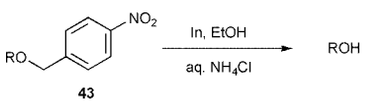
The 4-nitrobenzyl protecting group has seen use in the protection of alcohols, thiols, amines (as the 4-nitrobenzyl carbamates), and carboxylic acids.[80–82] For example, 4-nitrobenzyl esters are much more stable to acidic hydrolysis than other benzyl esters, and are recommended for glutamic acid and aspartic acid side chain protection in solid-phase peptide synthesis. Such protecting groups have also seen extensive use in the β-lactam field. Methods of deprotection include: Na_2S or $Na_2S_2O_4$ reduction, catalytic hydrogenolysis, TBAF, or oxidative cleavage with alkaline hydrogen peroxide. Electrochemical methods have also been used, especially for the unmasking of alcohols, either direct electrolytic reduction, or oxidative electrolysis following initial chemical reduction of the nitro group. Despite the undoubted usefulness of the 4-nitrobenzyl protecting group, many of the methods of deprotection have drawbacks in that they are not compatible with the presence of other functionality or protecting groups.

A series of alcohols, phenols and acids was protected as their corresponding 4-nitrobenzyl ethers and esters **43**. A variety of standard methods was used for the protection step with no attempt to optimise the yields (see Experimental section). The ethane-1,2-diol derivatives **43b–d** were used to probe the compatibility of other alcohol protecting groups. The deprotection reactions were carried out using indium metal under the usual aqueous conditions. Simple extractive work-up involving acid–base wash to remove the 4-toluidine by-product gave the deprotected material in good yield (Table 6).

In all cases, the substrates **43** were cleaved in good yield, although the *tert*-butyldimethylsilyl protected diol **43e** gave a mixture of products. (When the reaction was carried out at room temperature nitro compound **43e** was simply reduced to the corresponding aniline without further C–O bond cleavage.) Benzyl ethers and carbamates, and benzoate esters remained intact, and other functional groups were also unaffected by the conditions. Thus carbonyl groups (in the form of ketone **43h** and aldehyde **43i**) and chlorides were not reduced, and in the case of the quinoline derivative **43l**, the protecting group was removed faster than the reduction of the aromatic ring.

However, attempted removal of the 4-nitrobenzyl group from the cysteine thiol group or from the indole nitrogen were unsuccessful. The *S*-(4-nitrobenzyl)cysteine derivative **44** was reduced to the corresponding 4-aminobenzyl derivative in

Table 6 Deprotection of 4-nitrobenzyl ethers and esters

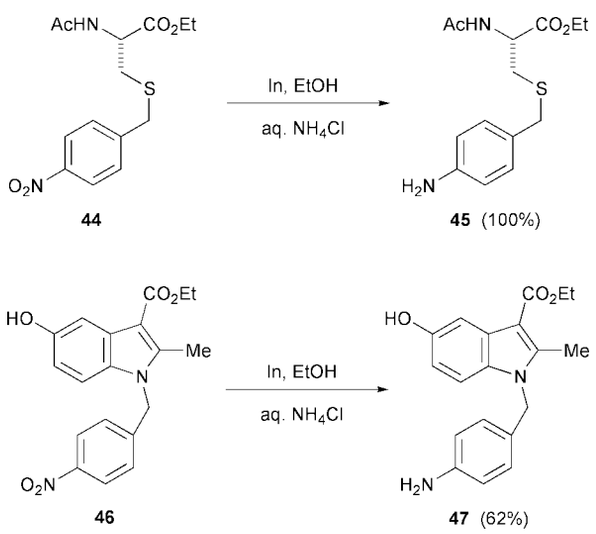


43

43	R	Yield (%)
a	$PhCH_2CH_2$	87
b	$PhOCH_2CH_2$	98
c	$PhCH_2OCH_2CH_2$	100
d	$PhCOOCH_2CH_2$	99
e	*t*-$BuMe_2SiOCH_2CH_2$	[a]
f	(1*R*,2*S*,5*R*)-2-Isopropyl-5-methylcyclohexyl	93
g	4-MeO-C_6H_4	81
h	4-Ac-C_6H_4	97
i	3-OHC-C_6H_4	61
j	2,3,5-Me_3-C_6H_2	100
k	2,4,5-Cl_3-C_6H_2	90
l	6-Quinolinyl	97
m	4-Cl-C_6H_4CO	90
n	(±)-CbzNHCHMeCO	96

[a] Inseparable mixture of desired product and *tert*-butyldimethylsilanol formed.

quantitative yield, and the 1-(4-nitrobenzyl)indole **46** similarly underwent simple nitro group reduction without further bond cleavage (Scheme 9).



44 **45** (100%)

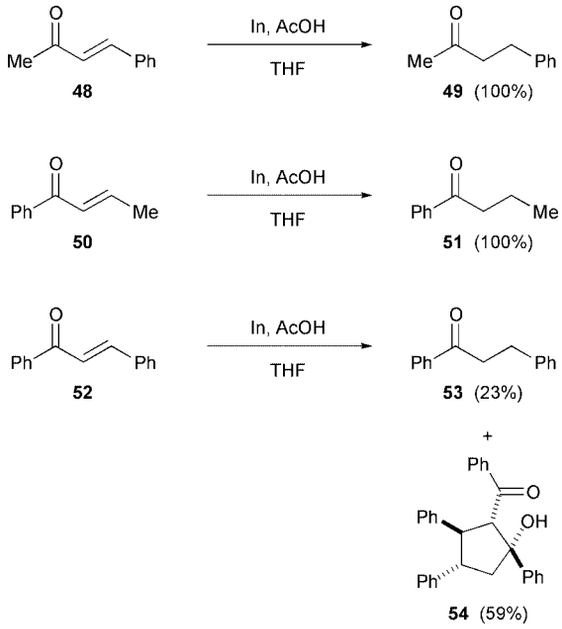
46 **47** (62%)

Scheme 9

Reduction of conjugated alkenes

The reduction of the C=C bond in conjugated alkenes, particularly α,β-unsaturated carbonyl compounds, is a much studied reaction in organic synthesis.[83] Although catalytic hydrogenation can be used, the methods of choice often involve electron transfer from appropriate metals. Examples include the well known reduction of α,β-unsaturated carbonyl compounds under Birch reduction conditions or using magnesium in methanol. In view of our success in using indium to replace such reducing metals in other reactions, we investigated its use in the reduction of conjugated alkenes.

The reaction was investigated using simple α,β-unsaturated ketones, and although the usual aqueous conditions were unsatisfactory, reduction using indium in THF in the presence of acetic acid was successful. Thus benzylideneacetone **48** and 1-phenylbut-2-en-1-one **50** were reduced to the corresponding ketones **49** and **51** in quantitative yield. However, when chalcone **52** was submitted to the same conditions only 23% of the corresponding ketone **53** was formed, the major product being the cyclopentane derivative **54** (59%) formed as a single diastereomer (Scheme 10). Such 'dimers' have been noted previously in the reduction of chalcone using samarium diiodide,[84] zinc[85] or electrochemistry,[86] and their stereochemistry and mechanism of formation discussed.[84] Presumably the indium mediated reaction follows a similar pathway initiated by single electron transfer from the metal to the conjugated system.



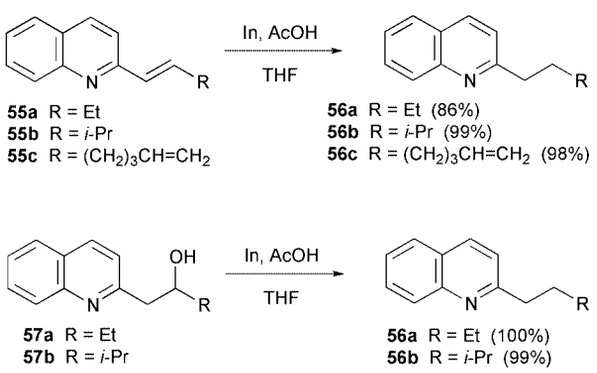
48 **49** (100%)

50 **51** (100%)

52 **53** (23%) + **54** (59%)

Scheme 10

Since an electron deficient heteroaromatic ring such as quinoline can fulfil the role of an electron withdrawing substituent, the reduction of alkenes conjugated to such rings was next investigated. The 2-(butenyl)quinoline **55a**, prepared by dehydration of the alcohol **57a** (see below), was readily reduced to the 2-butyl derivative **56a** (86%) on treatment with indium–AcOH–THF. Under these conditions no further reduction of the heteroaromatic ring was observed. Likewise, the 2-(alkenyl)-quinolines **55b** and **55c** were reduced to the 2-alkyl derivatives in excellent yield (Scheme 11). In the latter case, there was no evidence for interception of radical intermediates by cyclisation onto the terminal alkene. In accord with the requirement for an electron deficient aromatic ring to facilitate alkene reduction, 2-(3-methylbut-1-enyl)naphthalene was recovered unchanged.



55a R = Et
55b R = *i*-Pr
55c R = $(CH_2)_3CH=CH_2$

56a R = Et (86%)
56b R = *i*-Pr (99%)
56c R = $(CH_2)_3CH=CH_2$ (98%)

57a R = Et
57b R = *i*-Pr

56a R = Et (100%)
56b R = *i*-Pr (99%)

Scheme 11

The alkene **55a** was prepared by dehydration of the corresponding alcohol **57a**, itself available by reaction of the anion derived from 2-methylquinoline with propionaldehyde. Given the acidic nature of the indium reduction conditions, it was found that the alcohols **57** could be converted directly into the 2-alkylquinolines **56a** and **56b** in excellent yield (Scheme 11), the reaction proceeding by initial dehydration followed by reduction.

Conclusions

These studies have shown that indium metal can mediate a range of synthetically useful, selective reductions in both aqueous and non-aqueous systems. The reactions are usually high yielding, are easy to carry out usually avoiding the need for exclusion of air or moisture or any other special precautions, and involve simple work-up and product isolation.

Experimental

General

Commercially available reagents and solvents were used throughout without further purification other than those detailed below. Indium powder (100 mesh) was purchased from Aldrich. Silver(I) oxide was prepared freshly from the addition of sodium hydroxide solution to silver nitrate solution, collected by filtration, dried over P_2O_5, and stored in a brown glass jar. Light petroleum refers to the fraction that boils between 40 °C and 60 °C and was distilled from calcium chloride through a 36 cm Vigreux column before use. Diethyl ether (ether) and THF were distilled from sodium benzophenone ketyl under nitrogen prior to use. Dichloromethane was purified and dried by distillation from phosphorus pentoxide under nitrogen. Pyridine was distilled from calcium hydride whilst under nitrogen prior to use.

Analytical thin layer chromatography was carried out using aluminium or glass backed plates coated with Merck Kieselgel 60 GF_{254}. Developed plates were visualised under ultra-violet light (254 nm) and/or potassium permanganate or ninhydrin dip. Flash chromatography was carried out using Merck Kieselgel 60 H silica. Fully characterised compounds were chromatographically homogeneous.

IR Spectra were recorded on a Nicolet Magna 550 spectrometer with internal calibration. Spectra were recorded as thin films on sodium chloride plates, in solution or potassium bromide discs. NMR spectra were recorded on a Bruker AM 300 or Bruker Advance DRX 400 spectrometer at the frequencies stated. Chemical shifts are recorded in ppm and *J* values in Hz. Multiplets less than 0.2 ppm in width were recorded from the centre, those greater were reported as a range. Chemical shift values are referenced against chloroform at 7.27 ppm for $CDCl_3$, methanol at 3.35 ppm for CD_3OD, and DMSO at 2.50 ppm for d_6-DMSO, and are accurate to ±0.01 ppm (δ_H) and ±0.10 ppm (δ_C). High resolution mass spectra (CI and EI) were either obtained on a Kratos Profile HV3 spectrometer or at the EPSRC National Mass Spectrometry Service at the University of Wales, Swansea. Gas chromatography–mass spectrometry was carried out on a ThermoQuest Finnigan Trace 2000 series GCMS, with a 15 m Crossbond® 5% diphenyl–95% dimethylpolysiloxane column with a 0.25 mm internal diameter and CI/EI detection, which was used to obtain some of the low resolution spectra. Elemental analysis was carried out on a Perkin-Elmer 2400 CHN analyser to within ±0.3% of the theoretical values. Specific rotations were measured on an AA-1000 polarimeter and values are quoted in 10^{-1} deg cm^2 g^{-1}.

General procedures for indium metal reductions

General procedure 1: indium mediated reductions in aqueous ethanolic ammonium chloride. To a solution of the substrate (1.9 mmol) in ethanol (10 ml) was added saturated ammonium chloride solution (3 ml) and indium powder (2.0 g). The mixture was stirred under reflux. When the reaction appeared complete by TLC (typically 1–5 d), the cooled reaction mixture was diluted with water (50 ml) and filtered through Celite®. The aqueous filtrate was adjusted to pH ~ 9 with aqueous sodium hydroxide solution (4 M) and extracted with dichloromethane (3 × 15 ml). Combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by flash chromatography to yield the desired product.

General procedure 2: indium mediated reductions in THF–acetic acid. The substrate (1.0 mmol) was dissolved in THF (10 ml) with indium powder (1.0 g) and acetic acid (4.0 mmol–1 equivalent per proton required) under an atmosphere of nitrogen. The mixture was stirred under reflux. When the reaction appeared complete by TLC (typically 1–7 d) the cooled reaction mixture was diluted with water (50 ml) and ethyl acetate (25 ml) and decanted. The layers were separated and the aqueous layer further extracted with ethyl acetate (25 ml). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by flash chromatography to yield the desired product.

General procedure 3: indium reductions of isoquinolinium salts. The substrate (1.0 mmol) was dissolved in THF (10 ml) and indium powder (1.0 g) added. The mixture was heated at reflux under nitrogen for 4–5 d. The cooled reaction mixture was washed through Celite® with ethyl acetate (30 ml) and washed with water (30 ml) then dried ($MgSO_4$) and concentrated *in vacuo* to the product.

General procedure 4: indium reduction and acetylation of oximes. Indium powder (0.92 g, 8.0 mmol) was added to a solution of the oxime substrate (2.00 mmol), acetic anhydride (0.47 ml, ~0.51 g, 5.0 mmol) and acetic acid (0.46 ml, ~0.48 g, 8.0 mmol) in THF (10 ml) and the mixture heated at reflux for 18 h. Saturated aqueous sodium bicarbonate solution (10 ml) was carefully added to the cooled reaction mixture, and stirring continued for 1 h. The resulting mixture was diluted with water (30 ml) and extracted with ethyl acetate (3 × 15 ml). Combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. If required, the crude material was purified by flash column chromatography (silica eluting with ~20% ethyl acetate in dichloromethane) to give the desired product.

General procedure 5: indium reductions of nitro compounds. To a solution of the substrate (2.5 mmol) in ethanol (10 ml) was added saturated ammonium chloride solution (3 ml) and indium powder (2.0 g). The mixture was stirred under reflux. When the reaction appeared complete by TLC (typically 1–3 h) the cooled reaction mixture was diluted with water (50 ml) and filtered through Celite®. The aqueous filtrate was adjusted to pH ~ 9 with aqueous sodium hydroxide (4 M) and extracted with dichloromethane, ethyl acetate or ether (3 × 15 ml). Combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by flash chromatography to yield the desired product. Known products were confirmed by comparison with literature data for mp and ^{1}H NMR.

General procedure 6: reductive removal of 4-nitrobenzyl protecting groups. Indium powder (1.0 g) was added to a solution of the substrate (1.0 mmol) in methanol (10 ml) and saturated ammonium chloride solution (3 ml) and the mixture heated at reflux. After 18 h the cooled reaction mixture was filtered through Celite® with water (50 ml) and the pH adjusted to ~2 (7 for basic substrates) with hydrochloric acid (2 M) then extracted with dichloromethane (or ethyl acetate) (3 × 15 ml). Combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to give the desired product with no need for further purification. Deprotected compounds were compared with the original unprotected substrate and literature data.

General procedure 7: indium reduction of conjugated alkenes. The substrate (1.0 mmol) was dissolved in THF (10 ml) with indium powder (0.50 g) and acetic acid (4.0 mmol). The mixture was stirred under reflux. When the reaction appeared complete by TLC (typically 16 h–4 d), the cooled reaction mixture

was diluted with water (50 ml) and ethyl acetate (25 ml) and decanted. The layers were separated and the aqueous layer further extracted with ethyl acetate (25 ml). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. If required, the crude product was purified by flash chromatography to yield the desired product.

Preparation of imines

***N*,*N*′-Bis(4-methylphenyl)biphenyl-2,2′-dicarbaldehyde bisimine.** Biphenyl-2,2′-dicarbaldehyde, prepared by the ozonolysis of phenanthrene[87] (0.781 g, 3.72 mmol) and 4-toluidine (0.796 g, 7.44 mmol) were dissolved in benzene (30 ml) with a few crystals of toluene-4-sulfonic acid. The mixture was heated under reflux with a Dean–Stark trap for 2 d. The cooled reaction mixture was poured onto water (50 ml) and extracted with dichloromethane (3 × 20 ml). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was recrystallised twice from ether to give the *title compound* as colourless prisms (0.936 g, 65%); mp 155–157 °C (Found: C, 86.2; H, 6.2; N, 7.0. $C_{28}H_{24}N_2$ requires C, 86.6; H, 6.2; N, 7.2%) (Found: M^+, 388.1920. $C_{28}H_{24}N_2$ requires 388.1939); ν_{max} (KBr)/cm^{-1} 3065, 3020 (ArH), 2880, 1620 (imine), 1580, 1500 (Ar), 810 (ArH), 760 (ArH); δ_H (300 MHz; $CDCl_3$) 8.35 (2 H, dd, *J* 5.3, 4.0, 3-Ph-Ph), 8.22 (2 H, s, N=CH), 7.53 (4 H, m, 4&5-Ph-Ph), 7.35 (2 H, dd, *J* 5.3, 3.5, 6-Ph-Ph), 7.09 (4 H, d, *J* 8.3, 2&6-NArH), 6.93 (4 H, d, *J* 8.3, 3&5-NArH), 2.31 (6 H, s, Me); δ_C (75 MHz; $CDCl_3$) 158.0 (N=CH), 149.4 (C), 140.9 (C), 135.9 (C), 134.9 (C), 130.9 (CH), 130.6 (CH), 129.7 (CH), 128.4 (CH), 126.9 (CH), 120.8 (CH), 21.0 (Me); *m*/*z* (EI) 388 (M^+, 8%), 282 (84), 270 (30), 267 (81), 190 (17), 178 (24), 165 (48), 106 (38), 91 (100), 65 (62).

***N*,*N*′-Bis(4-methylbenzylidene)-*trans*-1,2-diaminocyclohexane 7.** 4-Tolualdehyde (5.0 ml, ~5.09 g, 42.4 mmol) and (+/−)-*trans*-1,2-diaminocyclohexane (2.53 ml, ~2.42 g, 21.2 mmol) were heated at reflux in benzene (30 ml) with a Dean–Stark trap for 24 h. The cooled mixture was concentrated *in vacuo* and the resulting crude material recrystallised from ether to give the title compound **7** as colourless prisms (5.53 g, 82%); mp 95–96 °C (lit.,[88] mp not given); δ_H (300 MHz; $CDCl_3$) 8.17 (2 H, s, N=CH), 7.48 (4 H, d, *J* 8.1, 2&6-ArH), 7.11 (4 H, d, *J* 8.1, 3&5-ArH), 3.48 (2 H, m, =N-CH), 2.31 (6 H, s, ArMe), 1.83 (6 H, m, ring-CH_2), 1.47 (2 H, ring-CH_2).

***N*,*N*′-Bis(4-methoxybenzylidene)-*trans*-1,2-diaminocyclohexane 8.** 4-Anisaldehyde (2.27 ml, ~2.54 g, 18.7 mmol) and (+/−)-*trans*-1,2-diaminocyclohexane (1.07 g, 9.4 mmol) were heated at reflux in benzene (30 ml) with a Dean–Stark trap for 22 h. The cooled mixture was concentrated *in vacuo* and the resulting crude material recrystallised from methanol to give the title compound **8** as colourless prisms (2.89 g, 88%); mp 169–170 °C (lit.,[88] mp not given); δ_H (300 MHz; $CDCl_3$) 8.13 (2 H, s, N=CH), 7.53 (4 H, m, 2&6-ArH), 6.82 (4 H, m, 3&5-ArH), 3.78 (6 H, s, OMe), 3.34 (2 H, m, =N-CH), 1.84 (6 H, m, ring-CH_2), 1.47 (2 H, ring-CH_2).

Reduction of imines

***N*,*N*′,1,2-Tetraphenylethane-1,2-diamine 2.** (a) According to the literature procedure,[36] the title compound was obtained as a 1 : 1 mixture of (±)/*meso* isomers from *N*-benzylideneaniline **1** as a colourless solid (87%); mp 157–160 °C (lit.,[89] mp *meso* 169–170 °C, (+),(−) 152.5–153.5 °C); δ_H (300 MHz; $CDCl_3$) 7.26–6.54 (20 H, m, ArH), 5.01 (1 H, d, *J* 6.8, [with D_2O shake—1 H, s] *meso*-NC*H*), 4.61 (3 H, br, [with D_2O shake—1 H, s] (+),(−)-NC*H* and N*H*).

(b) The title compound was also obtained directly from aniline and benzaldehyde (52%) by the same procedure (aniline 2.0 mmol and benzaldehyde 2.0 mmol).

***N*-Phenyl-3,4-dimethoxybenzylamine 4.** According to the general procedure 1, the title compound was obtained from *N*-(3,4-dimethoxybenzylidene)aniline **3** as a colourless oil (70%); δ_H (300 MHz; $CDCl_3$) 7.21–6.64 (8 H, m, ArH), 4.56 (2 H, s, CH_2), 3.88 (3 H, s, OMe), 3.87 (3 H, s, OMe), 1.64 (1 H, br s, NH) (*cf*. lit.[90]).

***N*-(4-Methoxyphenyl)-4-methylbenzylamine 6.** According to the general procedure 1, the title compound was obtained from *N*-(4-methylbenzylidene)-4-methoxyaniline **5** as a colourless oil (99%); δ_H (300 MHz; $CDCl_3$) 7.30 (2 H, d, *J* 6.3, 2&6-Ar*H*-CH_2N), 7.22 (2 H, d, *J* 6.3, 3&5-Ar*H*-CH_2N), 6.79 (2 H, m, 3&5-Ar*H*-N), 6.64 (2 H, m, 3&5-Ar*H*-N), 4.28 (2 H, s, CH_2), 3.77 (3 H, s, OMe), 3.11 (1 H, br s, NH), 2.37 (3 H, s, Ar*Me*) (*cf*. lit.[91]).

2,3-Bis(4-methylphenyl)-1,2,3,4,4a,5,6,7,8,8a-decahydroquinoxaline 9. Indium powder (2.00 g) was added to a solution of *N*,*N*′-(4-methylbenzylidene)-*trans*-1,2-diaminocyclohexane **7** (0.544 g, 1.71 mmol) and acetic acid (0.205 g, 3.42 mmol, ~0.20 ml) in THF (10 ml). The mixture was heated at reflux for 18 h then cooled and washed through Celite® with ethyl acetate (50 ml). The filtrate was washed with sodium hydroxide solution (1 M; 20 ml) and water (20 ml) then dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was passed down a flash chromatography column (silica, 2% methanol in chloroform) to give the *title compound* **9** as a clear oil which solidified on standing (0.440 g, 80%); mp 52–53 °C (Found: MH^+, 321.2337. $C_{22}H_{29}N_2$ requires 321.2331); ν_{max} (KBr)/cm^{-1} 3260 (NH), 3015 (ArH), 2920, 2840 (CH), 2810, 1515 (Ar), 820 (ArH); δ_H (300 MHz; $CDCl_3$) 7.02 (4 H, d, *J* 8.0, ArH), 6.93 (4 H, d, *J* 8.0, ArH), 3.82 (2 H, s, ArCH), 2.60 (2 H, m, CH_2C*H*N), 2.23 (6 H, s, ArMe), 1.84 (2 H, br s, NH), 1.73 (4 H, br m, CH_2CHN), 1.39 (4 H, br m, CH_2CH$_2$CHN); δ_C (100 MHz; $CDCl_3$) 138.6 (C), 136.5 (C), 128.5 (CH), 128.0 (CH), 67.9 (CH), 61.6 (CH), 31.8 (CH_2), 24.9 (CH_2), 21.1 (Me); *m*/*z* (EI) 320 (M^+, 12%), 201 (32), 186 (29), 120 (100), 105 (33), 91 (49); (CI) 321 (MH^+, 100), 200 (10), 120 (12).

2,3-Bis(4-methoxyphenyl)-1,2,3,4,4a,5,6,7,8,8a-decahydroquinoxaline 10. Indium powder (1.00 g) was added to a solution of *N*,*N*′-(4-methoxybenzylidene)-*trans*-1,2-diaminocyclohexane **8** (0.366 g, 1.05 mmol) and acetic acid (0.12 ml, ~0.13 g, 2.1 mmol) in THF (10 ml). The mixture was heated at reflux for 48 h then cooled and washed through Celite® with ethyl acetate (50 ml). The filtrate was washed with sodium hydroxide solution (1 M; 20 ml) and water (20 ml) then dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was passed down a flash chromatography column (silica, 2→10% methanol in chloroform) to give the *title compound* **10** as a colourless solid (0.20 g, 54%); mp 179–180 °C (Found: MH^+, 353.2226. $C_{22}H_{29}N_2O_2$ requires 353.2229); ν_{max} (KBr)/cm^{-1} 3230 (NH), 3005 (ArH), 2940, (CH), 2860, 1605, 1510 (Ar), 820 (ArH); δ_H (400 MHz; $CDCl_3$) 7.08 (4 H, d, *J* 8.6, ArH), 6.61 (4 H, d, *J* 8.6, ArH), 3.93 (2 H, s, ArCH), 3.71 (6 H, s, ArOMe), 3.31 (2 H, br s, NH), 2.75 (2 H, m, CH_2C*H*N), 1.70 (4 H, br m, CH_2CHN), 1.33 (4 H, br m, CH_2CH$_2$CHN); δ_C (100 MHz; $CDCl_3$) 158.8 (C), 131.6 (C), 129.3 (CH), 113.4 (CH), 66.4 (CH), 60.7 (CH), 55.1 (OMe), 30.8 (CH_2), 24.6 (CH_2); *m*/*z* (EI) 352 (M^+, 5%), 217 (15), 162 (22), 134 (100), 121 (39), 91 (40), 77 (41); (CI) 353 (MH^+, 100), 136 (22), 98 (29).

Preparation of nitrogen heterocycles

2-*n*-Propylquinoline 11f. *n*-Butyllithium (1.55 M in hexanes; 10.4 ml, ~16.1 mmol) was added to a stirred suspension of *n*-propyltriphenylphosphonium bromide (6.20 g, 16.1 mmol) in DME (30 ml) under a nitrogen atmosphere so as to keep the temperature at ~−35 °C. After 1 h, 2-chloroquinoline (1.32 g, 8.0 mmol) was added and the mixture allowed to warm to room

temperature over 2 h. The mixture was then heated at reflux for 18 h, then sodium carbonate (1.71 g, 16.1 mmol) in water (20 ml) was added and the mixture kept at reflux for a further 6 h. The cooled reaction mixture was diluted with dilute hydrochloric acid (0.5 M) until pH ~ 2 (*ca.* 100 ml), then washed with chloroform (3 × 30 ml). The aqueous layer was then adjusted to pH 8/9 with sodium carbonate and extracted with ether (3 × 50 ml). The combined ethereal layers were dried ($MgSO_4$), and concentrated *in vacuo*. The crude material was purified by flash column chromatography (silica, dichloromethane) to give the title compound **11f** as a colourless oil (0.23 g, 17%); δ_H (300 MHz; $CDCl_3$) 8.07 (1 H, d, *J* 8.3, 4-ArH), 8.05 (1 H, d, *J* 8.2, 8-ArH), 7.78 (1 H, dd, *J* 7.9, 1.4, 5-ArH), 7.69 (1 H, ddd, *J* 8.2, 7.2, 1.4, 7-ArH), 7.49 (1 H, ddd, *J* 7.9, 7.2, 0.8, 6-ArH), 7.30 (1 H, d, *J* 8.3, 3-ArH), 2.96 (2 H, m, $ArCH_2$), 1.86 (2 H, m, $ArCH_2CH_2$), 1.03 (3 H, t, *J* 7.4, Me) (*cf.* lit.[92]).

2-(Allyloxymethyl)quinoline 11h. Allyl alcohol (0.16 ml, ~0.14 g, 2.4 mmol) in DMF (20 ml) was added to sodium hydride (60% dispersion in mineral oil, 0.250 g, 6.25 mmol) previously rinsed with hexane under nitrogen. 2-(Chloromethyl)quinoline hydrochloride (0.48 g, 2.2 mmol) in DMF (15 ml) was added after 1 h and stirring continued for 1 h at room temperature, after which time TLC (silica, 40% ethyl acetate in light petroleum) showed completion. The reaction mixture was poured onto saturated ammonium chloride solution (50 ml). Water (20 ml) was added and the mixture extracted with ethyl acetate (3 × 15 ml). The combined organic layers were washed with brine (20 ml), dried ($MgSO_4$), and concentrated *in vacuo*. The crude product was purified by flash column chromatography (silica, 25% ethyl acetate in light petroleum) to give the *title compound* **11h** as a colourless oil (0.23 g, 52%) (Found: M^+, 199.0997. $C_{13}H_{13}NO$ requires 199.0997); ν_{max} (neat)/cm^{-1} 3054, 3008, 2846 (OCH_2), 1604, 1506, 1426, 1094, 987, 924, 822, 749 (ArH); δ_H (300 MHz; $CDCl_3$) 8.17 (1 H, d, *J* 8.5, 4-ArH), 8.06 (1 H, dd, *J* 8.4, 0.7, 8-ArH), 7.81 (1 H, br d, *J* 8.0, 5-ArH), 7.70 (1 H, ddd, *J* 8.4, 7.0, 1.4, 7-ArH), 7.63 (1 H, d, *J* 8.5, 3-ArH), 7.52 (1 H, br dd, *J* 8.0, 7.0, 6-ArH), 6.01 (1 H, ddt, *J* 10.4, 17.2, 5.7, C*H*=CH_2), 5.36 (1 H, ddt, *J* 3.0, 17.2, 1.6, *trans*-CH=CH*H*), 5.24 (1 H, ddt, *J* 3.0, 10.4, 1.6, *cis*-CH=C*H*H), 4.83 (2 H, s, $ArCH_2O$), 4.16 (2 H, ddd, *J* 1.6, 1.6, 5.7, $OCH_2CH=CH_2$); δ_C (100 MHz; $CDCl_3$) 159.2 (C), 147.6 (C), 136.7 (=CH), 134.4 (CH), 129.5 (CH), 129.0 (CH), 127.6 (CH), 127.5 (C), 126.3 (CH), 119.4 (CH), 117.4 (=CH_2), 73.7 (CH_2), 71.9 (CH_2); *m*/*z* (EI) 199 (M^+, 3%), 170 (2), 143 (100), 128 (9), 115 (11), 101 (4), 83 (6).

***N*-Quinolin-6-ylacetamide 11k.** To a stirred solution of 6-aminoquinoline (1.00 g, 6.9 mmol) in glacial acetic acid (10 ml) was added acetic anhydride (2.00 g, 19.6 mmol) in glacial acetic acid (5 ml). The solution was allowed to stir at room temperature for 5 h then poured onto ice–water (100 ml) and neutralised with aqueous ammonia. The crystals were collected by vacuum filtration and recrystallised twice from water to yield the title compound **11k** (0.68 g, 53%) as colourless needles, mp 138–139 °C (from water) (lit.,[93] mp 138 °C); ν_{max} (KBr)/cm^{-1} 3283 (NH), 3088, 1665, 1568, 1373, 1276, 871, 835, 820, 743; δ_H (400 MHz; $CDCl_3$) 8.80 (1 H, dd, *J* 4.2, 1.6, 2-ArH), 8.39 (1 H, br s, NH), 8.36 (1 H, d, *J* 2.2, 5-ArH), 8.07 (1 H, dd, *J* 8.4, 1.6, 4-ArH), 7.99 (1 H, d, *J* 9.0, 8-ArH), 7.57 (1 H, dd, *J* 9.0, 2.2, 7-ArH), 7.35 (1 H, dd, *J* 8.4, 4.2, 3-ArH), 2.23 (3 H, s, CH_3CO); δ_C (100 MHz; $CDCl_3$) 169.0 (C=O), 149.3 (CH), 145.4 (C), 136.1 (C), 135.9 (CH), 129.9 (CH), 128.9 (C), 123.3 (CH), 121.6 (CH), 116.2 (CH), 24.6 (Me).

1-Methylisoquinoline 13b. *n*-Butyllithium (1.6 M solution in hexanes; 15.0 ml, 24.0 mmol) was added to a stirred suspension of methyltriphenylphosphonium bromide (8.21 g, 23.0 mmol) in DME (30 ml) under an atmosphere of nitrogen, so as to keep the temperature at ~35 °C. After 1 h, 1-chloroisoquinoline (1.62 g, 9.9 mmol) was added and the mixture was allowed to stir at room temperature over 2 h, then heated under reflux for a further 16 h. Sodium carbonate (1.05 g, 9.91 mmol) in water (20 ml) was added, and reflux continued for 3 h. Hydrochloric acid (0.2 M) was added to the cooled reaction mixture to pH < 3 and the resulting solution was washed with chloroform (2 × 30 ml). The aqueous layer was basified with sodium carbonate to pH ~ 9, and extracted with ether (3 × 20 ml). The combined ethereal layers were dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was purified by flash column chromatography (silica, 1% methanol in chloroform) to give the title compound **13b** as a yellow oil (0.78 g, 55%); bp 110 °C/3.0 mmHg (lit.,[94] bp 71–72 °C/1.0 mmHg); δ_H (300 MHz; $CDCl_3$) 8.40 (1 H, d, *J* 5.8, 3-ArH), 8.14 (1 H, dd, *J* 8.2, 1.4, 8-ArH), 7.83 (1 H, dd, *J* 8.3, 1.4, 5-ArH), 7.69 (1 H, ddd, *J* 8.3, 6.9, 1.4, 6-ArH), 7.61 (1 H, ddd, *J* 8.2, 6.9, 1.4, 7-ArH), 7.53 (1 H, d, *J* 5.8, 4-ArH), 3.00 (3 H, s, Me).

2,3-Dimethylisoquinolinium iodide 13d. Methyl iodide (2.1 ml, ~4.78 g, 33.7 mmol) was added in one portion to a stirred solution of 3-methylisoquinoline **13c** (0.47 g, 3.3 mmol) in butanone (20 ml). The mixture was stirred and heated under reflux for 3 h. The resulting yellow precipitate was collected by filtration and washed with ether to give the title compound **13d** as yellow crystals (0.93 g, 98%); mp 228–230 °C (lit.,[95] mp 222–230 °C); δ_H (300 MHz; d_6-DMSO) 10.05 (1 H, s, 1-ArH), 8.47 (1 H, s, 4-ArH), 8.41 (1 H, d, *J* 8.3, 8-ArH), 8.21 (2 H, m, 5&6-ArH), 8.00 (1 H, ddd, *J* 8.3, 5.0, 3.3, 7-ArH), 4.40 (3 H, s, NMe), 2.85 (3 H, s, ArMe).

9-Methyl-1,2,3,4-tetrahydrocarbazole 17c. Methyl iodide (0.8 ml, 12.8 mmol) was added after 1 h to a stirred solution of 1,2,3,4-tetrahydrocarbazole (1.00 g, 5.8 mmol) and sodium hydride (60% dispersion in mineral oil, 0.50 g, 12.5 mmol) in anhydrous THF (10 ml) under nitrogen at room temperature. After 15 min the reaction was quenched with saturated ammonium chloride solution (40 ml), and extracted with dichloromethane (3 × 15 ml). The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The crude product was purified by flash chromatography (silica, 1 : 1 dichloromethane–light petroleum) to give the title compound **17c** as a colourless solid (1.01 g, 93%); mp 50–51 °C (lit.,[96] mp 50–51 °C); δ_H (300 MHz; $CDCl_3$) 7.56 (1 H, d, *J* 7.7, 8-ArH), 7.33 (1 H, d, *J* 8.2, 5-ArH), 7.24 (1 H, ddd, *J* 1.1, 7.7, 8.0, 7-ArH), 7.16 (1 H, ddd, *J* 1.1, 8.0, 8.2, 6-ArH), 3.63 (3 H, s, NMe), 2.74 (4H, m, CH_2), 1.92 (4 H, m, CH_2).

6,7-Dimethoxy-1-methyl-3,4-dihydroisoquinoline 22a. (a) Acetyl chloride (0.30 ml, ~0.33 g, 4.2 mmol) was added dropwise to a stirred solution of 2-(3,4-dimethoxyphenyl)ethylamine (0.495 g, 2.73 mmol) and triethylamine (0.275 g, ~0.38 ml, 2.72 mmol) in dichloromethane (10 ml). The mixture was stirred for 1.5 h then washed with water and concentrated *in vacuo* to give *N*-acetyl-3,4-dimethoxyphenethylamine (0.880 g, 100%) as a colourless solid, mp 95–96 °C (lit.,[97] 95–96 °C); δ_H (300 MHz; $CDCl_3$) 6.84–6.69 (3 H, m, ArH), 6.01 (1 H, br s, NH), 3.84 (3 H, s, OMe), 3.83 (3 H, s, OMe), 3.46 (2 H, m, CH_2N), 2.74 (2 H, t, *J* 6.9, $ArCH_2$), 1.95 (3 H, s, COMe).

(b) A solution of *N*-acetyl-3,4-dimethoxyphenethylamine (0.607 g, 2.72 mmol) in phosphoryl chloride (40 ml) was stirred at room temperature for 18 h, then the solution was heated at reflux for 2 h. The cooled mixture was concentrated *in vacuo* and the residue taken up in saturated aqueous sodium bicarbonate (40 ml) and extracted with dichloromethane (2 × 20 ml). Combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*, then purified by flash chromatography (silica, 5% methanol in chloroform) to give the title compound **22a** (0.307 g, 58%) as a colourless solid; mp 101–103 °C (lit.,[98] 102–104 °C); δ_H (300 MHz; $CDCl_3$) 6.98 (1 H, s, 5-ArH), 6.68 (1 H, s, 8-ArH), 3.91 (3 H, s, OMe), 3.90 (3 H, s, OMe), 3.62

(2 H, t, *J* 7.4, NCH_2), 2.63 (2 H, t, *J* 7.4, $ArCH_2$), 2.36 (3 H, s, Me).

6,7-Dimethoxy-1-(pent-4-enyl)-3,4-dihydroisoquinoline 22b. (a) 2-(3,4-Dimethoxyphenyl)ethylamine (1.12 g, 6.2 mmol) and hex-5-enoic acid (0.76 g, 6.6 mmol) were stirred together at 150 °C for 4 h. The cooled mixture was taken up in chloroform (25 ml) and washed successively with hydrochloric acid (2 M; 20 ml), dilute ammonia solution (20 ml) and water (20 ml). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo* to give *3,4-dimethoxy-N-(pent-4-enylcarbonyl)phenethylamine* (1.57 g, 91%) as a dark oil (Found: M^+, 277.1658. $C_{16}H_{23}NO_3$ requires 277.1678); ν_{max} (neat)/cm^{-1} 3294 (NH), 3079, 2931, 2828, 1658 (C=O), 1510, 1461, 1259, 1147, 1022, 914, 807, 762; δ_H (300 MHz; $CDCl_3$) 6.86 (1 H, d, *J* 8.7, ArH), 6.74 (1 H, dd, *J* 8.7, 1.8, ArH), 6.71 (1 H, d, *J* 1.8, ArH), 5.75 (1 H, ddt, *J* 17.1, 10.4, 6.7, C*H*=CH_2), 5.45 (1 H, br s, NH), 4.99 (1 H, dd, *J* 17.1, 1.7, *trans*-CH=CH*H*), 4.97 (1 H, dd, 10.4, 1.7, *cis*-CH=C*H*H), 3.86 (6 H, 2 s, 2 × OMe), 3.47 (2 H, dt, *J* 6.9, 6.9, $ArCH_2$), 2.76 (2 H, t, *J* 6.9, $ArCH_2$), 2.15 (2 H, t, *J* 7.7, $COCH_2$), 2.05 (2 H, dt, *J* 6.7, 7.7, CH_2CH=CH_2), 1.71 (2 H, quintet, *J* 7.7, CH_2CH_2CH=CH_2); δ_C (75 MHz; $CDCl_3$) 172.8 (CO), 149.0 (C), 147.7 (C), 137.9 (=CH), 131.4 (C), 120.6 (CH), 115.3 (=CH_2), 111.8 (CH), 111.3 (CH), 55.92 (OMe), 55.86 (OMe), 40.6 (CH_2), 36.0 (CH_2), 35.3 (CH_2), 33.1 (CH_2), 24.7 (CH_2); *m/z* (EI) 277 (M^+, 5%), 164 (100), 151 (31), 149 (16), 107 (9); (CI) 278 (MH^+, 100%).

(b) A solution of 3,4-dimethoxy-*N*-(pent-4-enylcarbonyl)-phenethylamine (0.430 g, 1.55 mmol) in phosphoryl chloride (20 ml) was stirred at room temperature for 4 d. The mixture was concentrated *in vacuo* and the residue taken up in saturated aqueous sodium bicarbonate (40 ml) and extracted with dichloromethane (2 × 15 ml). Combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*, then purified by flash chromatography (silica, 5% methanol in chloroform) to give the *title compound* **22b** (0.285 g, 71%) as a brown oil (Found: M^+, 259.1567. $C_{16}H_{21}NO_2$ requires 259.1572); ν_{max} (neat)/cm^{-1} 3067, 2929, 2828, 1510, 1464, 1271, 1208, 1141, 906, 864, 809; δ_H (300 MHz; $CDCl_3$) 6.99 (1 H, s, ArH), 6.70 (1 H, s, ArH), 5.84 (1 H, ddt, *J* 17.1, 10.3, 7.4, C*H*=CH_2), 5.04 (1 H, dd, *J* 17.1, 1.0, *trans*-CH=CH*H*), 4.98 (1 H, dd, *J* 10.3, 1.0, *cis*-CH=C*H*H), 3.92 (3 H, s, OMe), 3.90 (3 H, s, OMe), 3.64 (2 H, t, *J* 7.4, NCH_2), 2.72 (2 H, t, *J* 7.4, N=CCH_2), 2.63 (2 H, t, *J* 7.4, $ArCH_2$), 2.16 (2 H, q, *J* 7.4, CH_2CH=CH_2), 1.77 (2 H, quintet, *J* 7.4, CH_2CH_2CH=CH_2); δ_C (75 MHz; $CDCl_3$) 167.3 (C), 151.1 (C), 147.5 (C), 138.3 (=CH), 131.8 (C), 121.6 (C), 115.1 (=CH_2), 110.4 (CH), 108.9 (CH), 56.3 (OMe), 56.0 (OMe), 46.5 (CH_2), 35.0 (CH_2), 33.5 (CH_2), 26.5 (CH_2), 25.9 (CH_2); *m/z* (EI) 259 (M^+, 27%), 258 (47), 244 (26), 205 (100), 204 (78), 190 (50), 174 (53), 159 (31), 115 (37), 91 (30), 77 (50), 54 (43); (CI) 260 (MH^+, 100%).

6,7-Dimethoxy-1,2-dimethyl-3,4-dihydroisoquinolinium iodide 24a. Iodomethane (0.12 ml, ~0.27 g, 1.9 mmol) was added to a solution of 6,7-dimethoxy-1-methyl-3,4-dihydroisoquinoline **22a** (0.062 g, 0.30 mmol) in butanone (10 ml) and the solution was stirred and heated at reflux for 9 h. The cooled reaction mixture was concentrated *in vacuo* and the residue recrystallised from ethanol–light petroleum to give the title compound **24a** (0.101 g, 96%) as yellow needles, mp 100–101 °C (lit.,[99] 101–102 °C); δ_H (300 MHz; $CDCl_3$) 7.44 (1 H, s, 5-ArH), 7.08 (1 H, s, 8-ArH), 4.03 (2 H, t, *J* 7.7, CH_2N), 3.96 (3 H, s, OMe), 3.92 (3 H, s, OMe), 3.75 (3 H, s, MeN), 3.18 (2 H, t, *J* 7.7, $ArCH_2$), 2.85 (3 H, s, Me).

6,7-Dimethoxy-2-methyl-1-(pent-4-enyl)-3,4-dihydroisoquinolinium iodide 24b. Methyl iodide (0.85 ml, ~1.93 g, 13.6 mmol) was added to a stirred solution of 6,7-dimethoxy-1-(pent-4-enyl)-3,4-dihydroisoquinoline **22b** (0.880 g, 3.40 mmol) in acetone (20 ml). The mixture was heated at reflux for 24 h and the yellow precipitate was collected by filtration and washed with cold acetone then dried at 60 °C for 18 h to give the *title compound* **24b** (0.530 g, 39%) as yellow crystals; mp 168–170 °C (Found: $MH^+ - I$, 275.1878. $C_{17}H_{25}NO_2$ requires 275.1885); ν_{max} (KBr)/cm^{-1} 3001, 2966, 2935, 2822, 1634, 1568, 1526, 1383, 1280, 1220, 999, 886, 420; δ_H (300 MHz; d_6-DMSO) 7.41 (1 H, s, ArH), 7.15 (1 H, s, ArH), 5.87 (1 H, ddt, *J* 16.8, 10.2, 6.6, C*H*=CH_2), 5.08 (2 H, m, CH=CH_2), 3.96 (2 H, t, *J* 8.0, CH_2N), 3.91 (3 H, s, OMe), 3.86 (3 H, s, OMe), 3.71 (3 H, s, Me), 3.19 (2 H, t, *J* 7.7, CH_2C=N), 3.07 (2 H, t, *J* 8.0, $ArCH_2$), 2.21 (2 H, td, *J* 7.4, 6.6, CH_2CH=CH_2), 1.68 (2 H, tt, *J* 7.7, 7.4, CH_2-CH_2CH=CH_2); δ_C (100 MHz; d_6-DMSO) 176.5 (C=N), 155.9 (C), 148.5 (C), 138.0 (=CH), 133.7 (C), 118.8 (C), 116.6 (=CH_2), 113.1 (CH), 111.7 (CH), 56.8 (2 × OMe), 52.5 (CH_2-N), 44.5 (MeN), 33.0 (CH_2), 29.8 (CH_2), 26.7 (CH_2), 25.3 (CH_2); *m/z* (CI) 275 ($MH^+ - I^-$, 100%), 261 (6), 204 (9), 165 (12), 152 (16).

2-Cyclopropylquinoline 26. *n*-Butyllithium (1.6 M solution in hexanes; 12.0 ml, 19.2 mmol) was added to a stirred suspension of (cyclopropyl)triphenylphosphonium bromide (6.13 g, 16.0 mmol) in DME (30 ml) under an atmosphere of nitrogen, so as to keep the temperature at ~−35 °C. After 1 h, 2-chloroquinoline (1.03 g, 6.3 mmol) was added and the mixture allowed to stir to room temperature over 2 h, then heated under reflux for a further 19 h. Sodium carbonate (0.71 g, 6.7 mmol) in water (10 ml) was added, and reflux continued for 4 h. Hydrochloric acid (0.5 M; 100 ml) was added to the cooled reaction and the resulting solution was washed with chloroform (2 × 70 ml). The aqueous layer was basified with sodium carbonate to pH ~ 9, and extracted with ether (3 × 50 ml). The combined ethereal layers were dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was purified by flash column chromatography (silica, dichloromethane) to give the title compound **26** as a colourless oil (0.44 g, 41%) (lit.,[100] bp 145–148 °C at 17 mmHg); ν_{max} (neat)/cm^{-1} 3045 (cyclopropane), 3000 (ArH), 1600, 1500 (C=C), 815 (ArH), 750 (ArH); δ_H (300 MHz; $CDCl_3$) 8.00 (1 H, d, *J* 8.3, 4-ArH), 7.97 (1 H, d, *J* 8.5, 8-ArH), 7.74 (1 H, dd, *J* 8.0, 1.4, 5-ArH), 7.64 (1 H, ddd, *J* 8.5, 7.0, 1.4, 7-ArH), 7.43 (1 H, ddd, *J* 8.0, 7.0, 1.2, 6-ArH), 7.16 (1 H, d, *J* 8.3, 3-ArH), 2.25 (1 H, m, cyclopropane-CH), 1.13 (4 H, m, cyclopropane-CH_2); δ_C (75 MHz; $CDCl_3$) 163.4 (C), 147.9 (C), 135.9 (CH), 129.3 (CH), 128.6 (CH), 127.5 (CH), 126.7 (C), 125.2 (CH), 119.3 (CH), 18.1 (CH), 10.3 (CH_2).

Reduction of nitrogen heterocycles

1,2,3,4-Tetrahydroquinoline 12a. (a) According to the general procedure 1 the title compound was obtained as a yellow oil (52%) from quinoline **11a**; δ_H (400 MHz; $CDCl_3$) 6.95 (2 H, m, 7&5-ArH), 6.62 (1 H, ddd, *J* 7.6, 7.4, 1.1, 6-ArH), 6.47 (1 H, dd, *J* 7.5, 1.1, 8-ArH), 3.52 (1 H, br s, NH), 3.31 (2 H, m, $NHCH_2CH_2$), 2.77 (2 H, t, *J* 6.4, $ArCH_2$), 1.95 (2 H, m, $NHCH_2CH_2$) (*cf.* lit.[101]).

(b) The title compound was also formed in 79% yield from 2-chloroquinoline according to general procedure 1 (spectroscopic data identical).

2-Methyl-1,2,3,4-tetrahydroquinoline 12b. According to the general procedure 1 the title compound was obtained as a clear oil (46%) from 2-methylquinoline **11b**; δ_H (400 MHz; $CDCl_3$) 6.96 (2 H, m, 7&5-ArH), 6.62 (1 H, ddd, *J* 7.6, 7.4, 1.2, 6-ArH), 6.47 (1 H, dd, *J* 7.2, 1.2, 8-ArH), 3.67 (1 H, br s, NH), 3.41 (1 H, m, NHC*H*Me), 2.82 (1 H, m, ArC*H*H), 2.74 (1 H, m, ArCH*H*), 1.94 (1 H, m, $ArCH_2CHH$), 1.61 (1 H, m, $ArCH_2CHH$), 1.22 (3 H, dd, *J* 4.0, 2.3, Me) (*cf.* lit.[101]).

3-Methyl-1,2,3,4-tetrahydroquinoline 12c. (a) According to the general procedure 1 the title compound was obtained as a yellow oil (76%) from 3-methylquinoline **11c**; δ_H (400 MHz; $CDCl_3$) 6.95 (2 H, m, 7&5-ArH), 6.61 (1 H, ddd, *J* 7.4, 7.6, 1.2,

6-ArH), 6.48 (1 H, dd, *J* 7.4, 1.2, 8-ArH), 3.6-4.0 (1 H, br s, NH), 3.27 (1 H, ddd, *J* 11.0, 3.7, 2.0, NHC*H*H), 2.90 (1 H, dd, *J* 9.6, 10.9, ArCH*H*), 2.77 (1 H, ddd, *J* 16.0, 4.8, 1.8, NHCH*H*), 2.43 (1 H, dd, *J* 10.1, 16.0, ArC*H*H), 2.07 (1 H, m, C*H*Me), 1.06 (3 H, d, *J* 6.6, Me) (*cf*. lit.[102]).

(b) The title compound was formed in 30% yield using aqueous trimethylamine hydrogen chloride solution (4 M) in place of saturated aqueous ammonium chloride solution according to the general procedure 1 (spectroscopic data identical).

(c) The title compound was also formed in 21% yield according to the general procedure 2, after a reaction time of 7 days (spectroscopic data identical).

4-Methyl-1,2,3,4-tetrahydroquinoline 12d. According to the general procedure 1 the title compound was obtained as a yellow oil (73%) from 4-methylquinoline **11d**; δ_H (400 MHz; $CDCl_3$) 7.06 (1 H, ddd, *J* 7.4, 1.8, 0.9, 5-ArH), 6.97 (1 H, ddd, *J* 8.0, 7.8, 1.8, 7-ArH), 6.64 (1 H, ddd, *J* 7.8, 7.4, 1.2, 6-ArH), 6.48 (1 H, dd, *J* 8.0, 1.2, 8-ArH), 3.9 (1 H, br s, NH), 3.33 (2 H, m, NHCH_2), 2.93 (1 H, m, C*H*Me), 1.99 (1 H, m, NHCH$_2$-C*H*H), 1.70 (1 H, m, NHCH$_2$CH*H*), 1.30 (3 H, d, *J* 4.8, Me) (*cf*. lit.[103]).

***cis*-2,4-Dimethyl-1,2,3,4-tetrahydroquinoline 12e.** According to the general procedure 1 the *title compound* was obtained as a yellow oil (30%) from 2,4-dimethylquinoline **11e**; ν_{max} (neat)/cm^{-1} 3393 (NH), 3017, 2959, 2927, 2848, 1607, 740 (ArH); δ_H (400 MHz; $CDCl_3$) 7.19 (1 H, dd, *J* 7.6, 1.4, 5-ArH), 7.02 (1 H, ddd, *J* 8.0, 7.4, 1.4, 7-ArH), 6.71 (1 H, ddd, *J* 7.6, 7.4, 1.2, 6-ArH), 6.51 (1 H, dd, *J* 8.0, 1.2, 8-ArH), 3.9–3.2 (1 H, br s, NH), 3.51 (1 H, m, NHC*H*Me), 3.02 (1 H, m, ArC*H*Me), 1.98 (1 H, ddd, *J* 12.7, 5.4, 2.6, C*H*H), 1.39 (1 H, m (obscured), CH*H*), 1.38 (3 H, d, *J* 6.8, *cis* 4-Me), 1.25 (3 H, d, *J* 6.2, *cis* 2-Me) (*cf*. lit.[104]); δ_C (100 MHz; $CDCl_3$) 144.8 (C), 126.9 (CH), 126.8 (CH), 126.3 (C), 117.3 (CH), 113.9 (CH), 47.5 (CH), 40.7 (CH_2), 30.9 (CH), 22.8 (Me), 20.3 (Me).

2-*n*-Propyl-1,2,3,4-tetrahydroquinoline 12f. (a) According to the general procedure 1 the title compound was obtained as a clear oil (55%) from 2-*n*-propylquinoline **11f**; δ_H (300 MHz; $CDCl_3$) 6.98 (2 H, m, 7&5-ArH), 6.62 (1 H, ddd, *J* 7.4, 7.2, 1.1, 6-ArH), 6.49 (1 H, dd, *J* 8.3, 1.1, 8-ArH), 3.50 (1 H, br s, NH), 3.27 (1 H, m, NC*H*), 2.89–2.70 (2 H, m, ArCH_2), 2.00 (1 H, m, ArCH$_2$C*H*H), 1.63 (1 H, m, ArCH$_2$CH*H*), 1.58–1.41 (4 H, m, CH_2CH_2Me), 0.98 (3 H, t, *J* 6.9, Me) (*cf*. lit.[105]); δ_C (75 MHz; $CDCl_3$) 144.7 (C), 129.3 (CH), 126.7 (CH), 121.4 (C), 116.9 (CH), 114.1 (CH), 51.3 (CH), 38.9 (CH_2), 28.1 (CH_2), 26.5 (CH_2), 18.9 (CH_2), 14.2 (Me).

(b) The title compound was also obtained (24%) from 2-cyclopropylquinoline **26** according to general procedure 1 (spectroscopic data identical; see below).

2-(3-Methylbutyl)-1,2,3,4-tetrahydroquinoline 12g. According to the general procedure 1 the *title compound* was obtained as a colourless oil (49%) from 2-(3-methylbutyl)quinoline **11g** (Found: M$^+$, 203.1665. $C_{14}H_{21}N$ requires 203.1674); ν_{max} (neat)/cm^{-1} 3400 (NH), 3017, 2950, 2925, 2841, 1604, 1480, 1312, 745 (ArH); δ_H (300 MHz; $CDCl_3$) 6.97 (2 H, m, 5&7-ArH), 6.60 (1 H, ddd, *J* 7.4, 7.3, 1.1, 6-ArH), 6.47 (1 H, dd, *J* 6.3, 1.1, 8-ArH), 3.72 (1 H, br s, NH), 3.21 (1 H, m, NCH), 2.77 (2 H, m, ArCH_2CH$_2$), 1.98 (1 H, m, ArCH$_2$C*H*H), 1.46–1.67 (4 H, m, ArCH$_2$CH*H* and alkyl chain), 1.29 (2 H, m, CH_2CHMe$_2$), 1.00 (6 H, d, *J* 6.8, CH*Me*$_2$); δ_C (75 MHz; $CDCl_3$) 144.7 (C), 129.3 (CH), 126.7 (CH), 121.4 (C), 116.9 (CH), 114.0 (CH), 51.9 (CH), 34.9 (CH_2), 34.6 (CH_2), 28.3 (CH), 28.1 (CH_2), 26.5 (CH_2), 22.7 (Me); *m*/*z* (CI) 204 (MH$^+$, 100%); (EI) 203 (M$^+$, 8%), 132 (100), 117 (13).

2-(Allyloxymethyl)-1,2,3,4-tetrahydroquinoline 12h. According to the general procedure 1 the *title compound* was obtained as a clear oil (39%) from 2-allyloxymethylquinoline **11h** (Found: M$^+$, 203.1310. $C_{13}H_{17}NO$ requires 203.1310); ν_{max} (neat)/cm^{-1} 3396 (NH), 3020, 2925, 2843 (C–H), 1600, 1480, 1305, 1100 (C=O), 995, 935 (CH=CH$_2$), 738 (ArH); δ_H (300 MHz; $CDCl_3$) 7.01 (1 H, dd, *J* 8.6, 1.2, 5-ArH), 6.97 (1 H, ddd, *J* 8.0, 7.3, 1.2, 7-ArH), 6.63 (1 H, ddd, *J* 8.6, 7.3, 1.1, 6-ArH), 6.54 (1 H, d, *J* 8.0, 8-ArH), 5.97 (1 H, ddt, *J* 17.3, 10.5, 5.8, C*H*=CH$_2$), 5.33 (1 H, ddt, *J* 17.3, 1.7, 1.7, *trans*-CH=CH*H*), 5.24 (1 H, ddt, *J* 10.5, 1.7, 1.4, *cis*-CH=C*H*H), 4.20 (1 H, br s, NH), 4.06 (2 H, ddd, *J* 5.8, 1.7, 1.4, CH_2CH=CH$_2$), 3.57 (2 H, m, N-C*H* and NCHC*H*H), 3.37 (1 H, dd, *J* 10.2, 9.9, NCHCH*H*), 2.81 (2 H, m, ArCH_2), 1.91 (1 H, m, ArCH$_2$C*H*H), 1.65 (1 H, m, ArCH$_2$-CH*H*); δ_C (100 MHz; $CDCl_3$) 144.2 (C), 134.6 (=CH), 129.2 (CH), 126.8 (CH), 121.2 (C), 117.2 (=CH$_2$), 117.1 (CH), 114.2 (CH), 74.5 (OCH$_2$), 72.2 (OCH$_2$), 50.9 (CH), 26.0 (CH$_2$), 24.7 (CH$_2$); *m*/*z* (CI) 204 (MH$^+$, 100%), 146 (16), 132 (24); (EI) 203 (M$^+$, 7%), 132 (100), 130 (19), 117 (15), 91 (11), 77 (12).

2-Phenyl-1,2,3,4-tetrahydroquinoline 12i. According to the general procedure 1 the title compound was obtained as a yellow oil (40%) from 2-phenylquinoline **11i**; δ_H (400 MHz; $CDCl_3$) 7.42–7.29 (5 H, m, Ph), 7.01 (2 H, m, 7&5-ArH), 6.67 (1 H, dd, *J* 7.4, 1.1, 6-ArH), 6.55 (1 H, dd, *J* 7.5, 1.1, 8-ArH), 4.45 (1 H, dd, *J* 9.3, 3.3, NHC*H*Ph), 4.04 (1 H, br s, NH), 2.90 (1 H, m, ArC*H*H), 2.76 (1 H, m, ArCH*H*), 2.12 (1 H, m, ArCH$_2$C*H*H), 2.00 (1 H, m, ArCH$_2$CH*H*) (*cf*. lit.[106]).

6-Methoxy-1,2,3,4-tetrahydroquinoline 12j. According to the general procedure 1 the title compound was obtained as a yellow oil (42%) from 6-methoxyquinoline **11j**; δ_H (400 MHz; $CDCl_3$) 6.60 (1 H, dd, *J* 8.5, 2.7, 7-ArH), 6.57 (1 H, d, *J* 2.7, 5-ArH), 6.45 (1 H, d, *J* 8.5, 8-ArH), 3.73 (3 H, s, OMe), 3.69 (1 H, br s, NH), 3.26 (2 H, m, NHCH_2CH$_2$), 2.76 (2 H, t, *J* 6.5, ArCH_2), 1.93 (2 H, m, NHCH$_2$CH_2) (*cf*. lit.[107]).

***N*-(1,2,3,4-Tetrahydroquinolin-6-yl)acetamide 12k.** According to the general procedure 1 the title compound was obtained as a colourless oil following preparative TLC (60% by H NMR) from *N*-(quinolin-6-yl)acetamide **11k**; δ_H (300 MHz; $CDCl_3$) 7.14 (1 H, br s, CONH), 7.08 (1 H, d, *J* 2.5, 5-ArH), 6.97 (1 H, dd, *J* 8.5, 2.4, 7-ArH), 6.41 (1 H, d, *J* 8.5, 8-ArH), 3.78 (1 H, br s, NH), 3.26 (2 H, m, NHCH_2CH$_2$), 2.72 (2 H, t, *J* 6.4, ArCH_2), 2.11 (3 H, s, MeCO), 1.90 (2 H, m, NHCH$_2$CH_2) (*cf*. lit.[108]).

6-Chloro-1,2,3,4-tetrahydroquinoline 12l. According to the general procedure 1 the title compound was obtained as a clear oil (25%) from 6-chloroquinoline **11l**; δ_H (300 MHz; $CDCl_3$) 6.91 (1 H, dd, *J* 3.0, 1.5, 5-ArH), 6.90 (1 H, dd, *J* 7.3, 3.0, 7-ArH), 6.38 (1 H, dd, *J* 7.3, 1.5, 8-ArH), 3.50 (1 H, br s, NH), 3.27 (2 H, m, NHCH_2CH$_2$), 2.73 (2 H, t, *J* 6.5, ArCH_2), 1.92 (2 H, m, NHCH$_2$CH_2) (*cf*. lit.[109]).

1,2-Dihydrophenanthridine 12m. According to the general procedure 1 the title compound was obtained as a pale yellow solid (72%) from phenanthridine **11m**; mp 119–121 °C (lit.,[110] mp 123.5–124.5 °C); δ_H (300 MHz; $CDCl_3$) 7.69 (1 H, dd, *J* 7.7, 1.2, 6-ArH), 7.68 (1 H, dd, *J* 8.0, 1.5, 7-ArH), 7.31 (1 H, ddd, *J* 7.7, 7.3, 1.4, 5-ArH), 7.21 (1 H, ddd, *J* 7.5, 7.3, 1.2, 4-ArH), 7.11 (2 H, m, 9- and 3-ArH), 6.84 (1 H, ddd, *J* 8.0, 7.6, 1.1, 8-ArH), 6.67 (1 H, dd, *J* 7.9, 1.1, 10-ArH), 4.40 (2 H, s, CH$_2$), 3.94 (1 H, br s, NH).

1,2,3,4-Tetrahydroisoquinoline 14a. According to the general procedure 1 the title compound was obtained as a clear oil (78%) from isoquinoline **13a**; δ_H (300 MHz; $CDCl_3$) 7.15–7.00 (4 H, m, ArH), 4.02 (2 H, s, ArCH_2N), 3.14 (2 H, t, *J* 6.0, NHCH_2CH$_2$), 2.80 (2 H, t, *J* 6.0, NHCH$_2$CH_2), 1.95 (1 H, s, NH) (*cf*. lit.[111]).

1-Methyl-1,2,3,4-tetrahydroisoquinoline 14b. According to the general procedure 1 the title compound was obtained as a

colourless oil (74%) from 1-methylisoquinoline **13b**; bp 105 °C, 1.5 mmHg (lit.,[112] 78–80 °C, 0.06 mmHg); δ_H (300 MHz; $CDCl_3$) 7.17 (4 H, m, ArH), 4.12 (1 H, q, *J* 7.2, C*H*Me), 3.39–2.61 (4 H, m, CH_2CH_2), 1.82 (1 H, br s, NH), 1.51 (3 H, d, *J* 7.2, CH*Me*).

3-Methyl-1,2,3,4-tetrahydroisoquinoline 14c. According to the general procedure 1 the title compound was obtained as a yellow oil (71%) from 3-methylisoquinoline **13c**; δ_H (400 MHz; $CDCl_3$) 7.07–6.97 (4 H, m, ArH), 3.96 (2 H, 2d, *J* 15.8, ArCH_2N), 2.89 (1 H, m, C*H*CH_3), 2.69 (1 H, dd, *J* 12.5, 3.5, *anti*-ArC*H*HCH), 2.42 (1 H, dd, *J* 12.5, 5.5, *syn*-ArCH*H*CH), 1.16 (3 H, d, *J* 6.3, Me) (*cf*. lit.[113]).

2,3-Dimethyl-1,2,3,4-tetrahydroisoquinoline 14d. According to the general procedure 1 the title compound was obtained as a colourless oil (97%) from 2,3-dimethylisoquinolinium iodide **13d**; δ_H (300 MHz; $CDCl_3$) 7.15–7.00 (4 H, m, ArH), 3.82 (1 H, d, *J* 15.4, NC*H*H), 3.57 (1 H, d, *J* 15.4, NCH*H*), 2.85 (1 H, m, CHC*H*H), 2.68 (1 H, m, CHCH*H*), 2.63 (1 H, m, NC*H*), 2.42 (3 H, s, N-Me), 1.18 (3 H, d, *J* 6.1, CH-Me) (*cf*. lit.[114]).

1-Isoquinolinyl(phenyl)methanol. According to the general procedure 1 the title compound was obtained as a colourless solid (72%) from 1-isoquinolinyl phenyl ketone; mp 108–110 °C (lit.,[115] mp 108–109 °C); δ_H (400 MHz; $CDCl_3$) 8.55 (1 H, d, *J* 5.7, 3-ArH), 7.97 (1 H, dd, *J* 8.0, 1.0, 8-ArH), 7.83 (1 H, d, *J* 7.9, 5-ArH), 7.65 (1 H, d, *J* 5.7, 4-ArH), 7.63 (1 H, ddd, *J* 7.9, 6.0, 1.0, 6-ArH), 7.48 (1 H, ddd, *J* 8.0, 6.0, 1.1, 7-ArH), 7.36 (2 H, m, Ph), 7.27 (3 H, m, Ph), 6.39 (1 H, s, HOC*H*), 4.51 (1 H, br s, NH).

2-Methyl-1,2,3,4-tetrahydroquinoxaline 16a. According to the general procedure 1 the title compound was obtained as a brown solid (92%) from 2-methylquinoxaline **15a**; mp 71–72 °C (lit.,[116] mp 70 °C); δ_H (400 MHz; $CDCl_3$) 6.59 (2 H, m, ArH), 6.51 (2 H, m, ArH), 4.05 (2 H, br s, 2NH), 3.52 (1 H, m, NC*H*Me), 3.32 (1 H, dd, *J* 8.0, 2.2, *trans*-C*H*HCHMe), 3.04 (1 H, dd, *J* 8.0, 6.1, *cis*-CH*H*CHMe), 1.19 (3 H, d, *J* 6.3, Me).

2,3-Dimethyl-1,2,3,4-tetrahydroquinoxaline 16b. (a) According to the general procedure 1 the title compound was obtained as a yellow solid (90%) from 2,3-dimethylquinoxaline **15b**; 2 : 1 (*cis*/*trans*); mp 107–109 °C (lit.,[117] *cis*: 111–114 °C); ν_{max} (neat)/cm^{-1} 3337, 3280 (NH), 2973, 2850, 1599, 1514, 739 (ArH); δ_H (400 MHz; $CDCl_3$) 6.58 (2 H, m, ArH), 6.50 (2 H, m, ArH), 3.50 (2 H, br s, exchange in D_2O, 2NH), 3.48 (1.4 H, m, *cis*-NHC*H*Me), 3.02 (0.6 H, m, *trans*-NHC*H*Me), 1.17 (1.8 H, m, *trans*-Me), 1.12 (4.2 H, m, *cis*-Me) (*cf*. lit.[118]); δ_C (100 MHz; $CDCl_3$) 133.5 (C), 132.7 (C), 118.6 (CH), 118.5 (CH), 114.4 (CH), 113.9 (CH), 52.0 (*trans*-CH), 49.0 (*cis*-CH), 19.0 (*trans*-Me), 17.2 (*cis*-Me); *m*/*z* (EI) 162 (M^+, 57%), 147 (100), 132 (35), 119 (23), 66 (23).

(b) The title compound (2 : 1, *cis*/*trans*) was formed in 81% yield using aqueous trimethylamine hydrogen chloride solution (4 M) in place of saturated aqueous ammonium chloride solution according to the general procedure 1 (spectroscopic data identical).

(c) The title compound (2 : 1, *cis*/*trans*) was formed in 83% yield according to the general procedure 2 (spectroscopic data identical).

(d) The title compound (2 : 1, *cis*/*trans*) was formed in 8% yield with *tert*-butyl alcohol in place of acetic acid according to the general procedure 2 (spectroscopic data identical).

1,2-Dimethylindoline 18b. According to the general procedure 1 the title compound was obtained as a colourless oil (64%) from 1,2-dimethylindole **17b**; δ_H (300 MHz; $CDCl_3$) 7.07 (2 H, m, ArH), 6.68 (1 H, ddd, *J* 8.0, 7.4, 1.1, ArH), 6.47 (1 H, d, *J* 8.0, ArH), 3.41 (1 H, ddq, *J* 10.4, 8.2, 6.2, NC*H*Me), 3.10 (1 H, dd, *J* 15.4, 8.2, *cis*-NCHC*H*H), 2.74 (3 H, s, N-Me), 2.61 (1 H, dd, *J* 15.4, 10.4, *trans*-NCHCH*H*), 1.34 (3 H, d, *J* 6.2, NCH*Me*) (*cf*. lit.[119]); δ_C (75 MHz; $CDCl_3$) 196.4 (C), 129.3 (C), 127.3 (CH), 124.0 (CH), 117.8 (CH), 107.2 (CH), 62.9 (CH), 37.4 (Me), 33.8 (CH_2), 18.8 (Me).

4-Benzyloxy-1,2-dimethyl-5-methoxyindoline 18d. According to the general procedure 1 the *title compound* was obtained as a brown oil (23%) from 4-benzyloxy-1,2-dimethyl-5-methoxyindole **17d** (Found: M^+, 283.1578. $C_{18}H_{21}NO_2$ requires 283.1572); ν_{max} (neat)/cm^{-1} 3030, 2957, 2831, 2795, 1615, 1485, 1258, 1197, 1076, 1019, 739, 699; δ_H (300 MHz; $CDCl_3$) 7.40 (5 H, m, OCH_2*Ph*), 6.71 (1 H, d, *J* 8.3, 6-ArH), 6.16 (1 H, d, *J* 8.3, 7-ArH), 5.08 (1 H, d, *J* 11.1, OCH_2Ph), 5.06 (1 H, d, *J* 11.1, OCH_2Ph), 3.83 (3 H, s, OMe), 3.28 (1 H, m, NC*H*Me), 3.06 (1 H, dd, *J* 7.9, 12.0, *trans*-NCHCH*H*), 2.66 (3 H, s, NMe), 2.40 (1 H, dd, *J* 9.8, 12.0, *cis*-NCHC*H*H), 1.28 (3 H, d, *J* 6.1, NCH*Me*); δ_C (75 MHz; $CDCl_3$) 149.1 (C), 145.9 (C), 144.8 (C), 138.1 (C), 128.3 (CH), 128.2 (CH), 127.9 (CH), 122.8 (C), 112.5 (CH), 102.2 (CH), 74.5 (CH_2), 63.6 (CH), 57.1 (OMe), 34.9 (CH_2), 34.6 (NMe), 18.6 (Me); *m*/*z* (EI) 283 (M^+, 95%), 268 (40), 240 (12), 192 (17), 176 (13), 164 (88), 148 (26), 134 (21), 91 (100), 77 (10).

1-Methyl-6,7-dimethoxy-1,2,3,4-tetrahydroisoquinoline 23a. According to the general procedure 1 the title compound was obtained as a colourless oil (100%) from 1-methyl-6,7-dimethoxy-3,4-dihydroisoquinoline **22a**; δ_H (300 MHz; $CDCl_3$) 6.62 (1 H, s, ArH), 6.57 (1 H, s, ArH), 4.04 (1 H, q, *J* 6.6, C*H*Me), 3.86 (3 H, s, OMe), 3.85 (3 H, s, OMe), 3.25 (1 H, m, NC*H*H), 3.00 (1 H, m, NCH*H*), 2.79 (1 H, m, ArC*H*H), 2.64 (1 H, m, ArCH*H*), 1.68 (1 H, br s, NH), 1.44 (3 H, d, *J* 6.6, Me) (*cf*. lit.[120]).

6,7-Dimethoxy-1-(pent-4-enyl)-1,2,3,4-tetrahydroisoquinoline 23b. According to the general procedure 1 the *title compound* was obtained as a yellow oil (83%) from 6,7-dimethoxy-1-(pent-4-enyl)-3,4-dihydroisoquinoline **22b** (Found: M^+, 261.1720. $C_{16}H_{23}NO_2$ requires 261.1729); ν_{max} (neat)/cm^{-1} 3319 (NH), 3078, 2996, 2919, 2832, 1634, 1516, 1465, 1260, 1220, 1112, 912, 856, 789; δ_H (300 MHz; $CDCl_3$) 6.60 (1 H, s, ArH), 6.56 (1 H, s, ArH), 5.83 (1 H, m, C*H*=CH_2), 5.00 (2 H, m, CH=CH_2), 3.87 (1 H, m, ArC*H*N), 3.85 (3 H, s, OMe), 3.84 (3 H, s, OMe), 3.20 (1 H, m, NC*H*H), 2.96 (1 H, m, NCH*H*), 2.69 (2 H, m, ArCH_2), 2.13 (2 H, m, CH_2CH=CH_2), 1.62–1.48 (4 H, m, CH_2CH_2CHN), NH not observed; δ_C (75 MHz; $CDCl_3$) 147.2 (C), 147.1 (C), 138.7 (=CH), 131.5 (C), 127.2 (C), 114.7 (=CH_2), 111.7 (CH), 109.2 (CH), 56.0 (OMe), 55.8 (OMe), 55.3 (CH), 41.1 (CH_2), 35.9 (CH_2), 33.8 (CH_2), 29.5 (CH_2), 25.4 (CH_2); *m*/*z* (EI) 261 (M^+, 1%), 192 (100); (CI) 262 (MH^+, 100%).

6,7-Dimethoxy-1,2-dimethyl-1,2,3,4-tetrahydroisoquinoline (carnegine) 25a. According to the general procedure 3 the title compound was obtained as a yellow oil (83%) from 6,7-dimethoxy-1,2-dimethyl-3,4-dihydroisoquinolinium iodide **24a**; δ_H (300 MHz; $CDCl_3$) 6.58 (1 H, s, ArH), 6.56 (1 H, s, ArH), 3.842 (3 H, s, OMe), 3.838 (3 H, s, OMe), 3.56 (1 H, q, *J* 6.3, NCH), 3.04 (1 H, ddd, *J* 11.3, 6.0, 5.2, NC*H*H), 2.79 (2 H, m, ArCH_2), 2.65 (1 H, ddd, *J* 11.3, 7.1, 5.0, NCH*H*), 2.48 (3 H, s, NMe), 1.38 (3 H, d, *J* 6.3, CH*Me*) (*cf*. lit.[121]).

2-Cyclopropyl-1,2,3,4-tetrahydroquinoline 27. According to general procedure 1 the *title compound* was obtained as a colourless oil (35%) from 2-cyclopropylquinoline **26** (Found: MH^+, 174.1282. $C_{12}H_{16}N$ requires 174.1283); ν_{max} (neat)/cm^{-1} 3400 (NH), 3075 (cyclopropyl C–H), 2990, 2920, 2840 (C–H), 1600 (Ar), 745 (ArH); δ_H (300 MHz; $CDCl_3$) 6.99 (2 H, m, 7&5-ArH), 6.62 (1 H, ddd, *J* 7.5, 7.4, 1.1, 6-ArH), 6.52 (1 H, dd, *J* 7.7, 1.1, 8-ArH), 3.91 (1 H, br s, NH), 2.79 (2 H, m, ArCH_2), 2.43 (1 H, ddd, *J* 9.6, 9.1, 2.7, NCH), 2.11 (1 H, m, ArCH_2-

C*H*H), 1.83 (1 H, m, $ArCH_2CH$*H*), 0.93 (1 H, m, cyclopropyl CH), 0.55 (2 H, m, cyclopropyl CH_2), 0.27 (2 H, m, cyclopropyl CH_2); δ_C (75 MHz; $CDCl_3$) 144.6 (C), 129.3 (CH), 126.8 (CH), 121.3 (C), 116.9 (CH), 113.9 (CH), 57.5 (CH), 28.4 (CH_2), 26.7 (CH_2), 17.1 (CH), 3.0 (CH_2), 2.0 (CH_2); *m/z* (EI) 173 (M^+, 42%), 132 (100), 117 (13), 77 (10); (CI) 174 (MH^+, 100%).

2-*n*-Propyl-1,2,3,4-tetrahydroquinoline **12f** was also produced in this reaction (24%), see above for spectroscopic data.

Preparation of oximes

Dimethyl hydroxyiminomalonate 28a. A solution of sodium nitrite (1.40 g, 20.2 mmol) in water (3.2 ml) was added dropwise to a cooled (0 °C) solution of dimethyl malonate (2.0 ml, 17.5 mmol) in acetic acid (2.5 ml) so that the temperature of the reaction mixture did not rise above 20 °C. The reaction mixture was stirred at 0 °C for 30 min and then 1 h at room temperature. Water (9 ml) was added and the reaction mixture was stirred at room temperature overnight. The resulting solution was extracted with ether (3 × 15 ml). The combined organic phases were washed sequentially with water (15 ml), saturated aqueous sodium hydrogen carbonate (3 × 15 ml), water (15 ml) and brine (15 ml), dried ($MgSO_4$), concentrated and the residue purified by flash chromatography (50% ethyl acetate–light petroleum) to give the *oxime* as a colourless oil, which solidified on standing overnight in the freezer (1.108 g, 39%); mp 65–67 °C (lit.,[122] 66–67 °C); δ_H(300 MHz; $CDCl_3$) 10.56 (1 H, s, OH), 3.94 (3 H, s, OMe), 3.91 (3 H, s, OMe).

(*E*)- and (*Z*)-Methyl 2-hydroxyimino-3-oxo-4-methylpentanoate 28b. A solution of sodium nitrite (1.20 g, 17.4 mmol) in water (2.7 ml) was added dropwise to a cooled (0 °C) solution of methyl isobutyrylacetate (2.1657 g, 15.0 mmol) in acetic acid (2.1 ml) so that the temperature of the reaction mixture did not rise above 20 °C. The reaction mixture was stirred at 0 °C for 30 min and then 1 h at room temperature. Water (8 ml) was added and the reaction mixture was stirred at room temperature overnight. The resulting yellow solution was extracted with ether (3 × 15 ml). The combined organic phases were washed sequentially with water (15 ml), saturated aqueous sodium hydrogen carbonate (3 × 15 ml), water (15 ml) and brine (15 ml), dried ($MgSO_4$) and concentrated to give a colourless oil which was purified by flash chromatography (5% ether–dichloromethane) to give a mixture of isomeric *oximes* as a colourless oil (1.47 g, 57%). For analytical purposes, pure samples of each oxime isomer were obtained by further flash chromatography (2% ether–dichloromethane). The oximes were found to interconvert significantly within a few days on standing at room temperature either neat or in a solution of $CDCl_3$.

Less polar isomer. Colourless oil (Found: MH^+ (mixture of isomers), 174.0766. $C_7H_{12}NO_4$ requires 174.0766); R_f 0.4 (5% ether–dichloromethane); $\nu_{max}(CHCl_3)/cm^{-1}$ 3546s, 3315br, 2979, 1747vs (ester), 1695 (ketone), 1628w (oxime), 1363, 1302, 1213, 1005, 972; δ_H (300 MHz; $CDCl_3$) 9.88 (1 H, br s, OH), 3.91 (3 H, s, OMe), 3.43 (1 H, septet, *J* 6.9, C*H*Me_2), 1.16 (6 H, d, *J* 7.1, CH*Me*$_2$); δ_C (75 MHz; $CDCl_3$) 200.2 (ketone), 162.5 (ester), 149.5 (oxime), 52.9 (OMe), 35.5 (CH), 18.3 (CH_3); *m/z* (CI; mixture of isomers) 174 (MH^+, 80%), 158 (100).

More polar isomer. Colourless oil; R_f 0.2 (5% ether–dichloromethane); $\nu_{max}(CHCl_3)/cm^{-1}$ 3548, 3317br, 2978, 1736vs (ester), 1712s (ketone), 1628w (oxime), 1441, 1365, 1304, 1281, 1213, 1016s; δ_H (300 MHz; $CDCl_3$) 10.33 (1 H, br s, OH), 3.87 (3 H, s, OMe), 2.94 (1 H, septet, *J* 7.0, C*H*Me_2), 1.19 (6 H, d, *J* 7.1, CH*Me*$_2$); δ_C (75 MHz; $CDCl_3$) 198.2 (ketone), 161.3 (ester), 149.95 (oxime), 53.2 (OMe), 40.7 (CH), 16.7 (CH_3).

Ethyl pyruvate 2-oxime 28d. Hydroxylamine hydrochloride (1.59 g, 22.9 mmol) and sodium acetate (1.50 g, 18.3 mmol) in water (10 ml) were added to ethyl pyruvate (2.00 ml, 2.120 g, 18.3 mmol) in ethanol (10 ml). The mixture was stirred at room temperature for 3 h then extracted with dichloromethane (3 × 10 ml). The combined organic layers were washed with water (20 ml), dried ($MgSO_4$) and concentrated *in vacuo* to give the title compound **28d** as colourless crystals (*E*/*Z*, 8.3 : 1) (2.36 g, 98%); mp 94–96 °C (lit.,[123] mp 95 °C); δ_H (300 MHz; $CDCl_3$) 9.70 (1 H, br s, NOH), 4.30 (2 H, q, *J* 7.2, *E*-C*H*$_2$Me), 3.75 (0.24 H, q, *J* 7.2, *Z*-C*H*$_2$Me), 2.12 (0.36 H, s, *Z*-Me), 2.10 (3 H, s, *E*-Me), 1.34 (3 H, t, *J* 7.2, *E*-CH_2*Me*), 1.24 (0.36 H, t, *J* 7.2, *Z*-CH_2*Me*).

Reduction of oximes

Dimethyl acetamidomalonate 29a. According to general procedure 4, dimethyl hydroxyiminomalonate **28a** (0.213 g, 1.32 mmol) was reduced to give the acetamide **29a** (0.163 g, 65%) as a colourless solid after purification by flash chromatography (50% dichloromethane–ethyl acetate); mp 131–132 °C (lit.,[124] 130–132 °C); δ_H (300 MHz; $CDCl_3$) 6.71 (1 H, br d, *J ca.* 6, N*H*Ac), 5.21 (1 H, d, *J* 7.2, CH), 3.81 (6 H, s, 2 × OMe), 2.07 (3 H, s, $COCH_3$).

Methyl 2-acetamido-3-oxo-4-methylpentanoate 29b. According to general procedure 4, oxime **28b** as a mixture of isomers (0.353 g, 2.04 mmol) was reduced to give the *acetamide* **29b** (0.388 g, 95%) as a waxy colourless solid, which did not require chromatographic purification; mp 38–39 °C (lit.,[125] no mp); $\nu_{max}(CHCl_3)/cm^{-1}$ 3425 (NH), 2979, 1757s (ester), 1722s (ketone), 1678s (amide), 1498, 1436, 1333, 1213, 1165; δ_H (300 MHz; $CDCl_3$) 6.72 (1 H, br s, NHAc), 5.44 (1 H, d, *J* 6.9, C*H*NH), 3.81 (3 H, s, OMe), 3.07 (1 H, septet, *J* 6.9, C*H*Me_2), 2.08 (3 H, s, $COCH_3$), 1.21 (3 H, d, *J* 7.2, CH_3), 1.11 (3 H, d, *J* 6.9, CH_3); δ_C (75 MHz; $CDCl_3$) 205.2, 169.9, 167.0, 60.6, 53.2, 38.8, 22.7, 18.8, 17.6.

1-Phenyl-2-acetamidobutane-1,3-dione 29c. According to general procedure 4 the *title compound* was obtained as a colourless oil (69%) from 1-phenylbutane-1,2,3-trione 2-oxime **28c** (Found: MH^+, 220.0973. $C_{12}H_{14}NO_3$ requires 220.0974); ν_{max} (neat)/cm^{-1} 3290 (NH), 3050, 2920 (C–H), 1725 (C=O), 1655 (C=O), 1510 (NH), 1370 (COMe), 755, 700 (ArH); δ_H (300 MHz; $CDCl_3$) 8.11 (2 H, m, 2&6-PhH), 7.66 (1 H, m, 4-PhH), 7.54 (2 H, m, 3&5-PhH), 7.07 (1 H, br d, *J* 6.6, NH), 6.18 (1 H, d, *J* 6.6, NCH), 2.20 (3 H, s, COMe), 2.13 (3 H, s, NAc); δ_C (75 MHz; $CDCl_3$) 200.1 (C=O), 192.7 (C=O), 170.0 (NC=O), 134.6 (CH), 134.4 (C), 129.5 (CH), 129.0 (CH), 66.0 (CH), 27.3 (Me), 22.9 (Me); *m/z* (CI) 220 (MH^+, 14%), 178 (40), 105 (100).

The mass balance was found to be acetamidoacetophenone **29f**—spectroscopic data identical to below.

***N*-Acetyl-D,L-alanine ethyl ester 29d.** According to general procedure 4 the title compound was obtained as a colourless solid (98%) from ethyl pyruvate 2-oxime **28d**; mp 35–37 °C (from ether) (lit.,[126] 34–35 °C); δ_H (300 MHz; $CDCl_3$) 6.38 (1 H, br, NH), 4.51 (1 H, quintet, *J* 7.2, NCH), 4.14 (2 H, q, *J* 7.2, OC*H*$_2$Me), 1.97 (3 H, s, COMe), 1.34 (3 H, d, *J* 7.2, *Me*CH), 1.24 (3 H, t, *J* 7.2, OCH_2*Me*).

2-Acetamidopropiophenone 29e. According to general procedure 4 the title compound was obtained as a colourless solid (96%) from 1-phenylpropane-1,2-dione 2-oxime **28e**; mp 89–90 °C (lit.,[127] mp 87–89 °C); δ_H (300 MHz; $CDCl_3$) 7.98 (2 H, m, 2&6-PhH), 7.62 (1 H, m, 4-PhH), 7.50 (2 H, m, 3&5-PhH), 6.67 (1 H, br, NH), 5.57 (1 H, quintet, *J* 7.1, CHN), 2.06 (3 H, s, Ac), 1.43 (3 H, d, *J* 7.1, Me).

2-*N*-(*tert*-Butoxycarbonyl)aminopropiophenone. According to general procedure 4, but replacing acetic anhydride with di-*tert*-butyl dicarbonate (1.12 g, 5.1 mmol), the title compound was obtained as a colourless solid (92%) from 1-phenylpropane-1,2-dione 2-oxime **28e** after purification by flash

chromatography (10% ethyl acetate–light petroleum); mp 81–83 °C (lit.,[128] mp 81 °C); δ_H (400 MHz; $CDCl_3$) 7.97 (2 H, d, *J* 7.4, 2&6-PhH), 7.59 (1 H, dt, *J* 7.4, 1.1, 4-PhH), 7.48 (2 H, t, *J* 7.4, 3&5-PhH), 5.57 (1 H, br d, *J* 6.8, NH), 5.29 (1 H, quintet, *J* 7.3, CHN), 1.45 (9 H, s, C*Me*$_3$), 1.39 (3 H, d, *J* 7.1, CH*Me*).

Acetamidoacetophenone 29f. According to general procedure 4 the title compound was obtained as a colourless solid (100%) from phenylglyoxaldehyde oxime **28f**; mp 83–84 °C (lit.,[129] mp 83–84 °C); δ_H (300 MHz; $CDCl_3$) 7.98 (2 H, m, 2&6-PhH), 7.62 (1 H, m, 4-PhH), 7.49 (2 H, m, 3&5-PhH), 6.69 (1 H, br d, *J* 4.3, NH), 4.78 (2 H, d, *J* 4.3, $COCH_2N$), 2.09 (3 H, s, Ac).

3-(Acetamido)indol-2(3*H*)-one 29g. According to general procedure 4 the title compound was obtained as a colourless solid (69%) from isatin 3-oxime **28g**; mp 246–248 °C (from methanol–ethyl acetate) (lit.,[130] 248–249.5 °C (from isopropanol–benzene)); δ_H (300 MHz; d_6-DMSO) 10.42 (1 H, s, ArN*H*), 8.66 (1 H, d, *J* 7.9, N*H*Ac), 7.20 (1 H, dd, *J* 7.7, 7.5, 5-ArH), 7.12 (1 H, d, *J* 6.7, 7-ArH), 6.94 (1 H, dd, *J* 7.5, 6.7, 6-ArH), 6.81 (1 H, d, *J* 7.7, 4-ArH), 5.08 (1 H, d, *J* 7.9, NCHCO), 1.90 (3 H, s, COMe).

(1*S*)-(−)-3-*endo*-Acetamidocamphor 29h. According to general procedure 4 the *title compound* was obtained as a colourless solid (87%) from *anti*-(1*S*)-(−)-camphorquinone 3-oxime **28h**; mp 113–115 °C (from ether) (Found: C, 66.0; H, 9.5; N, 6.3. $C_{12}H_{19}NO_2{\cdot}0.5H_2O$ requires C, 66.0; H, 9.2; N, 6.4%) (Found: MH^+, 210.1491. $C_{12}H_{20}NO_2$ requires 210.1494); $[\alpha]_D^{20}$ −12.0 (*c* 0.75 in ethanol); ν_{max} (KBr)/cm^{-1} 3300 (amide), 3075, 2960 (C–H), 1750 (C=O), 1650 (amide), 1550, 1380, 1270, 705, 540; δ_H (400 MHz; $CDCl_3$) 6.10 (1 H, br, NH), 4.46 (1 H, m, NCH), 2.49 (1 H, m, NCHC*H*), 2.01 (3 H, s, NHCO*Me*), 1.77–1.21 (4 H, m, CH_2CH_2), 1.00 (3 H, s, *anti*-Me), 0.96 (3 H, s, *syn*-Me), 0.93 (3 H, s, COC*Me*) (*cf*. lit.[131]); δ_C (100 MHz; $CDCl_3$) 218.5 (C=O), 170.7 (NC=O), 58.9 (C), 58.6 (CH), 48.0 (CH), 44.3 (C), 32.4 (CH_2), 23.0 (Me), 19.7 (Me), 19.4 (CH_2), 19.0 (Me), 9.3 (Me); *m*/*z* (CI) 210 (MH^+, 100%), 122 (45).

Nitro group reductions

4-Chloroaniline 31a. According to the general procedure 5 the title compound was obtained as a colourless crystalline solid (95%) from 4-chloronitrobenzene **30a**; mp 69–70 °C (lit.,[132] mp 70–71 °C); δ_H (300 MHz; $CDCl_3$) 7.10 (2 H, dd, *J* 6.7, 2.2, ArH), 6.61 (2 H, dd, *J* 6.7, 2.1, ArH), 3.62 (2 H, br s, NH_2).

3-Chloro-2-methylaniline 31b. According to the general procedure 5 the title compound was obtained as a yellow oil (75%) from 6-chloro-2-nitrotoluene **30b**; δ_H (300 MHz; $CDCl_3$) 6.93 (1 H, dd, *J* 7.9, 7.8, ArH), 6.81 (1 H, d, *J* 7.8, ArH), 6.58 (1H, d, *J* 7.9, ArH), 3.75 (2 H, br s, NH_2), 2.23 (3 H, s, Me) (*cf*. lit.[133]).

5-Bromo-2-methylaniline 31c. According to the general procedure 5 the title compound was obtained as a pale crystalline solid (70%) from 2-nitro-4-bromotoluene **30c**; mp 32–33 °C (lit.,[134] mp 33 °C); δ_H (300 MHz; $CDCl_3$) 6.93 (1 H, d, *J* 7.2, ArH), 6.84 (2 H, m, ArH), 3.66 (2 H, br s, NH_2), 2.13 (3 H, s, Ar*Me*).

2-Iodoaniline 31d. According to the general procedure 5 the title compound was obtained as a colourless crystalline solid (60%) from 2-iodonitrobenzene **30d**; mp 56 °C (sharp) (lit.,[135] mp 56.5 °C); δ_H (300 MHz; $CDCl_3$) 7.64 (1 H, dd, *J* 7.9, 1.4, ArH), 7.13 (1 H, ddd, *J* 7.9, 7.3, 1.4, ArH), 6.75 (1 H, dd, *J* 7.9, 1.5, ArH), 6.47 (1 H, ddd, *J* 7.9, 7.3, 1.5, ArH), 3.90 (2 H, br s, NH_2).

3-Amino-4-methoxyphenyl methanesulfonate 31e. According to the general procedure 5 the title compound was obtained as a colourless crystalline solid (98%) from 4-methoxy-3-nitrophenyl methanesulfonate **30e**; mp 85–86 °C (from toluene) (lit.,[136] mp 84 °C (from benzene)); δ_H (300 MHz; $CDCl_3$) 6.73 (1 H, d, *J* 8.8, ArH), 6.64 (1 H, d, *J* 2.8, ArH), 6.60 (1 H, dd, *J* 8.8, 2.8, ArH), 3.85 (3 H, s, OMe), 3.09 (3 H, s, OSO_2Me).

4-Methylthioaniline 31f. According to the general procedure 5 the *title compound* was obtained as a brown oil (92%) from 4-methylthionitrobenzene **30f** (Found: M^+, 139.0453. C_7H_9NS requires 139.0454); ν_{max} (neat)/cm^{-1} 3447, 3350, 3217, 3022, 2981, 2910, 1620, 1588, 1490, 1275, 1170, 825; δ_H (300 MHz; $CDCl_3$) 7.17 (2 H, d, *J* 8.7, ArH), 6.64 (2 H, d, *J* 8.7, ArH), 3.60 (2 H, br s, NH_2), 2.42 (3 H, s, SMe); δ_C (75 MHz; $CDCl_3$) 145.1 (C), 131.1 (CH), 130.7 (C), 115.8 (CH), 18.8 (Me); *m*/*z* (EI) 139 (M^+, 87%), 124 (100), 97 (7), 80 (29), 65 (8).

3-Aminobenzonitrile 31g. According to the general procedure 5 the title compound was obtained as a colourless crystalline solid (95%) from 3-nitrobenzonitrile **30g**; mp 52–54 °C (from 1 : 1 ethanol–water) (lit.,[137] mp 53–54 °C); δ_H (300 MHz; $CDCl_3$) 7.22 (1 H, ddd, *J* 8.1, 7.6, 0.5, ArH), 7.01 (1 H, ddd, *J* 7.6, 1.4, 1.1, ArH), 6.90 (1 H, ddd, *J* 2.2, 1.4, 0.5, ArH), 6.86 (1 H, ddd, *J* 8.1, 2.2, 1.1, ArH), 3.95 (2 H, br s, NH_2).

3-Aminobenzoic acid 31h. According to the general procedure 5 the title compound was obtained as a colourless crystalline solid (90%) from 3-nitrobenzoic acid **30h**; mp 173–174 °C (lit.,[138] mp 174 °C); δ_H (300 MHz; d_4-MeOH) 7.38 (1 H, dd, *J* 1.3, 1.0, ArH), 7.32 (1 H, ddd, *J* 7.3, 1.3, 1.2, ArH), 7.16 (1 H, dd, *J* 7.3, 7.2, ArH), 6.90 (1 H, ddd, *J* 7.2, 1.2, 1.0, ArH).

Ethyl 4-Aminobenzoate 31i. According to the general procedure 5 the title compound was obtained as an orange crystalline solid (92%) from ethyl 4-nitrobenzoate **30i**; mp 87–89 °C (lit.,[139] mp 88–90 °C); δ_H (300 MHz; $CDCl_3$) 7.86 (2 H, d, *J* 8.8, ArH), 6.64 (2 H, d, *J* 8.8, ArH), 4.31 (2 H, q, *J* 7.1, OCH_2Me), 4.03 (2 H, br s, NH_2), 1.36 (2 H, t, *J* 7.1, OCH_2*Me*).

4-Aminoacetophenone 31j. According to the general procedure 5 the title compound was obtained as a colourless crystalline solid (83%) from 4-nitroacetophenone **30j**; mp 104–105 °C (lit.,[140] mp 104–106 °C); δ_H (300 MHz; $CDCl_3$) 7.80 (2 H, m, ArH), 6.64 (2 H, m, ArH), 4.24 (2 H, br s, NH_2), 2.50 (3 H, s, COMe).

4-Aminoacetanilide 31k. According to the general procedure 5 the title compound was obtained as a colourless crystalline solid (95%) from 4-nitroacetanilide **30k**; mp 161–163 °C (from water) (lit.,[141] mp 162 °C from water); δ_H (400 MHz; d_4-MeOH) 7.21 (2 H, 2 dd, *J* 8.7, 2.0, 8.7, 2.2, ArH), 6.68 (2 H, 2 dd, *J* 8.7, 2.0, 8.7, 2.2, ArH), 4.53 (2 H, br s, NH_2), 2.06 (3 H, s, NHCO*Me*).

The title compound was also formed in 100% yield from 4-nitroacetanilide **30k** with indium and acetic acid (6 equivalents) in THF (spectroscopic data identical).

4-(Methoxymethyl)aniline 31l. According to the general procedure 5 the title compound was obtained as a yellow oil (84%) from 4-(methoxymethyl)nitrobenzene **30l** (for preparation see below); bp 115–120 °C, 3 mmHg (lit.,[142] bp 131–132 °C, 11 mmHg); δ_H (300 MHz; $CDCl_3$) 7.13 (2 H, d, *J* 8.4, ArH), 6.66 (2 H, d, *J* 8.4, ArH), 4.34 (2 H, s, ArCH_2O), 3.50 (2 H, br s, NH_2), 3.34 (3 H, s, OMe).

2,6-Diaminotoluene 31m. 2,6-Dinitrotoluene **30m** (0.208 g, 1.14 mmol) was dissolved in THF (10 ml) with indium powder (−100 mesh, 1.0 g) and acetic acid (0.377 g, 0.36ml, 6.28 mmol) under nitrogen. The mixture was heated under reflux for 3 d.

The cooled reaction mixture was filtered through Celite® with water (50 ml). The filtrate was extracted with ethyl acetate (3 × 15 ml). Combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to yield the title compound **31m** as a colourless solid (0.125 g, 90%); mp 103–104 °C (lit.,[143] 106 °C); δ_H (300 MHz; $CHCl_3$) 6.84 (1 H, t, *J* 8.3, 4-ArH), 6.22 (2 H, d, *J* 8.3, 3&5-ArH), 5.06 (4 H, br s, NH_2), 1.98 (3 H, s, ArMe).

6-Aminoquinoline 33. According to the general procedure 5 the title compound was obtained as a colourless solid (82%) from 6-nitroquinoline **32**; mp 117–120 °C (lit.,[144] mp 116–118 °C); δ_H (300 MHz; $CDCl_3$) 8.65 (1 H, dd, *J* 4.3, 1.7, 2-ArH), 7.91 (1 H, d, *J* 9.0, 8-ArH), 7.89 (1 H, d, *J* 8.3, 4-ArH), 7.26 (1 H, dd, *J* 8.3, 4.3, 3-ArH), 7.15 (1 H, dd, *J* 9.0, 2.6, 7-ArH), 6.90 (1 H, d, *J* 2.6, 5-ArH), 3.95 (2 H, br s, NH_2).

5-Aminoisoquinoline 35. According to the general procedure 5 the title compound was obtained as a pale orange solid (99%) from 5-nitroisoquinoline **33**; mp 125–127 °C (lit.,[145] mp 128 °C); δ_H (300 MHz; $CDCl_3$) 9.18 (1 H, d, *J* 1.0, 1-ArH), 8.48 (1 H, dd, *J* 6.0, 1.0, 3-ArH), 7.57 (1 H, d, *J* 6.0, 4-ArH), 7.41 (2 H, 2d, *J* 4.2 and 4.1, 6&8-ArH), 6.95 (1 H, dd, *J* 4.2, 4.1, 7-ArH), 4.25 (2 H, br s, NH_2).

Ethyl 4-amino-5-methoxy-1,2-dimethylindole-3-carboxylate 37a. According to the general procedure 5 the title compound was obtained as a yellow crystalline solid (33%) from ethyl 5-methoxy-1,2-dimethyl-4-nitroindole-3-carboxylate **36a**;[146] δ_H (300 MHz; $CDCl_3$) 6.88 (1 H, d, *J* 8.6, indole ring), 6.52 (1 H, d, *J* 8.6, indole ring), 5.78 (2 H, br s, NH_2), 4.36 (2 H, q, *J* 7.1, OCH_2Me), 3.87 (3 H, s, OMe), 3.58 (3 H, s, NMe), 2.64 (3 H, s, indole-Me), 1.41 (3 H, t, *J* 7.1, OCH_2Me) (as authentic sample[146]).

Ethyl 4-amino-2-(biphenyl-4-yl)-5-methoxy-1-methylindole-3-carboxylate 37b. According to the general procedure 5 the title compound was obtained as a yellow crystalline solid (45%) from ethyl 2-(biphenyl-4-yl)-5-methoxy-1-methyl-4-nitroindole-3-carboxylate **36b**;[147] δ_H (300 MHz; $CDCl_3$) 7.68 (4 H, m, biPh), 7.54 (2 H, m, biPh), 7.50 (3 H, m, biPh), 7.02 (1 H, d, *J* 8.5, indole ring), 6.44 (1 H, d, *J* 8.5, indole ring), 5.89 (2 H, br s, NH_2), 3.99 (2 H, q, *J* 7.2, OCH_2Me), 3.91 (3 H, s, NMe), 3.48 (3 H, s, OMe), 0.81 (3 H, t, *J* 7.2, OCH_2Me) (as authentic sample[147]).

Cyclohexylamine 39a. According to the general procedure 5 the title compound **39a** was obtained as a clear oil (100%) from nitrocyclohexane **38a**; δ_H (300 MHz; $CDCl_3$) 2.61 (1 H, m, $CHNH_2$), 1.83–1.61 (6 H, m, CH_2 and NH_2), 1.28–1.00 (6 H, m, CH_2) (as authentic sample).

***n*-Hexylamine 39b.** According to the general procedure 5 the title compound **39b** was obtained as a clear oil (82%) from 1-nitrohexane **38b**; δ_H (300 MHz; $CDCl_3$) 2.61 (2 H, m, CH_2NH_2), 1.45 (2 H, m, $CH_2CH_2NH_2$), 1.40 (6 H, m, $CH_2CH_2CH_2$), 1.07 (2 H, br s, NH_2), 0.90 (3 H, t, *J* 7.2, Me) (as authentic sample).

1-Amino-3-methylbutan-2-ol 39c. According to general procedure 5 the title compound was obtained as a clear oil (59%) from 3-methyl-1-nitrobutan-2-ol **38c**; bp 125–130 °C, 60 mmHg; δ_H (300 MHz; $CDCl_3$) 5.01 (3 H, br, NH_2 & OH), 3.48 (1 H, ddd, *J* 7.8, 6.3, 4.7, CHOH), 2.87 (1 H, dd, *J* 11.6, 4.7, *syn*-CH(OH)$CHHNH_2$), 2.64 (1 H, dd, *J* 11.6, 7.8, *anti*-CH(OH)$CHHNH_2$), 1.68 (1 H, septet-d, *J* 6.9, 6.3, $CHMe_2$), 0.91 (3 H, d, *J* 6.9, Me), 0.97 (3 H, d, *J* 6.9, Me) (*cf.* lit.[148]).

The title compound was also obtained (84%) from 3-methyl-1-nitrobutan-2-ol **38c** by heating at reflux with indium (6 equivalents) and acetic acid (6 equivalents) in THF for 50 h.

Preparation of 4-nitrobenzyl derivatives

4-(Methoxymethyl)nitrobenzene 30l. Dimethyl sulfate (0.75 ml, ~1.00 g, 7.9 mmol) was added dropwise after 30 min to a stirred solution of 4-nitrobenzyl alcohol (0.53 g, 3.4 mmol) and potassium carbonate (0.73 g, 5.3 mmol) in acetone (20 ml) at 0 °C under an atmosphere of nitrogen until the orange colour no longer persisted. The mixture was allowed to stir to room temperature over 18 h, then diluted with aqueous sodium hydroxide solution (4 M; 20 ml) and extracted with dichloromethane (2 × 20 ml). Combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*, then purified by flash chromatography (silica, 20% ethyl acetate in light petroleum) to give the title compound **30l** as a yellow solid (0.42 g, 74%); mp 25–26 °C (lit.,[149] 23–24 °C); ν_{max} (neat)/cm^{-1} 2929, 2824 (OMe), 1603, 1523, 1347 (NO_2), 1103, 847 (ArH); δ_H (300 MHz; $CDCl_3$) 8.21 (2 H, dd, *J* 8.6, 1.9, ArH), 7.50 (2 H, d, *J* 8.6, ArH), 4.56 (2 H, s, $ArCH_2O$), 3.45 (3 H, s, OMe); δ_C (75 MHz; $CDCl_3$) 145.9 (C), 131.5 (C), 127.7 (CH), 123.6 (CH), 73.4 (CH_2), 58.7 (Me).

4-Nitrobenzyl acetate 41b. Acetyl chloride (0.52 ml, ~0.58 g, 7.4 mmol) was added to a stirred solution of 4-nitrobenzyl alcohol **41a** (0.750 g, 4.90 mmol) and triethylamine (1.02 ml, ~0.74 g, 7.4 mmol) in dichloromethane (30 ml) at room temperature. The mixture was stirred for 3 h, then washed with water (20 ml), dried ($MgSO_4$) and concentrated *in vacuo* to give the title compound **41b** as a yellow solid (0.96 g, 100%); mp 76–77 °C (from ether) (lit.,[150] mp 76–77 °C); δ_H (300 MHz; $CDCl_3$) 8.22 (2 H, m, 3&5-ArH), 7.52 (2 H, m, 2&4-ArH), 5.20 (2 H, s, CH_2O), 2.15 (3 H, s, MeCO).

4-(*N*,*N*-Dimethylamino)benzyl alcohol 42c. Sodium borohydride (0.74 g, 19.5 mmol) was added in portions to a stirred solution of 4-(*N*,*N*-dimethylamino)benzaldehyde (2.43 g, 16.3 mmol) in methanol (30 ml) at 0 °C. After 10 min, water (20 ml) was added and the resulting solution extracted with ethyl acetate (3 × 15 ml). Combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to give the title compound **42c** as a colourless oil (2.05 g, 83%); δ_H (300 MHz; $CDCl_3$) 7.26 (2 H, d, *J* 8.8, 3&5-ArH), 6.74 (2 H, d, *J* 8.8, 2&4-ArH), 4.58 (2 H, s, CH_2O), 2.96 (6 H, s, NMe_2), 1.65 (1 H, br s, OH) (*cf.* lit.[151]).

***O*-(4-Nitrobenzyl)-2-phenylethanol 43a.** Silver(I) oxide (1.04 g, 4.5 mmol) was added to a solution of 2-phenylethanol (0.54 g, 4.5 mmol) and 4-nitrobenzyl bromide (0.96 g, 4.4 mmol) in dichloromethane (10 ml). The mixture was heated at reflux under nitrogen for 5 d then cooled and filtered through Celite®, washed successively with hydrochloric acid (2 M; 15 ml), sodium hydroxide solution (4 M; 15 ml) and water (10 ml), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by flash column chromatography (silica, light petroleum–dichloromethane, 2 : 3) to give the *title compound* **43a** as a colourless oil (0.74 g, 65%) (Found: M^+, 257.1052. $C_{15}H_{15}NO_3$ requires 257.1052); ν_{max} (neat)/cm^{-1} 3034, 2917, 2853, 1598, 1516 (NO_2), 1340 (NO_2), 1103, 857, 844, 736, 698; δ_H (300 MHz; $CDCl_3$) 8.20 (2 H, d, *J* 8.2, 3&5-Ar*H*NO_2), 7.44 (2 H, d, *J* 8.2, 2&6-Ar*H*NO_2), 7.36–7.25 (5 H, m, Ph), 4.64 (2 H, s, OCH_2Ar), 3.77 (2 H, t, *J* 7.1, CH_2CH_2O), 2.99 (2 H, t, *J* 7.1, CH_2CH_2O); δ_C (75 MHz; $CDCl_3$) 147.6 (C), 146.2 (C), 138.7 (C), 129.0 (CH), 128.4 (CH), 127.6 (CH), 126.4 (CH), 123.6 (CH), 71.9 (OCH_2), 71.7 (OCH_2), 36.4 (CH_2); *m*/*z* (EI) 257 (M^+, 22%), 136 (31), 106 (33), 91 (100), 78 (28), 65 (11).

***O*-(4-Nitrobenzyl)-2-phenoxyethanol 43b.** Silver(I) oxide (0.600 g, 2.59 mmol) was added to a solution of 2-phenoxyethanol (0.350 g, 2.54 mmol) and 4-nitrobenzyl bromide (0.549 g, 2.54 mmol) in dichloromethane (10 ml). The mixture was heated at reflux under nitrogen for 6 d then cooled and filtered

through Celite®, washed successively with hydrochloric acid (1 M; 20 ml), sodium hydroxide solution (1 M; 20 ml) and water (10 ml), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by flash column chromatography (silica, light petroleum–dichloromethane, 1 : 1) to give the *title compound* **43b** as a colourless oil (0.483 g, 70%) (Found: M^+, 273.0995. $C_{15}H_{15}NO_4$ requires 273.1001); ν_{max} (neat)/cm^{-1} 3070, 2918, 2860, 1595, 1520 (NO_2), 1490, 1345 (NO_2), 1241, 1106, 858, 754, 688; δ_H (300 MHz; $CDCl_3$) 8.22 (2 H, d, *J* 8.5, 3&5-Ar*H*NO_2), 7.54 (2 H, d, *J* 8.5, 2&6-Ar*H*NO_2), 7.31 (2 H, m, 3&5-PhH), 6.96 (3 H, m, 2, 4&6-PhH), 4.76 (2 H, s, OCH_2Ar), 4.21 (2 H, m, PhOCH_2), 3.91 (2 H, m, PhOCH_2CH_2); δ_C (75 MHz; $CDCl_3$) 158.6 (C), 147.7 (C), 145.8 (C), 129.5 (CH), 127.7 (CH), 123.7 (CH), 121.1 (CH), 114.6 (CH), 72.1 (CH_2), 69.4 (CH_2), 67.3 (CH_2); *m*/*z* (EI) 273 (M^+, 69%), 229 (6), 151 (12), 136 (100), 120 (18), 106 (55), 94 (57), 90 (53), 77 (82), 65 (38), 51 (34).

***O*-(4-Nitrobenzyl)-2-benzyloxyethanol 43c.** Silver(I) oxide (0.870 g, 3.75 mmol) was added to a solution of 2-benzyloxyethanol (0.566 g, 3.72 mmol) and 4-nitrobenzyl bromide (0.808 g, 3.74 mmol) in dichloromethane (10 ml). The mixture was heated at reflux under nitrogen for 5 d. The cooled reaction mixture was filtered through Celite® and washed with hydrochloric acid (1 M; 20 ml), sodium hydroxide solution (2 M; 20 ml) and water (10 ml) then dried ($MgSO_4$), concentrated *in vacuo* and purified by flash chromatography (silica, dichloromethane–light petroleum, 2 : 1) to give the *title compound* **43c** as a colourless oil (0.893 g, 84%) (Found: M^+, 287.1155. $C_{16}H_{17}NO_4$ requires 287.1157); ν_{max} (neat)/cm^{-1} 3031, 2857, 1613, 1520 (NO_2), 1448, 1337 (NO_2), 1100, 838, 736, 698; δ_H (300 MHz; $CDCl_3$) 8.21 (2 H, d, *J* 8.8, 3&5-Ar*H*NO_2), 7.53 (2 H, d, *J* 8.8, 2&6-Ar*H*NO_2), 7.37–7.30 (5 H, m, PhH), 4.69 (2 H, s, OCH_2Ar), 4.60 (2 H, s, OCH_2Ph), 3.76–3.67 (4 H, m, OCH_2CH_2O); δ_C (100 MHz; $CDCl_3$) 147.4 (C), 146.1 (C), 138.1 (C), 128.4 (CH), 127.71 (2 × CH), 127.67 (CH), 123.6 (CH), 73.4 (CH_2), 72.0 (CH_2), 70.3 (CH_2), 69.5 (CH_2); *m*/*z* (EI) 287 (M^+, 1%), 196 (20), 151 (35), 136 (10), 107 (40), 91 (100), 78 (13), 65 (14), 51 (8).

2-(4-Nitrobenzyloxy)ethyl benzoate 43d. (a) Potassium hydroxide (0.290 g, 5.18 mmol) was added to a solution of 4-nitrobenzyl bromide (1.024 g, 4.74 mmol) in ethylene glycol (10 ml), and the resulting mixture heated at 80 °C for 20 h. The cooled reaction mixture was diluted with water (50 ml) and extracted with dichloromethane (2 × 30 ml). Combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to give *2-(4-nitrobenzyloxy)ethanol* as a colourless oil (0.856 g, 92%); δ_H (300 MHz; $CDCl_3$) 8.21 (2 H, m, 2&6-ArHNO_2), 7.52 (2 H, m, 3&5-ArHNO_2), 4.69 (2 H, s, ArCH_2), 3.83 (2 H, m, CH_2CH_2OH), 3.67 (2 H, m, C$H_2$$CH_2$OH), 2.01 (1 H, br s, OH) (*cf*. lit.[152]).

(b) Benzoyl chloride (0.125 ml, ~0.15 g, 1.1 mmol) was added to a stirred solution of 2-(4-nitrobenzyloxy)ethanol (0.211 g, 1.07 mmol) and triethylamine (0.15 ml, ~0.11 g, 1.1 mmol) in dichloromethane (10 ml) at room temperature. After 18 h water (50 ml) was added and the mixture extracted with further dichloromethane (2 × 15 ml). Combined organic extracts were dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash column chromatography (silica, light petroleum–dichloromethane, 1 : 2) to give the *title compound* **43d** as colourless needles (0.32 g, 99%); mp 74–75 °C (Found: C, 63.6; H, 4.9; N, 4.5. $C_{16}H_{15}NO_5$ requires C, 63.8; H, 5.0; N, 4.6%); ν_{max} (KBr)/cm^{-1} 2922, 2875, 2845 (C–H), 1717 (ester), 1509 (NO_2), 1442, 1345 (NO_2), 1273, 1100 (C=O), 850, 733, 720; δ_H (300 MHz; $CDCl_3$); 8.18 (2 H, m, 2&6-ArHNO_2), 8.06 (2 H, m, 2&6-ArHCOO), 7.59–7.44 (5 H, m, ArH), 4.71 (2 H, s, ArCH_2), 4.55 (2 H, m, COOCH_2), 3.88 (2 H, m, COOCH_2CH_2); δ_C (75 MHz; $CDCl_3$) 166.5 (C), 147.4 (C), 145.7 (C), 133.2 (CH), 129.9 (C), 129.7 (CH), 128.4 (CH), 127.7 (CH), 123.7 (CH), 71.9 (CH_2), 68.8 (CH_2), 63.9 (CH_2); *m*/*z* (CI) 302 (MH^+, 15%), 167 (23), 108 (21), 106 (100), 58 (94).

***O*-(*tert*-Butyldimethylsilyl)-2-(4-nitrobenzyloxy)ethanol 43e.** *tert*-Butyldimethylsilyl trifluoromethanesulfonate (1.73 ml, ~1.99 g, 7.5 mmol) was added dropwise to a stirred solution of 2-(4-nitrobenzyloxy)ethanol (0.74 g, 3.8 mmol) in pyridine (20 ml) under nitrogen at ~−35 °C. The mixture was stirred for 4 h then the pyridine was removed *in vacuo* and the residue triturated with ether (4 × 15 ml). The combined ethereal layers were washed with water (20 ml) and dried ($MgSO_4$) then concentrated *in vacuo*. The residue was purified by flash column chromatography (silica, light petroleum–dichloromethane, 1 : 1 (the column was prepared with the solvent system containing 0.001% triethylamine)) to give the *title compound* **43e** as a colourless oil (1.07 g, 92%) (Found: MH^+, 312.1628. $C_{15}H_{26}NO_4Si$ requires 312.1631); ν_{max} (neat)/cm^{-1} 2954, 2926, 2847 (C–H), 1516, 1340 (NO_2), 1104, 952, 836 and 776 (ArH); δ_H (300 MHz; $CDCl_3$) 8.20 (2 H, m, 3&5-ArHNO_2), 7.52 (2 H, m, 2&6-ArHNO_2), 4.68 (2 H, s, ArCH_2), 3.82 (2 H, m, C$H_2$$CH_2$OSi), 3.61 (2 H, m, CH_2CH_2OSi), 0.91 (9 H, s, Si^{t}Bu), 0.08 (6 H, s, $SiMe_2$); δ_C (75 MHz; $CDCl_3$) 147.5 (C), 146.4 (C), 127.6 (CH), 123.6 (CH), 72.4 (CH_2), 72.0 (CH_2), 62.8 (CH_2), 25.9 (Me_3), 18.4 (*C*Me_3), −5.3 (SiMe); *m*/*z* (CI) 312 (MH^+, 53%), 254 (13), 177 (40), 106 (100).

L-*O*-(4-Nitrobenzyl)menthol 43f. Silver(I) oxide (0.624 g, 2.69 mmol) was added to a solution of L-menthol (0.420 g, 2.69 mmol) and 4-nitrobenzyl bromide (0.580 g, 2.69 mmol) in dichloromethane (15 ml). The mixture was heated at reflux under nitrogen for 7 d then cooled and filtered through Celite®, washed successively with 1 M hydrochloric acid (20 ml), 1 M sodium hydroxide solution (20 ml) and water (10 ml), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by flash column chromatography (silica, light petroleum–dichloromethane, 2 : 1) to give the *title compound* **43f** as a colourless solid (0.453 g, 58%); mp 60–61 °C (from light petroleum); $[a]_D^{25}$ −80.0 (*c* 1.0 in ethanol) (Found: C, 70.0; H, 8.9; N, 4.6. $C_{17}H_{25}NO_3$ requires C, 70.1; H, 8.6; N, 4.8%) (Found: M^+, 291.1830. $C_{17}H_{25}NO_3$ requires 291.1834); ν_{max} (KBr)/cm^{-1} 2955, 2920, 2858, 1598, 1521 (NO_2), 1455, 1332 (NO_2), 1112, 835, 737, 570; δ_H (400 MHz; $CDCl_3$) 8.22 (2 H, d, *J* 8.5, 3&5-Ar*H*NO_2), 7.53 (2 H, d, *J* 8.5, 2&6-Ar*H*NO_2), 4.76 (1 H, d, *J* 13.0, OCH_2), 4.49 (1 H, d, *J* 13.0, OCH_2), 3.23 (1 H, td, *J* 10.4, 4.1, OCH), 2.30 (1 H, m, C*H*Me), 2.17 (1 H, m, CH_2CHOR), 1.67 (1 H, m, C*H*HCH_2CHMe), 1.65 (1 H, m, CH_2-C*H*HCHMe), 1.38 (1 H, m, C*H*Me_2), 1.30 (1 H, m, C*H*^{i}Pr), 1.03 (1 H, m, CH_2CH*H*CHMe), 0.95 (3 H, d, *J* 6.7, CH*Me*$_2$), 0.92 (3 H, d, *J* 6.7, CH*Me*$_2$), 0.90 (1 H, m, CH_2CHOR), 0.89 (1 H, m, CH*H*CH_2CHMe), 0.76 (3 H, d, *J* 7.0, CH*Me*); δ_C (100 MHz; $CDCl_3$) 147.2 (C), 147.0 (C), 127.8 (CH), 123.5 (CH), 79.7 (OCH), 69.1 (OCH_2), 48.3 (CH), 40.3 (CH_2), 34.5 (CH_2), 31.6 (CH), 25.7 (CH), 23.3 (CH_2), 22.3 (Me), 20.9 (Me), 16.2 (Me); *m*/*z* (EI) 291 (M^+, 5%), 261 (2), 206 (67), 138 (100), 136 (92), 123 (19), 106 (38), 95 (48), 81 (90), 69 (78).

***O*-(4-Nitrobenzyl)-4-methoxyphenol 43g.** Potassium hydroxide (0.230 g, 4.11 mmol) was added to a stirred solution of 4-methoxyphenol (0.508 g, 4.10 mmol) in ethanol (20 ml) at room temperature. After 1 h, 4-nitrobenzyl bromide (0.886 g, 4.10 mmol) was added and the mixture stirred and heated under reflux. After 72 h the cooled reaction mixture was diluted with water (30 ml) and extracted with dichloromethane (3 × 15 ml). Combined organic layers were dried ($MgSO_4$), concentrated *in vacuo* and purified by flash chromatography (silica, dichloromethane–light petroleum, 1 : 1) to give the title compound **43g** (1.021 g, 96%) as pale yellow crystals, mp 85–87 °C (lit.,[153] mp 88 °C); δ_H (300 MHz; $CDCl_3$), 8.24 (2 H, m, 3&5-Ar*H*NO_2), 7.60 (2 H, m, 2&6-Ar*H*NO_2), 6.92–6.83 (4 H, m, Ar*H*OMe), 5.13 (2 H, s, OCH_2), 3.78 (3 H, s, OMe).

3-(4-Nitrobenzyloxy)benzaldehyde 43i. Diethyl azodicarboxylate (0.63 ml, ~0.70 g, 4.0 mmol) was added quickly to a stirred solution of 3-hydroxybenzaldehyde (0.407 g, 3.34 mmol), 4-nitrobenzyl alcohol (0.507 g, 3.31 mmol) and triphenylphosphine (0.874 g, 3.34 mmol) in THF (15 ml) at room temperature. After 2 d the reaction mixture was concentrated *in vacuo* and the residue taken up in ethyl acetate (20 ml) and washed successively with sodium hydroxide solution (1 M; 50 ml), hydrochloric acid (1 M; 20 ml), water (15 ml) and brine (15 ml), dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by flash column chromatography (silica, dichloromethane) to give the *title compound* **43i** as a colourless solid (0.468 g, 55%); mp 109–110 °C (Found: C, 65.0; H, 4.2; N, 5.2. $C_{14}H_{11}NO_4$ requires C, 65.4; H, 4.3; N, 5.4%) (Found: M^+, 257.0690. $C_{14}H_{11}NO_4$ requires 257.0688); ν_{max} (KBr)/cm^{-1} 2920, 2835, 2742 (CHO), 1687 (CHO), 1590, 1513 (NO_2), 1450, 1345 (NO_2), 1260, 1150, 1045, 863, 836, 783, 760, 675; δ_H (300 MHz; $CDCl_3$) 10.0 (1 H, s, CHO), 8.29 (2 H, m, 3&5-Ar*H*NO_2), 7.65 (2 H, m, 2&6-Ar*H*NO_2), 7.52 (3 H, m, Ar*H*CHO), 7.29 (1 H, m, Ar*H*CHO), 5.26 (2 H, s, OCH_2); δ_C (75 MHz; $CDCl_3$) 191.9 (CHO), 158.7 (C), 147.7 (C), 143.7 (C), 137.9 (C), 130.4 (CH), 127.7 (CH), 124.6 (CH), 123.9 (CH), 122.2 (CH), 112.7 (CH), 68.8 (CH_2); *m*/*z* (EI) 257 (M^+, 32%), 229 (2), 136 (100), 121 (8), 106 (35), 90 (25), 89 (23), 78 (60), 63 (18).

***O*-(4-Nitrobenzyl)-2,3,5-trimethylphenol 43j.** Diethyl diazodicarboxylate (0.65 ml, ~0.72 g, 4.1 mmol) was added quickly to a stirred solution of 2,3,5-trimethylphenol (0.435 g, 3.20 mmol), 4-nitrobenzyl alcohol (0.487 g, 3.18 mmol) and triphenylphosphine (0.838 g, 3.20 mmol) in THF (20 ml) at room temperature. Stirring was continued for 3 h then the solution was concentrated *in vacuo*. The residue was taken up in ethyl acetate (30 ml) and washed successively with sodium hydroxide solution (1 M; 20 ml), hydrochloric acid (1 M; 20 ml), water (10 ml), and brine (10 ml), dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash column chromatography (silica, dichloromethane–light petroleum, 1 : 2) to give the *title compound* **43j** as a colourless solid (0.833 g, 96%); mp 128–129 °C (Found: C, 70.7; H, 6.4; N, 5.0. $C_{16}H_{17}NO_3$ requires C, 70.8; H, 6.3; N, 5.2%) (Found: M^+, 271.1219. $C_{16}H_{17}NO_3$ requires 271.1208); ν_{max} (KBr)/cm^{-1} 2976, 2919, 2843, 1603, 1573, 1516 (NO_2), 1342 (NO_2), 1142, 1107, 830, 727; δ_H (300 MHz; $CDCl_3$) 8.26 (2 H, d, *J* 8.2, 3&5-Ar*H*NO_2), 7.63 (2 H, d, *J* 8.2, 2&6-Ar*H*NO_2), 6.68 (1 H, s, ArH), 6.56 (1 H, s, ArH), 5.16 (2 H, s, OCH_2), 2.28 (3 H, s, Me), 2.27 (3 H, s, Me), 2.20 (3 H, s, Me); δ_C (100 MHz; $CDCl_3$) 156.0 (C), 147.5 (C), 145.2 (C), 138.0 (C), 135.6 (C), 127.3 (CH), 123.84 (CH), 123.77 (CH), 122.3 (C), 110.2 (CH), 68.9 (CH_2), 21.3 (Me), 20.0 (Me), 11.5 (Me); *m*/*z* (EI) 271 (M^+, 76%), 256 (12), 225 (7), 137 (61), 135 (100), 106 (31), 91 (40).

***O*-(4-Nitrobenzyl)-2,4,5-trichlorophenol 43k.** Potassium hydroxide (0.200 g, 3.57 mmol) was added to a stirred solution of 2,4,5-trichlorophenol (0.500 g, 2.53 mmol) and 4-nitrobenzyl chloride (0.434 g, 2.53 mmol) in ethanol (15 ml). The mixture was heated under reflux. After 30 min the reaction mixture was cooled and diluted with water (50 ml) then extracted with dichloromethane (3 × 15 ml). Combined organic layers were dried ($MgSO_4$), concentrated *in vacuo*, and purified by flash chromatography (silica, dichloromethane–light petroleum, 1 : 2) to give the title compound **43k** as a colourless solid (0.316 g, 38%); mp 139–142 °C (lit.,[154] mp 145–146 °C); δ_H (300 MHz; $CDCl_3$) 8.29 (2 H, d, *J* 8.8, 3&5-Ar*H*NO_2), 7.66 (2 H, d, *J* 8.8, 2&6-Ar*H*NO_2), 7.52 (1 H, s, ArH), 7.05 (1 H, s, ArH), 5.23 (2 H, s, OCH_2).

6-(4-Nitrobenzyloxy)quinoline 43l. 4-Nitrobenzyl bromide (0.458 g, 2.12 mmol) was added after 30 min at room temperature to a stirred solution of 6-hydroxyquinoline (0.308 g, 2.11 mmol) and potassium hydroxide (0.130 g, 2.32 mmol) in ethanol (20 ml) and the mixture heated under reflux. After 2 d the cooled reaction mixture was diluted with water (30 ml) and extracted with ethyl acetate (3 × 15 ml). Combined organic layers were dried ($MgSO_4$), concentrated *in vacuo*, then purified by flash chromatography (silica, ethyl acetate–light petroleum, 3 : 1) to give the *title compound* **43l** as a colourless solid (0.457 g, 77%); mp 159–160 °C (Found: C, 68.5; H, 4.1; N, 9.8. $C_{16}H_{12}N_2O_3$ requires C, 68.6; H, 4.3; N, 10.0%) (Found: M^+, 280.0850. $C_{16}H_{12}N_2O_3$ requires 280.0848); ν_{max} (KBr)/cm^{-1} 3013, 2900, 2837, 1625, 1503, 1335, 1230, 1045, 856, 835, 738, 620, 550, 460; δ_H (300 MHz; $CDCl_3$) 8.81 (1 H, dd, *J* 4.4, 1.7, 2-quinH), 8.29 (2 H, m, 3&5-Ar*H*NO_2), 8.06 (1 H, d, *J* 9.3, 8-quinH), 8.05 (1 H, dd, *J* 8.2, 1.7, 4-quinH), 7.68 (2 H, m, 2&6-Ar*H*NO_2), 7.48 (1 H, dd, *J* 9.3, 2.9, 7-quinH), 7.38 (1 H, dd, *J* 8.2, 4.4, 3-quinH), 7.13 (1 H, d, *J* 2.9, 5-quinH), 5.32 (2 H, s, OCH_2); δ_C (100 MHz; $CDCl_3$) 156.2 (C), 148.5 (CH), 146.9 (C), 144.7 (C), 143.9 (C), 134.8 (CH), 131.4 (CH), 129.1 (C), 127.7 (CH), 123.9 (CH), 122.2 (CH), 121.6 (CH), 106.7 (CH), 68.9 (CH_2); *m*/*z* (EI) 280 (M^+, 20%), 144 (61), 135 (100), 91 (30).

4-Nitrobenzyl 4-chlorobenzoate 43m. 4-*N*,*N*-Dimethylaminopyridine (DMAP, 0.75 g, 6.1 mmol) was added to a stirred solution of 4-nitrobenzyl alcohol (0.93 g, 6.1 mmol), 4-chlorobenzoic acid (0.95 g, 6.1 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI, 1.170 g, 6.1 mmol) in dichloromethane (20 ml). After 24 h the solution was washed with water (30 ml) and brine (15 ml), dried ($MgSO_4$) and concentrated *in vacuo.* The crude material was passed through a pad of silica with dichloromethane and concentrated *in vacuo* to yield the *title compound* **43m** as colourless crystals (1.62 g, 91%); mp 130–132 °C (Found: C, 57.6; H, 3.4; N, 4.7. $C_{14}H_{10}ClNO_4$ requires C, 57.6; H, 3.5; N, 4.8%) (Found: M^+, 291.0280. $C_{14}H_{10}ClNO_4$ requires 291.0298); ν_{max} (KBr)/cm^{-1} 3088, 3047, 2935, 2838, 1726 (C=O), 1588, 1516 (NO_2), 1338 (NO_2), 1255, 754; δ_H (300 MHz; $CDCl_3$) 8.26 (2 H, d, *J* 9.1, 3&5-Ar*H*NO_2), 8.02 (2 H, d, *J* 9.1, 3&5-Ar*H*Cl), 7.60 (2 H, d, *J* 9.1, 2&6-Ar*H*NO_2), 7.45 (2 H, d, *J* 9.1, 2&6-Ar*H*Cl), 5.45 (2 H, s, OCH_2Ar); δ_C (75 MHz; $CDCl_3$) 165.3 (C), 143.0 (C), 140.0 (C), 131.1 (CH), 129.0 (CH), 128.4 (CH), 127.9 (C), 123.9 (CH), 65.4 (CH_2); *m*/*z* (EI) 291 (M^+, 8%), 256 (5), 152 (3), 141 (30), 139 (92), 111 (16), 91 (22).

***N*-Benzyloxycarbonyl-D,L-alanine 4-nitrobenzyl ester 43n.** 4-Dimethylaminopyridine (0.098 g, 0.80 mmol) was added to a stirred solution of *N*-benzyloxycarbonyl-DL-alanine (0.176 g, 0.79 mmol), 4-nitrobenzyl alcohol (0.121 g, 0.79 mmol) and 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (EDCI, 0.156 g, 0.81 mmol) in dichloromethane (20 ml). After stirring at room temperature for 20 h the mixture was washed with hydrochloric acid (1 M; 20 ml), water (30 ml) and brine (20 ml), dried ($MgSO_4$), then concentrated *in vacuo* to give the title compound **43n** as a colourless solid (0.282 g, 100%); mp 78–79 °C (from ethyl acetate–light petroleum) (lit.,[155] mp 78–80 °C); δ_H (300 MHz; $CDCl_3$) 8.22 (2 H, d, *J* 8.7, 3&5-Ar*H*NO_2), 7.53 (2 H, d, *J* 8.7, 2&6-Ar*H*NO_2), 7.35 (5 H, m, Ph), 5.27 (2 H, s, OCH_2Ar), 5.11 (2 H, s, OCH_2Ph), 4.47 (1 H, m, C*H*Me), 1.65 (1 H, br s, NH), 1.45 (3 H, d, *J* 7.2, CH*Me*).

***N*-Acetyl-*S*-(4-nitrobenzyl)-L-cysteine ethyl ester 44.** (a) A solution of 4-nitrobenzyl chloride (0.775 g, 4.51 mmol) in 1,4-dioxane (10 ml) was added in 2 ml portions over 30 min to a vigorously stirred solution of *N*-acetyl-L-cysteine (0.735 g, 4.51 mmol) in sodium hydroxide solution (2 M; 2.25 ml) at 0 °C. The dioxane was removed *in vacuo* and the resulting solution diluted with water (50 ml), the pH adjusted to ~12 with 4 M sodium hydroxide solution and then extracted with ether (2 × 10 ml). The aqueous layer was acidified to pH ~ 2 with 2 M hydrochloric acid and extracted with dichloromethane (3 × 15 ml). Combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo* to give *N*-acetyl-*S*-(4-nitrobenzyl)-L-cysteine (0.518 g,

39%); mp 130–131 °C (lit.,[156] mp 132 °C); $[\alpha]_D^{23}$ −48.0 (*c* 1.0 in ethanol) (lit.,[156] $[\alpha]_D^{24}$ −53.8 (*c* 1.0 in ethanol)); δ_H (300 MHz; $CDCl_3$/d_6-DMSO) 8.22 (1 H, d, *J* 8.0, NH), 8.16 (2 H, m, 2&6-ArH), 7.58 (2 H, m, 3&5-ArH), 4.39 (1 H, ddd, *J* 8.3, 8.0, 5.2, C*H*CH_2S), 3.88 (2 H, s, ArCH_2), 3.33 (1 H, br s, COOH), 2.78 (1 H, dd, *J* 13.7, 5.2, *anti*-CHC*H*HS), 2.65 (1 H, dd, *J* 13.7, 8.3, *syn*-CHC*H*HS), 1.85 (3 H, s, MeCO).

(b) Thionyl chloride (0.21 ml, ~0.35 g, 2.9 mmol) was added to a stirred solution of *N*-acetyl-*S*-(4-nitrobenzyl)-L-cysteine (0.58 g, 1.95 mmol) in ethanol (20 ml). After 16 h the solvent was removed *in vacuo* and the residue was taken up in dichloromethane (50 ml) and washed with sodium hydroxide solution (2 M; 20 ml). The organic layer was dried ($MgSO_4$) and concentrated *in vacuo* to give the *title compound* **44** as a yellow solid (0.53 g, 83%); mp 87–88 °C; $[\alpha]_D^{22}$ −26.0 (*c* 1.04 in chloroform) (Found: C, 51.4; H, 5.4; N, 8.4. $C_{14}H_{18}N_2O_5S$ requires C, 51.5; H, 5.6; N, 8.6%); ν_{max} (KBr)/cm^{-1} 3335 (NH), 3005, 2930, 1770 (ester), 1655 (amide), 1510, 1350 (NO_2), 1020, 855, 800, 585; δ_H (300 MHz; $CDCl_3$) 8.18 (2 H, m, 2&6-ArH), 7.48 (2 H, m, 3&5-ArH), 6.28 (1 H, br d, *J* 7.3, NH), 4.80 (1 H, ddd, *J* 7.3, 5.7, 5.1, C*H*CH_2S), 4.22 (2 H, m, CH_2Me), 3.79 (2 H, s, CH_2Ar), 2.93 (1 H, dd, *J* 13.9, 5.1, *anti*-CHCH*H*S), 2.80 (1 H, dd, *J* 13.9, 5.7, *syn*-CHC*H*HS), 2.03 (3 H, s, MeCO), 1.27 (3 H, t, *J* 7.1, CH_2*Me*); δ_C (75 MHz; $CDCl_3$) 170.7 (CO), 169.9 (CO), 147.1 (C), 145.5 (C), 129.8 (CH), 123.9 (CH), 62.1 (CH_2), 51.6 (CH), 35.9 (CH_2), 33.7 (CH_2), 23.2 (Me), 14.2 (Me); *m*/*z* (CI) 327 (MH^+, 6%), 164 (11), 122 (17), 112 (23), 108 (65), 106 (100).

Ethyl 1-(4-nitrobenzyl)-5-hydroxy-2-methylindole-3-carboxylate 46. Ethyl acetoacetate (1.20 ml, ~1.24 g, 9.5 mmol), was added to a stirred mixture of 4-nitrobenzylamine hydrochloride (1.79 g, 9.5 mmol) and triethylamine (1.32 ml, ~0.96 g, 9.5 mmol) at room temperature. After the initial exothermic reaction had subsided (~1 h), the mixture was diluted with ether (40 ml) and after a further 30 min the resulting solution was washed with water (20 ml). The ether layer was dried ($MgSO_4$) and concentrated *in vacuo*. The resulting crude ethyl 3-(4-nitrobenzylamino)but-2-enoate (2.51 g, 9.5 mmol) was added to a solution of *p*-benzoquinone (1.03 g, 9.5 mmol) in nitromethane (10 ml) and allowed to stand at room temperature for 18 h. The solvent was removed under a stream of nitrogen and the residue recrystallised from ethyl acetate to give the title compound **46** as a yellow powder (0.81 g, 24%); mp 221–222 °C (from ethyl acetate) (lit.,[157] mp 222–224 °C); δ_H (300 MHz; $CDCl_3$/d_6-DMSO) 7.97 (1 H, s, OH), 7.20 (2 H, m, 3&5-ArHNO_2), 6.47 (1 H, d, *J* 2.4, 4-indoleH), 6.25 (2 H, m, 2&6-ArHNO_2), 6.22 (1 H, d, *J* 8.7, 7-indoleH), 5.67 (1 H, dd, *J* 8.7, 2.4, 6-indoleH), 4.63 (2 H, s, NCH_2Ar), 3.33 (2 H, q, *J* 7.1, CH_2Me), 1.68 (3 H, s, Me), 0.43 (3 H, t, *J* 7.1, CH_2*Me*).

Reduction of 4-nitrobenzyl derivatives

4-Methylaniline 40a. (a) The title compound was also obtained (72%) from 4-(methoxymethyl)nitrobenzene **30l** according to the general procedure 5 after a reaction time of 18 h (rather than 1–2 h).

(b) According to the general procedure 5 the title compound was obtained as a colourless crystalline solid (47%) from 4-nitrobenzyl alcohol **41a**; mp 41–42 °C (lit.,[158] mp 42 °C); δ_H (300 MHz; $CDCl_3$) 6.98 (2 H, d, *J* 7.8, ArH), 6.62 (2 H, d, *J* 7.8, ArH), 3.42 (2 H, br s, NH_2), 2.25 (3 H, s, ArMe).

(c) The title compound was also obtained (83%) from 4-(acetoxymethyl)nitrobenzene **41b** according to the general procedure 5.

(d) The title compound was also obtained (82%) from 4-aminobenzyl alcohol **42a** according to the general procedure 5.

4-Ethylaniline 40b. According to the general procedure 5 the title compound was obtained as a yellow oil (31%) from 1-(4-aminophenyl)ethanol **42b**; δ_H (300 MHz; $CDCl_3$) 7.02 (2 H, d, *J* 8.6, ArH), 6.64 (2 H, d, *J* 8.6, ArH), 3.48 (2 H, br s, NH_2), 2.56 (2 H, q, *J* 7.4, CH_2Me), 1.20 (3 H, t, *J* 7.4, CH_2*Me*) (*cf*. lit.[159]).

4-Methyl-*N*,*N*-dimethylaniline 40c. According to the general procedure 5 the title compound was obtained as a dark oil (53%) from 4-*N*,*N*-dimethylaminobenzyl alcohol **42c**; δ_H (300 MHz; $CDCl_3$) 7.07 (2 H, d, *J* 8.5, ArH), 6.71 (2 H, d, *J* 8.5, ArH), 2.91 (6 H, s, NMe_2), 2.27 (3 H, s, Ar*Me*) (*cf*. lit.[160]).

1,2-Bis-(4-aminophenyl)ethane. According to the general procedure 5 the title compound was obtained as a colourless solid (32%) from 4-nitrobenzyl chloride (also obtained was 4-methylaniline (46%), spectroscopic data as above); mp 133–134 °C (lit.,[161] mp 134 °C); δ_H (300 MHz; $CDCl_3$) 6.99 (4 H, d, *J* 8.3, ArH), 6.64 (4 H, d, *J* 8.3, ArH), 3.57 (4 H, br s, NH_2), 2.78 (4 H, s, CH_2).

2-Phenylethanol. According to the general procedure 6 the title compound was obtained as a colourless oil (87%) from *O*-(4-nitrobenzyl)-2-phenylethanol **43a**; δ_H (300 MHz; $CDCl_3$) 7.37–7.25 (5 H, m, PhH), 3.89 (2 H, t, *J* 6.6, OCH_2), 2.90 (2 H, t, *J* 6.6, PhCH_2), 1.62 (1 H, br s, OH)—(as original sample).

2-Phenoxyethanol. According to the general procedure 6 the title compound was obtained as a colourless oil (98%) from *O*-(4-nitrobenzyl)-2-phenoxyethanol **43b**; δ_H (300 MHz; $CDCl_3$) 7.32 (2 H, m, 3&5-ArH), 6.98 (3 H, m, 2, 4&6-ArH), 4.11 (2 H, m, CH_2OH), 3.99 (2 H, m, PhOCH_2), 2.24 (1 H, br s, OH)—(as original sample).

2-Benzyloxyethanol. According to the general procedure 6 the title compound was obtained as a colourless oil (100%) from *O*-(4-nitrobenzyl)-2-benzyloxyethanol **43c**; δ_H (300 MHz; $CDCl_3$) 7.42–7.28 (5 H, m, PhH), 4.57 (2 H, s, PhCH_2), 3.76 (2 H, t, *J* 4.1, CH_2OH), 3.60 (2 H, t, *J* 4.1, CH_2OBn), 2.23 (1 H, br s, OH)—(as original sample).

2-Hydroxyethyl benzoate. According to the general procedure 6 the title compound was obtained as a colourless solid (99%) from 2-(4-nitrobenzyloxy)ethyl benzoate **43d**; mp 35–36 °C (lit.,[162] mp 36–37 °C); δ_H (300 MHz; $CDCl_3$) 8.06 (2 H, m, 2&6-ArH), 7.60 (1 H, m, 4-ArH), 7.45 (2 H, m, 3&5-ArH), 4.47 (2 H, m, C$H_2$$CH_2$OH), 3.97 (2 H, m, CH_2CH_2OH), 2.24 (1 H, br s, OH).

***O*-(*tert*-Butyldimethylsilyl)-2-(4-aminobenzyloxy)ethanol.** According to the general procedure 6 (reaction stirred at room temperature—not refluxed) the *title compound* was obtained as a colourless oil (80%) from *O*-(*tert*-butyldimethylsilyl)-2-(4-nitrobenzyloxy)ethanol **43e** (Found: MH^+, 282.1891. $C_{15}H_{28}NO_2Si$ requires 282.1889); ν_{max} (neat)/cm^{-1} 3448, 3360 (NH_2), 3222, 2954, 2917, 2856, 1608, 1515, 1464, 1250, 938, 827, 776; δ_H (300 MHz; $CDCl_3$) 7.14 (2 H, m, 2&6-ArH), 6.66 (2 H, m, 3&5-ArH), 4.45 (2 H, s, ArCH_2), 3.80 (2 H, t, *J* 5.5, C$H_2$$CH_2$OSi), 3.52 (2 H, t, *J* 5.5, CH_2CH_2OSi), 0.90 (9 H, s, t-Bu), 0.07 (6 H, s, $SiMe_2$), NH_2 not observed; δ_C (75 MHz; $CDCl_3$) 146.5 (C), 129.4 (CH), 128.7 (C), 115.0 (CH), 73.2 (CH_2), 71.1 (CH_2), 62.8 (CH_2), 26.0 (C*Me*$_3$), 18.6 (*C*Me$_3$), −5.2 (Si*Me*$_2$); *m*/*z* (CI) 282 (MH^+, 41%), 176 (43), 167 (20), 115 (13) and 106 (100).

L-Menthol. According to the general procedure 6 the title compound was obtained as colourless needles (93%) from L-*O*-(4-nitrobenzyl)menthol **43f**; mp 42–43 °C (lit.,[163] mp 43 °C); $[\alpha]_D^{25}$ −49.0 (*c* 1.0 in ethanol) (lit.,[164] $[\alpha]_D$ −50.0 (*c* 10 in ethanol)); δ_H (300 MHz; $CDCl_3$) 3.44 (1 H, td, *J* 10.7, 4.4, OCH), 2.19 (1 H, m, C*H*Me), 1.98 (1 H, m, CH_2CHOR), 1.67 (1 H, m, C$H_2$$CH_2$CHMe), 1.65 (1 H, m, CH_2CH_2CHMe), 1.44 (1 H, m,

C*H*Me$_2$), 1.13 (1 H, m, C*H*^{i}Pr), 1.03 (1 H, m, CH$_2$C*H*$_2$CHMe), 0.95 (3 H, d, *J* 7.2, CH*Me*$_2$), 0.93 (3 H, d, *J* 7.2, CH*Me*$_2$), 0.92 (1 H, m, C*H*$_2$CHOR), 0.89 (1 H, m, C*H*$_2$CH$_2$CHMe), 0.83 (3 H, d, *J* 6.9, CH*Me*)—(as original sample).

4-Methoxyphenol. According to the general procedure 6 the title compound was obtained as colourless crystals (81%) from *O*-(4-nitrobenzyl)-4-methoxyphenol **43g**; mp 54–55 °C (lit.,[165] mp 54 °C); δ_H (300 MHz; $CDCl_3$) 6.79 (4 H, m, ArH), 4.52 (1 H, br s, OH), 3.77 (3 H, s, OMe)—(as original sample).

4-Hydroxyacetophenone. According to the general procedure 6 the title compound was obtained as a colourless solid (97%) from 4-(4-nitrobenzyloxy)acetophenone **43h**; mp 107–108 °C (lit.,[166] mp 107–109 °C); δ_H (300 MHz; $CDCl_3$) 10.35 (1 H, br s, OH), 7.83 (2 H, m, ArH), 6.85 (2 H, m, ArH), 2.46 (3 H, s, COMe)—(as original sample).

3-Hydroxybenzaldehyde. According to the general procedure 6 the title compound was obtained as a colourless solid (61%) from 3-(4-nitrobenzyloxy)benzaldehyde **43i**; mp 104–106 °C (lit.,[167] mp 103–105 °C); δ_H (300 MHz; d_4-MeOH) 9.89 (1 H, s, CHO), 7.37 (2 H, m, ArH), 7.27 (1 H, m, ArH), 7.08 (1 H, m, ArH), 4.93 (1 H, br s, OH)—(as original sample).

2,3,5-Trimethylphenol. According to the general procedure 6 the title compound was obtained as a pale solid (100%) from *O*-(4-nitrobenzyl)-2,3,5-trimethylphenol **43j**; mp 93–95 °C (lit.,[168] mp 94–95 °C); δ_H (300 MHz; $CDCl_3$) 6.63 (1 H, s, ArH), 6.49 (1 H, s, ArH), 4.88 (1 H, br s, OH), 2.27 (6 H, s, Me), 2.16 (3 H, s, Me)—(as original sample).

2,4,5-Trichlorophenol. According to the general procedure 6 the title compound was obtained as a colourless solid (90%) from *O*-(4-nitrobenzyl)-2,4,5-trichlorophenol **43k**; mp 63–64 °C (lit.,[169] mp 63–65 °C); δ_H (300 MHz; $CDCl_3$) 7.43 (1 H, s, ArH), 7.15 (1 H, s, ArH), 5.63 (1 H, br s, OH)—(as original sample).

6-Hydroxyquinoline. According to the general procedure 6 the title compound was obtained as an orange solid (97%) from 6-(4-nitrobenzyloxy)quinoline **43l**; mp 191–193 °C (from ether) (lit.,[170] mp 193 °C); δ_H (300 MHz; d_6-DMSO) 10.06 (1 H, br s, OH), 8.65 (1 H, dd, *J* 4.1, 1.6, 2-ArH), 8.13 (1 H, dd, *J* 8.6, 1.6, 4-ArH), 7.86 (1 H, d, *J* 9.1, 8-ArH), 7.39 (1 H, dd, *J* 8.6, 4.1, 3-ArH), 7.31 (1 H, dd, *J* 9.1, 2.8, 7-ArH), 7.14 (1 H, d, *J* 2.8, 5-ArH)—(as original sample).

4-Chlorobenzoic acid. According to the general procedure 6 the title compound was obtained as a colourless solid (90%) from 4-nitrobenzyl 4-chlorobenzoate **43m**; mp 240–241 °C (lit.,[171] mp 240 °C); δ_H (300 MHz; d_6-DMSO) 8.79 (1 H, br s, COOH), 7.95 (2 H, m, ArH), 7.58 (2 H, m, ArH)—(as original sample).

***N*-Benzyloxycarbonyl-D,L-alanine.** According to the general procedure 6 the title compound was obtained as a colourless solid (96%) from *N*-benzyloxycarbonyl-DL-alanine 4-nitrobenzyl ester **43n**; mp 112–113 °C (lit.,[172] mp 112–114 °C); δ_H (300 MHz; $CDCl_3$) 7.36 (5 H, m, PhH), 6.52 (1 H, br s, COOH), 5.31 (1 H, d, *J* 7.4, NH), 5.13 (2 H, m, CH_2), 4.43 (1 H, quintet, *J* 7.4, C*H*Me), 1.48 (3 H, d, *J* 7.4, CH*Me*)—(as original sample).

***N*-Acetyl-*S*-(4-aminobenzyl)-L-cysteine ethyl ester 45.** According to the general procedure 6 the *title compound* was obtained as a yellow solid (100%) from *N*-acetyl-*S*-(4-nitrobenzyl)-L-cysteine ethyl ester **44**; mp 89–91 °C; $[a]_D^{24}$ +23.7 (*c* 0.97 in chloroform) (Found: C, 56.9; H, 6.8; N, 9.2. $C_{14}H_{20}N_2O_3S$ requires C, 56.7; H, 6.8; N, 9.5%); ν_{max} (KBr)/cm^{-1} 3470 (amide), 3385, 3345 (NH_2), 2985, 2915, 1735 (ester), 1635 (NH_2), 1510, 1370, 1025, 830 (ArH); δ_H (300 MHz; $CDCl_3$) 7.12–7.07 (2 H, m, 3&5-ArH), 6.68–6.64 (2 H, m, 2&6-ArH), 6.18 (1 H, br d, *J* 7.6, NH), 4.79 (1 H, dt, *J* 7.6, 5.1, NCH), 4.21 (2 H, q, *J* 7.2, C*H*$_2$Me), 3.64 (2 H, s, SC*H*$_2$Ar), 2.90 (2 H, d, *J* 5.1, NCHC*H*$_2$S), 2.02 (3 H, s, MeCO), 1.30 (3 H, t, *J* 7.2, CH$_2$*Me*), NH_2 not observed; δ_C (75 MHz; $CDCl_3$) 170.9 (CO), 169.9 (CO), 145.6 (C), 130.0 (CH), 127.3 (C), 115.2 (CH), 61.8 (CH_2), 51.7 (CH), 36.4 (CH_2), 33.4 (CH_2), 23.1 (Me), 14.1 (Me); *m*/*z* (CI) 297 (MH^+, 1%), 158 (100), 116 (29).

Ethyl 1-(4-aminobenzyl)-5-hydroxy-2-methylindole-3-carboxylate 47. According to the general procedure 6 the *title compound* was obtained as a colourless solid (62%) from ethyl-*N*-(4-nitrobenzyl)-5-hydroxy-2-methylindole-3-carboxylate **46**; mp 196–198 °C (Found: M^+, 324.1475. $C_{19}H_{20}N_2O_3$ requires 324.1474); ν_{max} (KBr)/cm^{-1} 3415, 3335 (NH_2), 3230 (OH), 2970, 2920, 2850, 1650, 1610, 1515, 1470, 1250, 1026, 877 (ArH); δ_H (300 MHz; d_6-DMSO) 8.95 (1 H, br s, OH), 7.37 (1 H, d, *J* 2.5, 4-indoleH), 7.28 (1 H, d, *J* 8.5, 7-indoleH), 6.74 (2 H, m, 3&5-Ar*H*NH_2), 6.62 (1 H, dd, *J* 8.5, 2.5, 6-indoleH), 6.46 (2 H, m, 2&6-Ar*H*NH_2), 5.20 (2 H, s, NCH_2), 5.03 (2 H, br s, NH_2), 4.26 (2 H, q, *J* 7.2, C*H*$_2$Me), 2.66 (3 H, s, Me), 1.35 (3 H, t, *J* 7.2, CH$_2$*Me*); δ_C (100 MHz; d_6-DMSO) 165.6 (C), 153.1 (C), 148.2 (C), 145.3 (C), 130.8 (C), 127.7 (CH), 124.5 (C), 114.5 (CH), 111.9 (CH), 111.3 (CH), 105.9 (CH), 102.8 (C), 79.6 (C), 59.1 (CH_2), 46.2 (CH_2), 15.0 (Me), 12.4 (Me); *m*/*z* (EI) 324 (M^+, 12%), 309 (10), 295 (12), 218 (57), 203 (100), 145 (60), 91 (42).

Preparation of conjugated alkenes

1-Phenylbut-2-en-1-one 50. Aluminium trichloride (freshly ground, 5.48 g, 41.1 mmol) was suspended in benzene (20 ml), then stirred vigorously at room temperature while *trans*-crotonyl chloride (3.09 ml, ~3.35 g, 32.1 mmol) was added dropwise over 5 min. After a further 15 min the resulting clear solution was poured onto a mixture of ice (100 ml) and hydrochloric acid solution (2 M; 50 ml). The resulting mixture was extracted with ether (2 × 30 ml), washed with sodium hydroxide solution (4 M; 30 ml), dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was purified by distillation to give the title compound **50** as a clear oil (2.86 g, 61%); bp 85–90 °C, 0.7 mmHg (lit.,[173] bp 90–95 °C, 2.0 mmHg); δ_H (300 MHz; $CDCl_3$) 7.93 (2 H, m, 3&5-ArH), 7.55 (1 H, m, 4-ArH), 7.47 (2 H, m, 2&6-ArH), 7.09 (1 H, dq, *J* 15.4, 6.9, MeC*H*=CH), 6.92 (1 H, dq, *J* 15.4, 1.7, MeCH=C*H*), 2.01 (6 H, dd, *J* 6.9, 1.7, *Me*CH=CH).

2-(*trans*-But-1-enyl)quinoline 55a. According to general procedure 7 *without* indium (reflux for 4 days) the *title compound* **55a** was obtained as a clear oil (56%) from 1-(quinolin-2-yl)-butan-2-ol **57a** (prepared as described below); δ_H (300 MHz; $CDCl_3$) 8.05 (1 H, d, *J* 8.7, 4-ArH), 8.03 (1 H, dd, *J* 8.5, 1.0, 8-ArH), 7.74 (1 H, dd, *J* 8.0, 1.5, 5-ArH), 7.66 (1 H, ddd, *J* 8.5, 7.1, 1.5, 7-ArH), 7.52 (1 H, d, *J* 8.7, 3-ArH), 7.45 (1 H, ddd, *J* 8.0, 7.1, 1.0, 6-ArH), 6.87 (1 H, dt, *J* 16.0, 6.2, ArCH=C*H*), 6.72 (1 H, dt, *J* 16.0, 1.4, ArC*H*=CH), 2.35 (2 H, qdd, *J* 7.5, 6.2, 1.4, C*H*$_2$Me), 1.17 (3 H, t, *J* 7.5, CH$_2$*Me*) (*cf*. lit.[52]).

***trans*-3-Methyl-1-(quinolin-2-yl)but-1-ene 55b.** (a) *n*-Butyllithium (1.6 M in hexanes; 3.0 ml, 4.8 mmol) was added to a stirred suspension of (isobutyl)triphenylphosphonium bromide (1.83 g, 4.6 mmol) in dry ether (20 ml) under an atmosphere of nitrogen at 0 °C. After 30 min the mixture was cooled to −78 °C and quinoline-2-carbaldehyde (0.72 g, 4.6 mmol) in dry ether (10 ml) was added dropwise over 30 min. The reaction mixture was stirred, while warming to room temperature over 3 h, washed with water (50 ml), dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was purified by flash column chromatography (silica, 6% ethyl acetate in light petroleum) to

give *cis-3-methyl-1-(quinolin-2-yl)but-1-ene* as a colourless oil (0.53 g, 59%) (Found: MH^+, 198.1283. $C_{14}H_{16}N$ requires 198.1285); ν_{max} (neat)/cm^{-1} 3060 (=C–H), 2955, 2860 (C–H), 1650 (C=C), 1600, 1500 (Ar), 800 (*cis* CH=CH), 815, 750 (ArH); δ_H (300 MHz; $CDCl_3$) 8.09 (1 H, d, *J* 8.5, 4-ArH), 8.06 (1 H, dd, *J* 8.6, 1.0, 8-ArH), 7.78 (1 H, dd, *J* 7.9, 1.2, 5-ArH), 7.69 (1 H, ddd, *J* 8.6, 7.0, 1.2, 7-ArH), 7.50 (1 H, ddd, *J* 7.9, 7.0, 1.0, 6-ArH), 7.39 (1 H, d, *J* 8.5, 3-ArH), 6.54 (1 H, dd, *J* 11.7, 1.1, ArC*H*=CH), 5.83 (1 H, dd, *J* 11.7, 10.1, ArCH=C*H*), 3.50 (1 H, d-septet-d, *J* 10.1, 6.6, 1.1, C*H*Me$_2$), 1.13 (6 H, d, *J* 6.6, CH*Me*$_2$); δ_C (75 MHz; $CDCl_3$) 157.1 (C), 148.1 (C), 145.8 (CH), 135.8 (=CH), 129.42 (CH), 129.38 (CH), 127.4 (CH), 126.7 (CH), 126.5 (C), 126.0 (=CH), 122.2 (CH), 27.6 (CH), 22.9 (Me); *m*/*z* (CI) 198 (MH^+, 100%).

(b) Acetic acid (0.50 ml, ~0.53 g, 8.8 mmol) and *cis*-3-methyl-1-(quinolin-2-yl)but-1-ene (0.515 g, 2.61 mmol) were heated at reflux in THF (20 ml) for 94 h. The cooled solution was washed with saturated sodium bicarbonate solution (20 ml), dried ($MgSO_4$) and concentrated *in vacuo* to give the *title compound* **55b** as a colourless oil (0.495 g, 96%) (Found: MH^+, 198.1282. $C_{14}H_{16}N$ requires 198.1285); ν_{max} (neat)/cm^{-1} 3060 (=C–H), 2950, 2860 (C–H), 1650 (C=C), 1600, 1500 (Ar), 970 (*trans* CH=CH), 815, 750 (ArH); δ_H (300 MHz; $CDCl_3$) 8.07 (1 H, d, *J* 8.6, 4-ArH), 8.03 (1 H, dd, *J* 8.4, 1.0, 8-ArH), 7.75 (1 H, dd, *J* 7.9, 1.3, 5-ArH), 7.67 (1 H, ddd, *J* 8.4, 7.0, 1.3, 7-ArH), 7.55 (1 H, d, *J* 8.6, 3-ArH), 7.47 (1 H, ddd, *J* 7.9, 7.0, 1.0, 6-ArH), 6.81 (1 H, dd, *J* 16.0, 6.2, ArCH=C*H*), 6.68 (1 H, d, *J* 16.0, ArC*H*=CH), 2.59 (1 H, septet-d, *J* 6.8, 6.2, C*H*Me$_2$), 1.17 (6 H, d, *J* 6.8, CH*Me*$_2$); δ_C (75 MHz; $CDCl_3$) 156.7 (C), 148.1 (C), 144.5 (CH), 136.2 (=CH), 129.5 (CH), 129.1 (CH), 128.3 (CH), 127.4 (CH), 127.1 (C), 125.8 (=CH), 118.7 (CH), 31.6 (CH), 22.1 (Me); *m*/*z* (CI) 198 (MH^+, 100%).

***cis*-1-(Quinolin-2-yl)hepta-1,6-diene 55c.** *n*-Butyllithium (1.6 M solution in hexanes; 0.76 ml, 1.21 mmol) was added to a stirred suspension of (hex-5-enyl)triphenylphosphonium bromide (0.514 g, 1.21 mmol) in ether (15 ml) at 0 °C under an atmosphere of nitrogen. After 15 min, the mixture was cooled to −78 °C and quinoline-2-carbaldehyde (0.190 g, 1.21 mmol) in ether (15 ml) was added over 10 min. The reaction mixture was allowed to warm to room temperature over 4 h, and then water (50 ml) was added and the layers separated. The aqueous layer was further extracted with ether (2 × 15 ml). Combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was passed down a flash chromatography column (silica, 5% ethyl acetate in light petroleum) to give the *title compound* **55c** as a colourless oil (0.087 g, 32%) (Found: MH^+, 224.1443. $C_{16}H_{18}N$ requires 224.1439); ν_{max} (neat)/cm^{-1} 3060 (=CH), 3010 (ArH), 2915, 2850 (CH_2), 1625 (C=C), 1600, 1500 (Ar), 970 (CH=CH_2), 750 (HC=CH); δ_H (300 MHz; $CDCl_3$) 8.10 (1 H, d, *J* 8.5, 4-ArH), 8.07 (1 H, dd, *J* 8.3, 1.0, 8-ArH), 7.79 (1 H, dd, *J* 8.1, 1.3, 5-ArH), 7.70 (1 H, ddd, *J* 8.3, 7.0, 1.3, 7-ArH), 7.50 (1 H, ddd, *J* 8.1, 7.0, 1.0, 6-ArH), 7.39 (1 H, d, *J* 8.5, 3-ArH), 6.66 (1 H, dt, *J* 11.8, 1.8, ArC*H*=CH), 6.04 (1 H, dt, *J* 11.8, 7.4, ArCH=C*H*), 5.84 (1 H, ddt, *J* 17.0, 10.2, 6.6, C*H*=CH_2), 5.01 (1 H, ddt, *J* 17.0, 2.0, 1.5, *trans*-CH=CH*H*), 4.95 (1 H, ddt, *J* 10.2, 2.0, 1.5, *cis*-CH=C*H*H), 2.73 (2 H, m, ArCH=CHCH_2), 2.17 (2 H, m, CH_2CH=CH_2), 1.64 (2 H, m, CH_2CH_2CH=CH_2); δ_C (100 MHz; $CDCl_3$) 156.4 (C), 148.0 (C), 138.4 (CH), 137.7 (CH), 136.3 (CH), 131.2 (CH), 129.6 (CH), 129.1 (CH), 129.0 (CH), 127.2 (CH), 126.0 (C), 118.7 (CH), 114.8 (=CH_2), 33.3 (CH_2), 32.4 (CH_2), 28.1 (CH_2); *m*/*z* (CI) 224 (MH^+, 100%).

3-Methyl-1-(2-naphthyl)but-1-ene. *n*-Butyllithium (1.6 M solution in hexanes; 1.50 ml, 2.4 mmol) was added to a stirred suspension of isobutyltriphenylphosphonium bromide (0.889 g, 2.23 mmol) in ether (30 ml) at ~10 °C under an atmosphere of nitrogen. After 30 min, the mixture was cooled to −78 °C and 2-naphthaldehyde (0.348 g, 2.23 mmol) in ether (10 ml) was added over 10 min. The reaction mixture was allowed to warm to room temperature over 4 h, and then water (50 ml) was added and the layers separated. The aqueous layer was further extracted with ether (2 × 15 ml). Combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was passed down a flash chromatography column (silica, light petroleum) to give the *title compound* as a colourless solid (0.261 g, 60%), a mixture of *cis* and *trans* isomers (4.5 : 1); mp 36–38 °C (lit.,[174] mp 38.5–39 °C); δ_H (300 MHz; $CDCl_3$) *cis* 7.81 (3 H, m, ArH), 7.71 (1 H, s, 1-ArH), 7.45 (3 H, m, ArH), 6.46 (1 H, d, *J* 11.6, ArC*H*=CH), 5.57 (1 H, dd, *J* 11.6, 10.3, ArCH=C*H*), 3.02 (1 H, d-septet, *J* 10.3, 6.6, C*H*Me$_2$), 1.09 (6 H, d, *J* 6.6, CH*Me*$_2$); *trans* 7.83–7.38 (7 H, m, ArH), 6.52 (1 H, d, *J* 15.9, ArC*H*=CH), 6.33 (1 H, dd, *J* 15.9, 6.7, ArCH=C*H*), 2.53 (1 H, septet, *J* 6.8, C*H*Me$_2$), 1.09 (6 H, d, *J* 6.8, CH*Me*$_2$).

1-(Quinolin-2-yl)butan-2-ol 57a. *n*-Butyllithium (1.6 M in hexanes; 3.5 ml, 5.6 mmol) was added slowly to a stirred solution of 2-methylquinoline (0.68 ml, ~0.72 g, 5.0 mmol) in ether (20 ml) at 0 °C under an atmosphere of nitrogen. After stirring for 30 min, the reaction mixture was cooled to −78 °C and propionaldehyde (0.36 ml, ~0.29 g, 5.0 mmol) was added dropwise over 5 min. Stirring was continued at −78 °C for 1 h, then the mixture was allowed to warm to room temperature, poured onto saturated ammonium fluoride solution (100 ml), and extracted with ether (2 × 30 ml). Combined ethereal layers were dried ($MgSO_4$), and concentrated *in vacuo*. The residue was purified by flash column chromatography (silica, 10% ethyl acetate in light petroleum) to give the *title compound* **57a** as a colourless solid (0.61 g, 61%); mp 36–37 °C (Found: C, 77.1; H, 7.7; N, 6.6. $C_{13}H_{15}NO{\cdot}0.1H_2O$ requires C, 76.9; H, 7.5; N, 6.9%); ν_{max} (KBr)/cm^{-1} 3360 (OH), 3050, 2950, 2920, 1600, 1505, 1425, 1115, 820, 755 (ArH); δ_H (300 MHz; $CDCl_3$) 8.08 (1 H, d, *J* 8.3, 4-ArH), 8.01 (1 H, dd, *J* 8.6, 1.1, 8-ArH), 7.78 (1 H, dd, *J* 8.2, 1.4, 5-ArH), 7.69 (1 H, ddd, *J* 8.6, 7.0, 1.4, 7-ArH), 7.50 (1 H, ddd, *J* 8.2, 7.0, 1.1, 6-ArH), 7.26 (1 H, d, *J* 8.3, 5-ArH), 5.65 (1 H, br s, OH), 4.14 (1 H, m, C*H*OH), 3.11 (1 H, dd, *J* 15.6, 2.9, *anti*-ArC*H*HCHOH), 3.01 (1 H, dd, *J* 15.6, 8.9, *syn*-ArCH*H*CHOH), 1.76-1.53 (2 H, m, CHOH-CH_2Me), 1.05 (3 H, t, *J* 7.4, Me); δ_C (75 MHz; $CDCl_3$) 161.1 (C), 147.0 (C), 136.6 (CH), 129.7 (CH), 128.7 (CH), 127.6 (CH), 126.7 (C), 126.1 (CH), 122.1 (CH), 72.0 (CHOH), 43.2 (CH_2), 29.9 (CH_2), 10.1 (Me); *m*/*z* (CI) 202 (MH^+, 100%), 184 (70), 144 (61), 143 (28), 57 (90).

3-Methyl-1-(quinolin-2-yl)butan-2-ol 57b. *n*-Butyllithium (1.6 M in hexanes; 3.5 ml, 5.6 mmol) was added slowly to a solution of 2-methylquinoline (0.715 g, 5.00 mmol, 0.68 ml) in ether (20 ml) at 0 °C under an atmosphere of nitrogen. After 30 min the solution was cooled to −78 °C. Isobutyraldehyde (0.45 ml, ~0.36 g, 5.0 mmol) was added dropwise over 10 min. Stirring was continued for 1 h at −78 °C, then the mixture was allowed to warm to room temperature over 2 h. The reaction mixture was quenched by pouring onto saturated ammonium fluoride solution (100 ml). The layers were separated and the aqueous layer extracted with ether (2 × 50 ml). The combined ethereal layers were dried ($MgSO_4$), and concentrated *in vacuo*. The crude material was recrystallised from ether to give the title compound **57b** as a colourless solid (0.634 g, 59%); mp 94–96 °C (lit.,[175] mp 93 °C); ν_{max} (KBr)/cm^{-1} 3237 (OH), 2945, 2875 (C–H), 1600, 1505 (Ar), 1430, 1380, 1045 (C–O), 810, 750 (ArH); δ_H (300 MHz; $CDCl_3$) 8.09 (1 H, d, *J* 8.5, 4–ArH), 8.01 (1 H, d, *J* 8.4, 8-ArH), 7.79 (1 H, d, *J* 8.2, 5-ArH), 7.70 (1 H, dd, *J* 8.4, 8.2, 7-ArH), 7.51 (1 H, dd, *J* 8.2, 8.2, 6-ArH), 7.28 (1 H, d, *J* 8.5, 3-ArH), 5.65 (1 H, br s, OH), 3.95 (1 H, ddd, *J* 8.9, 5.8, 2.8, C*H*OH), 3.09 (1 H, dd, *J* 15.5, 2.8, *anti*-ArC*H*HCHOH), 3.03 (1 H, dd, *J* 15.5, 8.9, *syn*-ArCH*H*CHOH), 1.81 (1 H, septet-d, *J* 6.8, 5.8, CHMe$_2$), 1.07 (3 H, d, *J* 6.8, Me), 1.04 (3 H, d, *J* 6.8, Me); δ_C (75 MHz; $CDCl_3$) 161.5 (C), 147.1 (C), 136.7

(CH), 129.7 (CH), 128.7 (CH), 127.6 (CH), 126.8 (C), 126.1 (CH), 122.2 (CH), 75.5 (CHOH), 40.7 (CH_2), 33.6 (CH), 18.7 (Me), 18.1 (Me).

Reduction of conjugated alkenes

Benzylacetone 49. According to general procedure 7, the title compound **49** was obtained as a colourless oil (100%) from benzylideneacetone **48**; δ_H (300 MHz; $CDCl_3$) 7.29 (2 H, m, ArH), 7.20 (3 H, m, ArH), 2.89 (2 H, m, PhCH_2), 2.77 (2 H, m, $COCH_2$), 2.16 (3 H, s, Me) (*cf*. lit.[176]).

1-Phenylbutan-1-one 51. According to general procedure 7, the title compound **51** was obtained as a colourless oil (100%) from 1-phenylbut-2-en-1-one **50**; δ_H (300 MHz; $CDCl_3$) 7.97 (2 H, m, ArH), 7.55 (1 H, m, ArH), 7.46 (2 H, m, ArH), 2.96 (2 H, t, *J* 7.3, COCH_2), 1.78 (2 H, sextet, *J* 7.3, $COCH_2CH_2$), 1.01 (3 H, t, *J* 7.3, Me) (*cf*. lit.[177]).

Reaction of chalcone 52 with indium. (a) Indium powder (1.00 g) was added to a stirred solution of chalcone **52** (0.345 g, 1.66 mmol) in ethanol (10 ml) and saturated ammonium chloride solution (3 ml). The mixture was heated under reflux. After 24 h the cooled reaction mixture was washed through Celite® with dichloromethane (30 ml) and water (50 ml). The layers were separated and the aqueous layer extracted with further portions of dichloromethane (2 × 10 ml). Combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The crude material was passed down a flash chromatography column (silica, dichloromethane–light petroleum 2 : 1) to give two products: 1,3-diphenylpropan-1-one **53** (0.053 g, 15%) and (1*S*,2*R*,3*S*,4*R*/1*R*,2*S*,3*R*,4*S*)-2-benzoyl-1,3,4-triphenylcyclopentan-1-ol **54** (0.215 g, 62%).

(b) The same two products were obtained from chalcone **52** according to general procedure 7 (2 equivalents of acetic acid): 1,3-diphenylpropan-1-one **53** (23%) and (1*S*,2*R*,3*S*,4*R*/1*R*,2*S*,3*R*,4*S*)-2-benzoyl-1,3,4-triphenylcyclopentan-1-ol **54** (59%).

1,3-Diphenylpropan-1-one ***53***. mp 70–71 °C (lit.,[178] mp 71–72 °C); δ_H (300 MHz; $CDCl_3$) 8.03–7.24 (10 H, m, 2 × Ph), 3.35 (2 H, m, COCH_2), 3.13 (2 H, m, PhCH_2).

(1S,2R,3S,4R/1R,2S,3R,4S)-2-Benzoyl-1,3,4-triphenylcyclopentan-1-ol ***54***. mp 196–198 °C (from ether–light petroleum) (lit.,[86] mp 195 °C); ν_{max} (KBr)/cm^{-1} 3430 (OH), 3060, 3020, 2970, 2945, 2920, 1640 (C=O), 1590, 1490, 1380, 1050 (C–O), 750, 700 (ArH); δ_H (400 MHz; $CDCl_3$) 7.68–7.09 (20 H, m, 4 × Ph), 5.20 (1 H, d, *J* 1.3, OH), 4.54 (1 H, d, *J* 12.0, C*H*COPh), 4.11 (1 H, dd, *J* 12.0, 10.2, C*H*CHCOPh), 3.79 (1 H, ddd, *J* 11.4, 10.2, 6.1, CH_2CHPh), 3.01 (1 H, ddd, *J* 14.6, 11.4, 1.3, C*H*HCHPh), 2.59 (1 H, dd, *J* 14.6, 6.1, CH*H*CHPh) (*cf*. lit.[84]); δ_C (100 MHz; $CDCl_3$) 204.9 (CO), 145.3 (C), 144.0 (C), 139.9 (C), 137.6 (C), 133.2 (CH), 128.43 (CH), 128.37 (CH), 128.3 (CH), 128.13 (CH), 128.07 (CH), 127.9 (CH), 127.6 (CH), 127.0 (CH), 126.9 (CH), 126.3 (CH), 124.9 (CH), 84.3 (C), 63.6 (CH), 59.5 (CH), 51.4 (CH_2 and CH).

2-*n*-Butylquinoline 56a. (a) According to the general procedure 7 the title compound **56a** was obtained as a clear oil (86%) from 2-(*trans*-but-1-enyl)quinoline **55a**; δ_H (300 MHz; $CDCl_3$) 8.08 (1 H, d, *J* 8.3, 4-ArH), 8.06 (1 H, dd, *J* 8.2, 1.2, 8-ArH), 7.79 (1 H, dd, *J* 8.0, 1.5, 5-ArH), 7.69 (1 H, ddd, *J* 8.2, 6.9, 1.5, 7-ArH), 7.49 (1 H, ddd, *J* 8.0, 6.9, 1.2, 6-ArH), 7.32 (1 H, d, *J* 8.3, 3-ArH), 2.99 (2 H, dd, *J* 8.1, 7.6, ArCH_2), 1.80 (2 H, m, $ArCH_2CH_2$), 1.46 (2 H, qt, *J* 7.5, 7.4, CH_2CH_2Me), 0.97 (3 H, t, *J* 7.5, CH_2CH_3) (*cf*. lit.[179]).

(b) The title compound was also obtained directly from 1-(quinolin-2-yl)butan-2-ol **57a** (100%) according to procedure 7 (spectroscopic data identical).

2-(3-Methylbutyl)quinoline 56b. (a) The title compound was obtained from *trans*-3-methyl-1-(quinolin-2-yl)but-1-ene **55b** (99%) according to general procedure 7 (reflux for 4 d) (spectroscopic data below).

(b) According to the general procedure 7 the title compound **56b** was obtained as a yellow oil (99%) from 3-methyl-1-(quinolin-2-yl)butan-2-ol **57b** after 17 h (lit.,[180] bp not given); ν_{max} (neat)/cm^{-1} 2960, 2910 (C–H), 1620, 1600, 1500 (Ar), 1465, 1370, 815, 745 (ArH); δ_H (300 MHz; $CDCl_3$) 8.10 (2 H, m, 4-ArH), 7.79 (1 H, dd, *J* 8.0, 1.4, 5-ArH), 7.70 (1 H, ddd, *J* 8.5, 7.1, 1.4, 7-ArH), 7.50 (1 H, ddd, *J* 8.0, 7.1, 1.4, 6-ArH), 7.33 (1 H, d, *J* 8.2, 3-ArH), 3.00 (2 H, m, ArCH_2), 1.69 (3 H, m, CH_2CHMe_2), 0.99 (6 H, d, *J* 6.6, Me_2) (*cf*. lit.[179]); δ_C (100 MHz; $CDCl_3$) 163.4 (C), 147.9 (C), 136.2 (CH), 129.3 (CH), 128.8 (CH), 127.5 (CH), 126.7 (C), 125.6 (CH), 121.4 (CH), 39.3 (CH_2), 37.5 (CH_2), 28.0 (CH), 22.6 (Me).

2-(Hept-6-enyl)quinoline 56c. According to general procedure 7 the *title compound* **56c** was obtained as a colourless oil (98%) from *cis*-1-(quinolin-2-yl)hepta-1,6-diene **55c** (Found: MH^+, 226.1595. $C_{16}H_{20}N$ requires 226.1596); ν_{max} (neat)/cm^{-1} 3050 (=CH), 3010 (ArH), 2920, 2850 (CH_2), 1715, 1620 (C=C), 1595, 1500 (Ar), 1430 (CH_2), 910 ($CH=CH_2$), 825, 755 (ArH); δ_H (300 MHz; $CDCl_3$) 8.08 (1 H, d, *J* 8.4, 4-ArH), 8.07 (1 H, dd, *J* 8.3, 1.0, 8-ArH), 7.78 (1 H, dd, *J* 8.1, 1.4, 5-ArH), 7.69 (1 H, ddd, *J* 8.3, 7.0, 1.4, 7-ArH), 7.49 (1 H, ddd, *J* 8.1, 7.0, 1.0, 6-ArH), 7.31 (1 H, d, *J* 8.4, 3-ArH), 5.80 (1 H, ddt, *J* 17.1, 10.1, 6.6, C*H*=CH_2), 4.99 (1 H, ddt, *J* 17.1, 2.6, 1.6, *trans*-CH=CH*H*), 4.93 (1 H, ddt, *J* 10.1, 2.6, 1.6, *cis*-CH=C*H*H), 2.99 (2 H, m, ArCH_2), 2.07 (2 H, m, $CH_2CH=CH_2$), 1.90–1.42 (6 H, m, $CH_2CH_2CH_2$); δ_C (100 MHz; $CDCl_3$) 153.0 (C), 147.6 (C), 139.0 (=CH), 136.5 (CH), 129.5 (CH), 128.5 (CH), 127.5 (CH), 126.7 (C), 125.7 (CH), 121.4 (CH), 114.3 (=CH_2), 39.0 (CH_2), 33.6 (CH_2), 29.9 (CH_2), 29.0 (CH_2), 28.8 (CH_2); *m*/*z* (CI) 226 (MH^+, 100%), 143 (6), 52 (28).

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