A New Oxindole Synthesis

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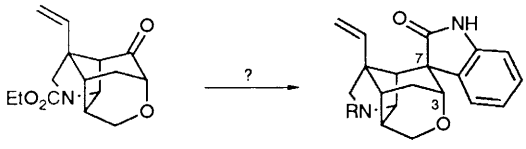
A quaternary carbon atom can be set up by irradiation of the *N*-methylaniline enamine **5** of adamantane-2-carbaldehyde giving the indoline **6** in poor yield. This product was converted into the spiro-oxindole **8**, but only in very low yield. Quaternary carbon atoms can be set up more efficiently from the ketone group of adamantanone in two high-yielding steps by conjugate addition of appropriate organometallic carbon nucleophiles to the electrophilic alkenes **9** and **25**, obtained by condensation of adamantanone with either Meldrum's acid or nitromethane. By use of the latter intermediate **25**, a high yielding, eight-step conversion of adamantanone into the corresponding spiro-oxindole **8** can be carried out. Conjugate addition of triphenylaluminium to the corresponding nitroalkene **33** derived from 2-oxaadamantan-4-one **32** takes place with high stereoselectivity in the sense appropriate for a synthesis of gelsemine, with the phenyl group in the product **34** *cis* to the oxygen bridge.

In our approach [1] to the synthesis of the alkaloid gelsemine **3**,[2] we plan to convert the ketone **1** into the spiro-oxindole **2**. Several years ago, we reported a pair of stereochemically complementary oxindole syntheses of this type,[3] one of which, we hoped, would have the correct stereoselectivity to achieve this end. A little later, we reported the synthesis of the ketone **1**,[1] but, to our dismay, neither oxindole synthesis was successful in giving either the oxindole **2** or its stereoisomer at C-7. Although we had no evidence on this point, we argued that the neighbouring C–O bond might be detrimental in some way to the carbocation chemistry used in the two routes, both of which depended upon the orderly behaviour of a cation at C-7.[4,†] To avoid carbocation chemistry, we tried a Brunner oxindole synthesis, for which we prepared the way[6] by improving upon the rather harsh conditions under which it had traditionally been carried out.[7] The modified Brunner synthesis also failed,[8] most likely because the neighbouring oxygen departed as a nucleofuge from the intermediate, which is a carbanion at C-7.

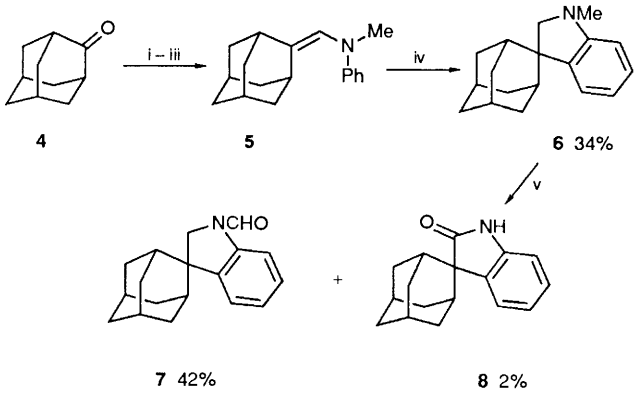


1 **2** R = EtO_2C, **3** R = Me

We faced, then, the need for a new oxindole synthesis. It should allow the creation of the quaternary centre without, if possible, using carbocation chemistry. It should also avoid carbanion chemistry at C-7, although this was not an overwhelmingly compelling constraint, since the reversibility of the oxygen leaving as a nucleofuge might make it inoffensive, and the Brunner synthesis, using harsh conditions and a di- or tri-anion, might not be typical. It should also introduce the aryl group onto C-7 after the other C–C bond has been formed, because it is likely that the lower surface of the molecule (as drawn) is the less hindered. Our originally having *two* oxindole syntheses lined up was precautionary: at that stage in our work we did not know that the vinyl group would already have been established on the top surface, shielding an incoming aryl group from attacking C-7 with a 1,3-diaxial interaction. Other people, facing the same problem, have developed solutions using radical chemistry [9] or a Heck reaction,[10] but these possibilities are not available to us without considerable backtracking, because they require a double bond between C-3 and C-7.

The sum of all these constraints looks formidable, but we have found two ways of staying within them, and report our results here, using adamantanone **4** as a model for the ketone **1**. We have found three methods for establishing a quaternary centre, and one that has led to a good oxindole synthesis.

One way is to use a pericyclic process, and the version that we have had some success with is the [$_\pi$6] photochemical cyclisation[11] of the enamine **5**, which established the quaternary centre in the indoline **6** in 33% yield. Oxidation of this compound was selective for the formation of the *N*-formylindoline **7**, but the oxindole **8** was a minor by-product (Scheme 1), readily recognisable, because we had made it before.[3] Although this route is fairly short, involving the homologation of adamantanone **4** to adamantane-2-carbaldehyde,[12] two low yields in a row, and the prospect that the lower pyrrolidine ring in the ketone **1** might interfere with the oxidation reaction that we would have to carry out in the full synthesis, led us not to pursue this route.



4 **5** **6** 34% **7** 42% **8** 2%

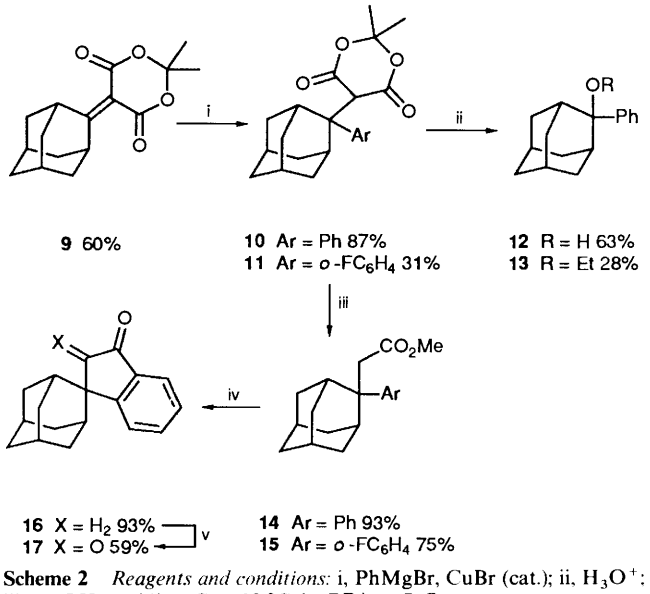
Scheme 1 *Reagents and conditions:* i, $Me_2S(:O)=CH_2$; ii, BF_3·Et_2O; iii, PhNHMe; iv, *hν*; v, MnO_2

A more powerful approach that stays within our constraints is to use the conjugate addition of an organometallic aryl nucleophile to an electrophilic alkene to be derived by condensation of the ketone with malonate derivatives or with

† However, we may be overestimating this problem (see ref. 5).

nitromethane. This avoids cationic, anionic and even radical chemistry at C-7, and seemed likely to lead to the aryl ring arriving on the lower face. Accordingly, we invested more of our time on this approach than on any other.

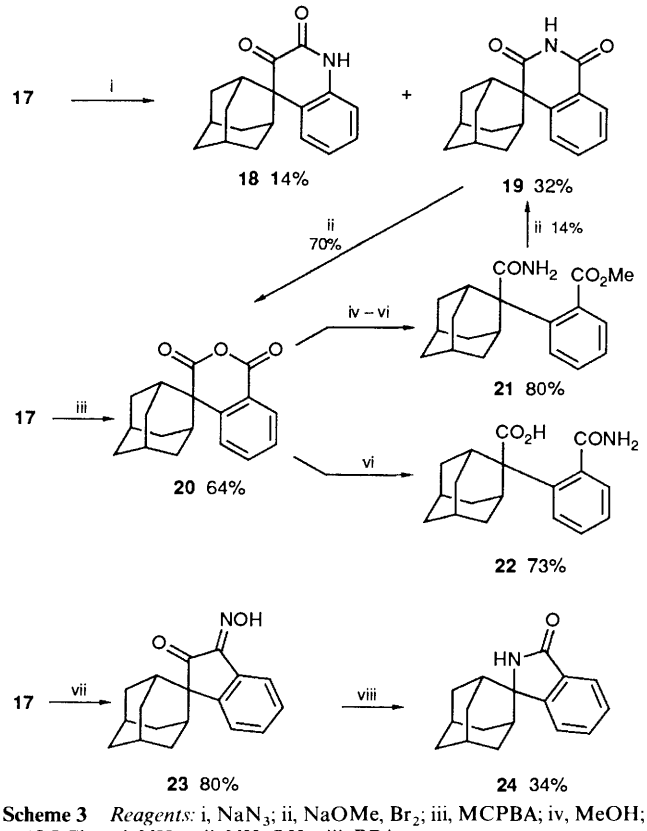
Our first substrate was the known[13] alkene **9** derived from adamantanone and Meldrum's acid, to which conjugate addition ought to be particularly easy.[14] Copper-catalysed addition of phenylmagnesium bromide gave the ester **10** in 87% yield, and the yield was only a little diminished, to 73%, when the copper salt was left out. Setting up the quaternary centre had been easy, but the rest of the work on this approach proved to be more difficult. There were two recognisable problems, one in each of the branches at the quaternary centre: the phenyl ring was unfunctionalised,[15] and the carbon chain was one carbon atom too long. However, before we dealt with these, we met another problem: an attempt at acid-catalysed hydrolysis and decarboxylation of the Meldrum's acid group gave the alcohol **12**, a compound that had also been an unavoidable and puzzling minor by-product in the preparation of the ester **10**. For, no matter how carefully we purified the starting material **9** to free it of adamanatanone, certainly well enough for there to be $<2\%$ of compound **4**, we always found that the product contained 4–5% of the alcohol **12**. It was now clear that this by-product must have been produced in the acidic aq. work-up of the reaction mixture. This is a remarkable reaction, for it implies *an S_N1 process with a carbon nucleofugal group*, a rare event, although more understandable here with Meldrum's acid as the nucleofuge than with most carbon groups. In more detail, the acidic hydrolysis of the ester **10** actually gave a mixture of the alcohol **12** and the ether **13**, the latter coming from the ethanol present in the chloroform used to extract the product, and the combined yield was high. Fortunately this particular problem responded to a procedure of Oikawa's, in which the decarboxylation is combined with methanolysis under basic conditions, giving the ester **14** in 93% yield.[16] We were still left with the two remaining problems. *ortho*-Functionalisation of the phenyl ring was probably going to be easy; thus we were able to add *o*-fluorophenyllithium to the ester **9** by keeping the temperature at -50 °C, above which benzyne formation becomes relatively rapid,[17] and by using boron trifluoride–diethyl ether as a Lewis acid catalyst. The yield of the ester **11** was only 31%, but, for reasons that will become apparent, we did not try to optimise this reaction. The methanolysis–decarboxylation reaction also worked in this series, giving the ester **15** (Scheme 2).



Scheme 2 *Reagents and conditions:* i, PhMgBr, CuBr (cat.); ii, H_3O^+; iii, MeOH–pyridine, Cu, 100 °C; iv, PPA; v, SeO_2

The contraction of the two-carbon chain to a one-carbon chain was not so easy. Routes based on successive reduction, dehydration, and ozonolysis are undesirable, because they are not compatible with the presence of the vinyl group in the ketone **1** that we would eventually have to work with. We tried many oxidations under basic conditions, hoping to attack the enolate of the ester **14**, to no avail. The problem was that the enolate did not form, even under rather forcing conditions, such as refluxing with potassium hydride in tetrahydrofuran (THF) for several hours. To avoid this problem, we tried to oxidise directly the anion of the Meldrum's acid derivative **10**, either *in situ*, immediately after its formation in the conjugate addition, or by regenerating it from compound **10**. Thus, after bubbling air through the reaction mixture following the conjugate addition, and by using a reductive work-up with hydrogen sulphite, we isolated the alcohol **12** (44%), showing that the C–C bond had again cleaved too easily for our purposes, together with a reduction product, dihydro-**9** (21%), that must have come from unchanged starting material. The anion formed from the ester **10** was insoluble, it did not react with oxygen, and other oxidising agents were equally ineffective.

To get round this problem, and simultaneously to solve the *ortho*-functionalisation problem, we carried out a Friedel–Crafts reaction on the ester **14** to give the indanone **16** in 93% yield. We hoped that enolisation would now be easier than it had been with the ester **14**; in the first place the carbonyl group is now a ketone, and furthermore it is constrained in a ring, making enolisation easier still. In the event, the diketone **17** formed easily in 59% yield, but we were unable to make an oxindole from this intermediate, as summarised in Scheme 3.



Scheme 3 *Reagents:* i, NaN_3; ii, NaOMe, Br_2; iii, MCPBA; iv, MeOH; v, $(COCl)_2$; vi, NH_3; vii, NH_2OH; viii, PPA

Schmidt reaction on the diketone **17** gave two products (**18** and **19**), but the former did not decarbonylate on heating, as pyruvate derivatives sometimes do,[18] and the latter did not give the oxindole on treatment with bromine and base, although there was good precedent for it to have done so.[19] The product in the latter case was the anhydride **20**, which was also the

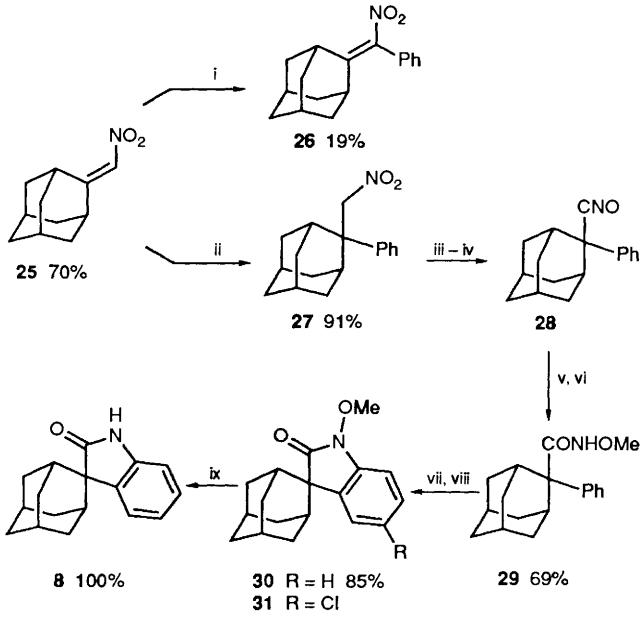
product from treatment of the diketone **17** with peracid. Although this anhydride did react with ammonia to give an amido acid (**22**), the amido acid did not give the oxindole on Hofmann reaction. The assignment of regiochemistry to the opening of the anhydride was not entirely unambiguous, and we therefore opened it first with methoxide ion, on the assumption that the product would have the same regiochemistry. We then made the amido ester **21** from this half-acid half-ester. Hofmann reaction on this amide only led back to the imide **19**, with a Thorpe–Ingold effect so encouraging ring formation that the bromine is unable to attack the anionic intermediate before it cyclises. Even if we have the structures drawn for the amido acid and the amido ester the wrong way round, this route does not look promising.

Finally, the only reaction to achieve the loss of a carbon atom, but unfortunately the wrong one, was the Beckmann rearrangement carried out on the oxime **23** of the diketone **17**. This oxime was formed by nucleophilic attack with opposite regioselectivity to that which we had observed with the anhydride **20**. This might have allowed us to synthesize the lactam **18** in better yield, and so to pursue its chemistry with more conviction, but the product of the Beckmann rearrangement proved to be the isomer **24** of the oxindole, formed by decarbonylation, a retro-Koch–Haaf reaction, from C-2 of the adamantane system.

Our second substrate, the known[20] αβ-unsaturated nitro compound **25**, avoids the problem of the extra carbon atom, but the problem now was to achieve the conjugate addition of an aryl nucleophile. Although we did occasionally prepare the nitroalkane **27**, in our early efforts, it was usually in negligible yield, never better than 15% (PhMgBr, CuBr·DMS, TMSCl). A curious by-product in a few of these runs, and a major product (19%) in one of them (PhLi, THF), appeared to be the nitroalkene **26**, formally corresponding to Michael addition with unconventional regiochemistry followed by oxidation. However, following Pecunioso and Menicagli,[21] we found that conjugate addition of triphenylaluminium to this Michael acceptor was much more successful, and gave the nitroalkane **27** in 91% yield. Our original plan at this stage had been to convert the nitroalkane directly into the oxindole in one pot, for they are at the same oxidation level, and a reaction existed that seemed promising.[22] It is based on Royer's conversion of β-nitrostyrene into 3-chlorooxindole using acetyl chloride and iron(III) chloride,[23] and involved first forming the nitronate with sodium hydride, followed by treatment with acetyl chloride and iron(III) chloride. After a lot of work, we were able to make this reaction work for the conversion of 2-nitroethylbenzene into oxindole itself, but only in 10% yield. Worse still, although we had hoped that a Thorpe–Ingold effect might make the adamantane-based reaction better than the unsubstituted model, even our best reaction conditions completely failed to convert the nitroalkane **27** into the oxindole **8**, which we could have detected in trace amounts.

Consideration of some of the intermediates that might be involved in the one-pot procedure[24–26] led us to a stepwise version that does work. One of the many by-products in our attempts at the one-pot reaction was the nitrile oxide **28**. Although nitrile oxides have been strongly implicated as intermediates in the reaction of nitronates with acetyl chloride,[24,27] this is the first time that one has been isolated. Deliberate dehydration of the nitroalkane **27**, using successively sodium methoxide and acetyl chloride, since phenyl isocyanate and triethylamine[28] were ineffective, gave the nitrile oxide **28** in 66% yield. Addition of acetic acid to the nitrile oxide gave the *O*-acetyl hydroxamate, but this too did not cyclise[25] on treatment with iron(III) chloride, giving perhaps only traces of the oxindole **8**. Hydration of the nitrile oxide gave the hydroxamic acid itself in 56% yield, and methylation of this compound gave the methyl hydroxamate **29** in 93% yield. When the three steps from the nitroalkane **27** to the methyl hydroxamate **29** were combined, without purification of the intermediates, the overall yield was 69%.

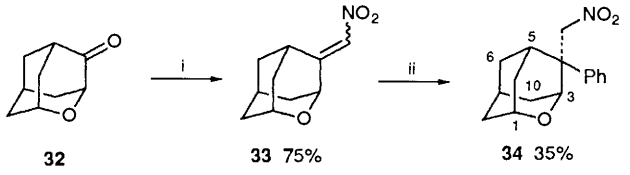
We were now able to connect to Kikugawa's *N*-methoxyoxindole synthesis, in which methyl *N*-chlorohydroxamates are cyclised with silver(I) as a Lewis acid catalyst.[29] In our case, the chlorination of the methyl hydroxamate **29** was slower than Kikugawa's, but the cyclisation to the *N*-methoxyoxindole **30** was faster, the Thorpe–Ingold effect coming to our aid this time. When carried out with a small excess of t-butyl hypochlorite, the reaction gave some of the chlorinated *N*-methoxyoxindole **31**, in which the chlorine atom was *para* to the nitrogen, implying that some chlorination had taken place after cyclisation. This was easily minimised by careful control of the amount of hypochlorite, and the *N*-methoxyoxindole **30** was formed, upon using zinc acetate as the Lewis acid, in 85% yield. Finally, reduction of the N–O bond with sodium amalgam, which had previously been established as a reducing agent for a number of similar substrates,[30] worked cleanly to give the oxindole **8** in quantitative yield (Scheme 4). The overall yield from adamantanone was 47%.



Scheme 4 *Reagents:* i, PhLi; ii, Ph_3Al; iii, NaOMe; iv, AcCl; v, H_2SO_4; vi, Na_2CO_3, MeI; vii, Bu^{t}OCl; viii, $Zn(OAc)_2$; ix, Na/Hg

Before we moved on to the main synthesis itself, there remained the possibility that the stereochemistry of attack on C-7 of the nitroalkene to be derived from the definitive ketone **1** might be affected by the presence of the oxygen substituent on C-3; whether helpfully or adversely we did not know. In applying the Heck reaction to oxindole syntheses, in which this bridging substituent was not present, but the axial vinyl group was, Overman and co-workers[10] found little selectivity (1.4:1) in favour of attack of the aryl group from the lower surface, and Speckamp and co-workers found surprisingly, that the aryl group attacked only on the upper surface, *syn* to the vinyl group, to give the wrong oxindole.[10] We wanted to know whether the oxygen bridge would be helpful in our system, as it might well be, given that it can co-ordinate to the aluminium reagent. Furthermore, it is known that several nucleophiles, including some that are not capable of co-ordination, attack the ketone **32** *syn* to the bridging oxygen atom.[5] Accordingly, we prepared the mixture of nitroalkenes **33** from the ketone **32**, and treated it with triphenylaluminium at as low a temperature as we could,

given that the triphenylaluminium–xylene mixture solidifies at −10 °C. We obtained largely (90:1) the nitroalkane **34**, although only in 35% yield (Scheme 5). The crystals did not prove to be suitable for X-ray structure analysis, but an argument based on combined COSY and difference NOE experiments convinced us that the structure was that which we had hoped for. The stage was now set for us to turn to the synthesis of gelsemine itself.



32 **33** 75% **34** 35%

Scheme 5 *Reagents:* i, $MeNO_2$; ii, Ph_3Al

Experimental

2-(N-*Methylanilinomethylene*)*adamantane* **5**.—*N*-Methylaniline (3.65 cm^3, 32 mmol) was added to a solution of adamantane-2-carbaldehyde[12] (*ca.* 5.25 g, *ca.* 32 mmol) in benzene (400 cm^3) and the mixture was refluxed (Soxhlet, 4 Å sieves) for 3 days. The solvent was evaporated off under reduced pressure, and the residue was distilled (Kugelrohr, 100 °C/0.02 mmHg) to give the *enamine* **5** (4.99 g, *ca.* 62%) as a yellow oil, ν_{max}(film)/cm^{-1} 1580 (C=C) and 680 (Ph); $\delta_H(CDCl_3)$ 6.50–7.30 (5 H, m, Ph), 5.75 (1 H, s, =CHN), 3.00 (3 H, s, NMe) and 2.39–1.50 (14 H, m) (Found: M^+, 253.1812. $C_{18}H_{23}N$ requires M, 253.1830).

Tricyclo[3.3.1.$1^{3,7}$]*decane-2-spiro-3′-2′,3′-dihydro-N-methylindole* **6**.—A solution of the enamine **5** (3.09 g, 12.21 mmol) in dry diethyl ether (300 cm^3) was purged with nitrogen for 30 min, and irradiated in Pyrex apparatus with a 450 W mercury vapour lamp at 20 °C for 7 days. The mixture was then extracted with hydrochloric acid (3 mol dm^{-3}; 3 × 100 cm^3). The extracts were washed with diethyl ether (100 cm^3), basified with solid sodium hydroxide, and extracted with diethyl ether (3 × 100 cm^3). The extracts were washed with brine (100 cm^3), dried ($MgSO_4$), and evaporated under reduced pressure. Distillation of the residue (Kugelrohr, 100 °C/0.02 mmHg) gave the *indoline* **6** (1.06 g, 34%) as an oil, R_f [light petroleum–EtOAc (4:1)] 0.71; ν_{max}(film)/cm^{-1} 1590, 1450, 1370, 1270, 1095, 960, 750 and 735; $\delta_H(CDCl_3)$ 7.64 (1 H, dd, *J* 7.6 and 0.9, 7′-H), 7.14 (1 H, dt, *J* 7.6 and 0.9, 5′-H), 6.71 (1 H, dt, *J* 7.6 and 1.2, 6′-H), 6.52 (1 H, dd, *J* 7.8 and 0.9, 4′-H), 3.31 (2 H, s, CH_2N), 2.76 (3 H, s, NMe), 2.52–2.46 (2 H, m) and 2.05–1.65 (12 H, m); $\delta_C(CDCl_3)$ 153.30, 137.20, 127.39, 126.98, 117.02, 107.55, 66.98, 50.21 39.26, 36.16, 35.38, 34.97, 33.12, 27.55 and 27.41 (Found: M^+, 253.1844. $C_{18}H_{23}N$ requires M, 253.1830).

Tricyclo[3.3.1.$1^{3,7}$]*decane-2-spiro-3′-2′,3′-dihydroindole-N-carbaldehyde* **7**.—Following the procedure of Henbest and Thomas,[31] the indole **6** (0.96 g, 3.80 mmol) and manganese dioxide (22.60 g, 256.8 mmol) were stirred in chloroform (45 cm^3) at 20 °C for 16 h. The mixture was filtered through Celite, which was then washed with chloroform, the combined filtrate and washings were evaporated under reduced pressure, and the residue was flash chromatographed [light petroleum–EtOAc (4:1)] to give the oxindole **8** (20 mg, 2%), identical (TLC, NMR and MS) with an authentic sample,[3] followed by the *amide* **7** (0.43 g, 42%), R_f [light petroleum–EtOAc (4:1)] 0.41; ν_{max}(film)/cm^{-1} 2900, 1665 (C=O), 1580, 1480, 1360 and 750; $\delta_H(CDCl_3)$ 8.91–7.63 (3 H, s, br s, s, d, d, d and d, aromatic CH and NCHO, mixture of two rotameric forms), 7.38–7.02 (2 H, m), 4.02 (2 H, d, *J* 1.0, NCH_2R) and 2.58–1.60 (14 H, m) (Found: M^+, 267.1625. $C_{18}Y_{21}NO$ requires M, 267.1623); *m*/*z* 267 (24%, M^+), 266 (100) and 237 (26, M − CHO).

2,2-*Dimethyl*-5-(2-*phenyltricyclo*[3.3.1.$1^{3,7}$]*decan-2-yl*)-1,3-*dioxane*-4,6-*dione* **10**.—A solution of 2,2-dimethyl-5-(tricyclo-[3.3.1.$1^{3,7}$]decanylidene)-1,3-dioxane-4,6-dione **9**[13] (200 mg, 0.72 mmol) in the minimum of diethyl ether (40 cm^3) was added dropwise during 18 min to a mixture of phenylmagnesium bromide [1.5 cm^3 of a 1.5 mol dm^{-3} solution in diethyl ether, prepared from bromobenzene (2.63 cm^3, 25 mmol) and magnesium (0.73 g, 30 mmol)] and copper(I) bromide (5 mg) in diethyl ether (5 cm^3) under nitrogen at 0 °C. The reaction mixture was allowed to warm to room temperature during 20 min and was then heated to 40 °C for 6 h to complete consumption of the adduct **9** (TLC). The reaction was quenched by the addition of brine (containing 2% conc. sulphuric acid) and extracted with diethyl ether. The extracts were washed with brine and dried ($MgSO_4$), the solvent was evaporated off, and the residue was flash chromatographed [hexane–Et_2O (7:1)] to give the *diester* **10** (224 mg, 87%). A recrystallised sample (from hexane–EtOAc) gave prisms, m.p. 163–164 °C (Found: C, 74.3; H, 7.5. $C_{22}H_{26}O_4$ requires C, 74.6; H, 7.4%); R_f [hexane–Et_2O (1:1)] 0.47; $\nu_{max}(CHCl_3)$/cm^{-1} 1730 (C=O); $\delta_H(CDCl_3)$ 7.31–7.14 (5 H, m, Ph), 4.27 (1 H, s, CHCO), 2.97 (2 H, s, 2 × CH α to CPh), 2.34 (2 H, br d, *J* 13.3, 2 × CH), 1.99–1.56 (10 H, m, adamantyl CH and CH_2), 1.41 (3 H, s, Me *trans* to Ph) and 0.57 (3 H, s, Me *cis* to Ph); $\delta_C(CDCl_3)$ 164.5 (CO), 140.5 (*ipso*-C), 128.6 and 127.2 (*o*-, *m*-C), 127.0 (*p*-C), 105.2 (CMe_2), 52.6 (C-2), 51.2 (*C*HCO), 38.3 (C-6), 33.5 and 33.2 (C-4 and -9, and C-8 and -10), 31.4 (C-1 and -3), and 30.5, 26.9, 26.8 and 26.2 (C-5, -7 and CMe_2) (Found: $M^+ - C_4H_6O_3$, 252.1512. $C_{18}H_{20}O$ requires *m*/*z* 252.1514); *m*/*z* 268 (2%, M − $C_4H_6O_2$), 252 (1, M − $C_4H_6O_3$) and 211 (100, $C_{16}H_{19}$). Chromatography also gave the alcohol **12** (7 mg, 4%), identical (TLC, ^1H NMR) with the sample prepared below.

Attempted Phenyl-addition to the Ester **9** *and* in situ *Oxidation of the Intermediate Enolate*.—The ester **9** (0.3 g, 1.1 mmol) was treated with phenyllithium (1.3 mmol) in diethyl ether at 0 °C until the adduct was consumed (TLC). The reaction mixture was flushed with oxygen and allowed to warm to room temperature overnight, then quenched with aq. sodium sulphite, and worked up to give a solid. Separation by dry-column flash chromatography[32] [hexane–Et_2O (10:1)] gave the alcohol **12** (107 mg, 44%) as prisms, m.p. 79.5–80.5 °C [from light petroleum (b.p. 40–60 °C)] (lit.,[33] 80.5–81 °C); R_f [hexane–Et_2O (4:1)] 0.30, $\nu_{max}(CCl_4)$/cm^{-1} 3610 (OH); $\delta_H(CDCl_3)$ 7.54 (2 H, d, *J* 8, *o*-Ph), 7.37 (2 H, t, *J* 7.4, *m*-Ph), 7.30–7.24 (1 H, m, *p*-Ph), 2.56 (2 H, br s, 2 × CH α to CPh), 2.41 (2 H, br d, *J* 12, 2 × CH), 1.91 (1 H, br s, CH), 1.72 (9 H, br s, CH and CH_2) and 1.60 (1 H, br s, OH, exchanges in D_2O); *m*/*z* 228 (100%, M^+), 210 (100, M − H_2O) and 133 (20, $C_{10}H_{13}$); and 2,2-dimethyl-5-(tricyclo[3.3.1.$1^{3,7}$]decan-2-yl)-1,3-dioxane-4,6-dione[34] (64 mg, 21%) as needles, m.p. 150.5–152 °C (from hexane); R_f [hexane–Et_2O (4:1)] 0.17; $\nu_{max}(CCl_4)$/cm^{-1} 1760 (C=O); $\delta_H(CDCl_3)$ 3.75 (1 H, d, *J* 11.1, CHCO), 2.23 (1 H, d, *J* 11.1, *CH*CHCO), 2.08–1.57 (14 H, m, CH and CH_2), 1.78 (3 H, s, Me) and 1.73 (3 H, s, Me); *m*/*z* 278 (4%, M^+), 263 (4, M − Me), 220 (100, M − C_3H_6O), and 192 (100, M − $C_4H_6O_2$).

Attempted Hydrolysis and Decarboxylation of the Ester **10**.—A suspension of the ester **10** (0.2 g, 0.56 mmol) in hydrochloric acid (10 cm^3; 6 mol dm^{-3}) was boiled for 16 h. The cooled mixture was then extracted with chloroform (3 × 10 cm^3). The extracts were dried ($MgSO_4$), and evaporated under reduced pressure. Chromatography [TLC; light petroleum–EtOAc (4:1)] gave the alcohol **12** (0.08 g, 63%), R_f [light

petroleum–EtOAc (4:1)] 0.53, identical (TLC, IR, ^{1}H NMR) with the sample described above; and *2-ethoxy-2-phenyladamantane* **13** (0.04 g, 28%), R_f [light petroleum–EtOAc (4:1)] 0.75; ν_{max}(film)/cm^{-1} 2900, 1440, 1065, 760 and 695; δ_H($CDCl_3$) 7.49–7.21 (5 H, m), 2.92 (2 H, q, *J* 6.9, OCH_2Me), 2.62 (2 H, br s), 2.34 (2 H, br d), 1.88 (1 H, br s), 1.58–1.74 (9 H, m) and 0.96 (3 H, t, *J* 7.0 OCH_2Me) (Found: M^+, 256.1817. $C_{18}H_{24}O$ requires M, 256.1827).

Methyl (2-*Phenyltricyclo*[3.3.1.1^{3,7}]*decan*-2-*yl*)*acetate* **14**.—Following the method of Oikawa *et al.*,[16] the ester **10** (100 mg, 0.28 mmol) and copper powder (8 mg) were heated in pyridine (4 cm^3)–methanol (1 cm^3) at 100 °C for 9 h. The solvent was evaporated off, the residue taken up in dichloromethane, the copper was filtered off, and the solvent was evaporated off to give the *ester* **14** (75 mg, 93%). A recrystallised sample gave needles, m.p. 126.5–127.5 °C (from hexane) (Found: C, 80.3; H, 8.7. $C_{19}H_{24}O_2$ requires C, 80.2; H, 8.5%); R_f [hexane–Et_2O (2:1)] 0.49; ν_{max}($CHCl_3$)/cm^{-1} 1730 (C=O); δ_H($CDCl_3$) 7.31–7.27 (4 H, m, 4 × ArH), 7.19–7.14 (1 H, m, ArH), 3.26 (3 H, s, OMe), 2.70 (2 H, s, CH_2CO), 2.61 (2 H, br s, 2 × CH α to CPh), 2.23 (2 H, br d, *J* 11.7, 2 × CH_AH_B), 1.96–1.71 (8 H, m, CH and CH_2) and 1.57 (2 H, br d, *J* 11.7, 2 × CH_AH_B); δ_C($CDCl_3$) 172.1 (CO), 145.1 (*ipso*-C), 128.0 and 126.3 (*o*-, *m*-C), 125.6 (*p*-C), 50.8 (OMe), 46.0 (C-2), 45.7 (CH_2CO), 38.6 (C-6), 33.5 and 32.9 (C-4 and -9, and C-8 and -10), 32.7 (C-1 and -3) and 27.8 and 27.1 (C-5 and -7) (Found: M^+, 284.1775. $C_{19}H_{24}O_2$ requires M, 284.1776); *m/z* 284 (1%, M^+), 269 (1, M − Me), 224 (1, M − HCO_2Me) and 211 (100, $C_{16}H_{19}$).

5-(2-o-*Fluorophenyltricyclo*[3.3.1.1^{3,7}]*decan*-2-*yl*)-2,2-*dimethyl*-1,3-*dioxane*-4,5-*dione* **11**.—A solution of *o*-bromofluorobenzene (317 mg, 1.81 mmol) in diethyl ether (2 cm^3) was added dropwise during 6 min to a solution of butyllithium (1.13 cm^3 of a 1.6 mol dm^{-3} solution in hexane, 1.81 mmol) in diethyl ether (20 cm^3) under nitrogen, while the internal temperature was kept below −65 °C, and the mixture was then kept for 50 min at < −65 °C. The adduct **9** (100 mg, 0.36 mmol) and a solution of boron trifluoride–diethyl ether (0.09 cm^3, 0.72 mmol, freshly distilled) in diethyl ether (20 cm^3) were added dropwise during 15 min, while the internal temperature was kept below −65 °C. The mixture was brought to −45 °C (solid CO_2–MeCN) and stirred for 2 h, then quenched with aq. ammonium chloride and allowed to warm to room temperature. The mixture was extracted with diethyl ether, the extracts were washed with brine and dried ($MgSO_4$), and the solvent was evaporated off. The residue was chromatographed [TLC, hexane–Et_2O (1:1)] to give the *ester* **11** (42 mg, 31%) as prisms, m.p. 164–168 °C (from hexane) (Found: C, 71.0; H, 6.65. $C_{22}H_{25}FO_4$ requires C, 71.0; H, 6.8%); R_f [hexane–Et_2O (1:1)] 0.38; ν_{max}(CCl_4)/cm^{-1} 1775 (C=O) and 1735 (C=O); δ_H($CDCl_3$) 7.24–6.96 (4 H, m, 4 × ArH), 4.29 (1 H, s, CHCO), 3.22 (1 H, br s, CH α to CPh), 2.95 (1 H, br s, CH α to CPh), 2.42–2.34 (2 H, m, 2 × CH), 1.98–1.65 (10 H, m, CH and CH_2), 1.49 (3 H, s, Me *trans* to Ar) and 0.79 (3 H, s, Me *cis* to Ar) (Found: $M^+ - C_3H_6O$, 314.1317. $C_{19}H_{19}FO_3$ requires *m/z*, 314.1318); *m/z* 314 (1%, $M - C_3H_6O$), 286 (13, $M - C_4H_6O_2$) and 229 (100, $C_{16}H_{18}F$).

Methyl (2-o-*Fluorophenyltricyclo*[3.3.1.1^{3,7}]*decan*-2-*yl*)*acetate* **15**.—The ester **11** (42 mg, 0.11 mmol) was heated with copper in pyridine–methanol, as described for the preparation of the ester **14**, to give the *ester* **15** (25 mg, 75%) as an oil, R_f [hexane–Et_2O (2:1)] 0.46; ν_{max}(CCl_4)/cm^{-1} 1730 (C=O); δ_H($CDCl_3$) 7.26 (1 H, dt, *J* 1.8 and 8.1, ArH), 7.21–7.12 (1 H, m, ArH), 7.08–6.92 (2 H, m, ArH), 3.28 (3 H, s, OMe), 3.03 (1 H, d, *J* 13.2, CH_ACH_BCO), 2.82 (1 H, br s, CHα to CAr), 2.71 (1 H, d, *J* 13.2, CH_ACH_BCO), 2.67 (1 H, br s, CH α to CAr), 2.34–2.27 (1 H, m, CH), 2.17–2.04 (2 H, m, 2 × CH or CH_2) and 1.95–1.57 (9 H, m, CH and CH_2) (Found: M^+, 302.1672. $C_{19}H_{23}FO_2$ requires M, 302.1682); *m/z* 302 (3%, M^+), 287 (1, M − Me) and 229 (100, $C_{16}H_{18}F$).

Attempted Deuteriation of the Ester **14**.—A solution of the ester **14** (200 mg, 0.70 mmol) in THF (5 cm^3) was added slowly to a suspension of potassium hydride (282 mg of a 20% dispersion in oil; 1.4 mmol, washed with THF) in THF (3 cm^3) under nitrogen, and the mixture was refluxed for 4 h. Deuterium oxide (0.4 cm^3) was added slowly to the mixture at 0 °C and the mixture was extracted with diethyl ether. The extracts were washed with brine, dried ($MgSO_4$), and the solvent was evaporated off to give recovered ester (168 mg, 84%) with no deuterium incorporation (^{1}H NMR).

Tricyclo[3.3.1.1^{3,7}]*decane*-2-*spiro*-1′-*indan*-3′-*one* **16**.—By adaptation of the method of Koo,[35] the methyl ester **14** (2.03 g, 7.15 mmol) was heated in polyphosphoric acid (PPA) (30 cm^3) at 100 °C, and occasionally stirred. When all the solid had dissolved (5 h), the hot mixture was poured onto crushed ice (500 g) and extracted with chloroform (5 × 50 cm^3). The extracts were washed with brine (100 cm^3), dried ($MgSO_4$), and evaporated under reduced pressure, to give the *ketone* **16** (1.68 g, 93%). A sample purified by TLC [light petroleum–EtOAc (9:1)] had R_f [light petroleum–EtOAc (9:1)] 0.40; ν_{max}(film)/cm^1 2880, 1695 (C=O), 1590, 1450, 1310, 1080 and 845; δ_H($CDCl_3$) 8.09 (1 H, d, *J* 8.0, 4′-H), 7.75 (1 H, m), 7.57 (1 H, m), 7.38 (1 H, m), 2.83 (2 H, s, CH_2CO), 2.58 (2 H, br d) and 2.09–1.69 (12 H, m); δ_C($CDCl_3$) 205.98 (C=O), 161.11 (2 C), 136.80 and 133.60 (4 × CH), 129.26, 127.30, 123.58, 51.40 (CH_2CO), 49.31 (C-2), 39.51 (5 × CH_2), 37.21 (two signals), 36.08 (two signals) and 32.79 (two signals) (4 × CH), 27.12 and 26.76 (Found: M^+, 252.1519. $C_{18}H_{20}O$ requires M, 252.1514); *oxime* (61%) needles, m.p. 188–191 °C (from aq. EtOH); R_f [$CHCl_3$–MeOH (9:1)] 0.50; ν_{max}(film)/cm^1 3560, 3350, 2880 and 1580; δ_H($CDCl_3$) 7.93 (1 H, d, *J* 7.7, 4′-H), 7.72 (1 H, dd, *J* 7.3 and 0.9), 7.25–7.40 (2 H, m), 3.08 (2 H, s, CH_2C=N), 2.62–2.57 (2 H, br d) and 2.19–1.67 (12 H, m) (Found: M^+, 267.1619. $C_{18}H_{21}NO$ requires M, 267.1623).

Tricyclo[3.3.1.1^{3,7}]*decane*-2-*spiro*-1′-*indan*-2′,3′-*dione* **17**.—The indanone **16** (0.52 g, 2.06 mmol) and selenium dioxide (0.57 g, 5.15 mmol) were stirred in acetic anhydride (30 cm^3) at 90 °C for 12 h. The mixture was then evaporated under reduced pressure, and the residue was partitioned between the diethyl ether (100 cm^3) and aq. sodium hydroxide (40 cm^3; 2 mol dm^{-3}). The ether layer was washed with brine (40 cm^3), dried ($MgSO_4$), and evaporated under reduced pressure. The residue was then filtered through silica gel, the filter was washed with dichloromethane, and the combined filtrate and washings were evaporated under reduced pressure to give the α-*diketone* **17** (0.22 g, 40.1%) as red needles, m.p. 139–143 °C (from hexane); R_f [light petroleum–EtOAc (9:1)] 0.40; ν_{max}(Nujol)/cm^{-1} 2895, 1715 (C=O), 1590 and 1185; δ_H($CDCl_3$) 8.21 (1 H, d, *J* 8.2, 4′-H), 7.94 (1 H, dd, *J* 7.6 and 1.3), 7.79–7.72 (1 H, m), 7.50 (1 H, t), 2.75 (2 H, 2 d), 2.56 (2 H, 2 d) and 2.14–1.60 (10 H, m) (Found: M^+, 266.1319. $C_{18}H_{18}O_2$ requires M, 266.1307); *m/z* 266 (5%, M^+) and 238 (100, M − CO).

Schmidt Reaction of the α-Diketone **17**.—Sodium azide (0.37 g, 5.65 mmol) was added in small portions during 1 h to a stirred solution of the diketone **17** (0.93 g, 3.50 mmol) in a mixture of trichloroacetic acid (9.3 g) and sulphuric acid (98%; 1.02 g) at 60 °C. After a further 24 h, the mixture was poured onto ice (100 g) and extracted with dichloromethane (3 × 40 cm^3). The extracts were dried ($MgSO_4$), then evaporated under reduced pressure, and the residue was filtered through silica gel, and the filter was worked with dichloromethane–methanol (1:1 v/v). The combined filtrate and washings were evaporated

under reduced pressure and the residue was distilled (Kugelrohr, 200 °C/0.01 mmHg). The distillate was dry-column flash chromatographed (CH_2Cl_2) to give the anhydride **20** (114 mg, 12%), identical (TLC, NMR, IR and MS) with the sample described below; 1,2,3,4-*tetrahydro*-1,3-*dioxoisoquindine*-4-*spiro*-2′-*tricyclo*[3.3.1.1^{3,7}]*decane* **19** (0.31 g, 32%), R_f [$CHCl_3$–MeOH (19:1)] 0.35; $\nu_{max}(CD_2Cl_2)/cm^{-1}$ 3340 (NH), 2880, 2830, 1710 (C=O), 1688, 1330, 1185, 1070 and 890; $\delta_H(CDCl_3)$ 8.04 (1 H, dd, *J* 7.5 and 1.5, 8-H), 7.72 (1 H, d, *J* 7.8), 7.51 (2 H, dt and br s, *J* 7.5 and 1.5, NH and ArH), 7.38 (1 H, dt, *J* 7.5 and 1.0) and 2.57–1.58 (14 H, m); $\delta_C(CDCl_3)$ 178.30 (3 C), 166.09, 144.30 and 131.70 (2 × CH), 129.41, 128.47 (C), 127.67 (2 × CH), 127.05, 55.24 (C), 37.70 (4 × CH_2), 34.95, 33.76, 29.69 and 27.15 (2 × CH) and 27.10 (Found: M^+, 281.1403. $C_{18}H_{19}NO_2$ requires M, 281.1416.

Further elution [CH_2Cl_2–MeOH (19:1)] gave 1,2,3,4-*tetrahydro*-2,3-*dioxoquinoline*-4-*spiro*-2′-*tricyclo*[3.3.1.1^{3,7}]*decane* **18** (142 mg, 14%) as a powder, m.p. >200 °C (decomp.) (from hexane–EtOAc); R_f [$CHCl_3$–MeOH (19:1)] 0.32; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3430, 3200, 2895, 2850, 1720 (C=O), 1675 (C=O), 1350, 1090 and 1035; $\delta_H(CDCl_3)$ 7.91–7.84 (2 H, m), 7.60–7.42 (3 H, m, including NH), 2.53 (2 H, d, *J* 13), 2.2–2.0 (4 H, m), 1.86 (2 H, d, *J* 13), 1.84 (4 H, br s) and 1.74 (2 H, br s) (Found: $M^+ - CO$, 253.1446. $C_{17}H_{19}NO$ requires *m/z*, 253.1467).

3,4-*Dihydro*-1,3-*dioxo*-1H-2-*oxanaphthalene*-4-*spiro*-2′-*tricyclo*[3.3.1.1^{3,7}]*decane* **20**.—The α-diketone **17** (1.27 g, 4.77 mmol) and *m*-chloroperoxybenzoic acid (MCPBA) (85%; 1.07 g, 6.20 mmol) were stirred in chloroform (50 cm^3) at 20 °C for 4 days, the mixture was washed successively with aq. sodium hydrogen sulphite (30 cm^3) and brine (30 cm^3) and dried ($MgSO_4$), the solvent was partly evaporated off under reduced pressure, and the residue was filtered through silica gel, and the filter washed with dichloromethane (200 cm^3). The combined filtrate and washings were evaporated under reduced pressure to give the *anhydride* **20** (0.86 g, 64%) as needles, m.p. 154–155 °C (from hexane); R_f [$CHCl_3$–MeOH (19:1)] 0.65; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 2900, 2840, 1795 (C=O), 1745 (C=O), 1590, 1000, 965 and 945; $\delta_H(CDCl_3)$ 7.98 (1 H, d, 8-H), 7.74 (1 H, d), 7.61 (1 H, dt), 7.44 (1 H, dt) and 2.50–1.73 (14 H, m) (Found: M^+, 282.1284. $C_{18}H_{18}O_3$ requires M, 282.1256); *m/z* 282 (0.6%, M^+), 254 (1.5, M − CO) and 238 (100, M − CO_2).

Methyl 2-(2′-*Carbamoyltricyclo*[3.3.1.1^{3,7}]*decan*-2′-*yl*)-*benzoate* **21**.—Sodium methoxide (5 cm^3 of a 1 mol dm^{-3} solution in methanol) and the anhydride (80 mg, 0.28 mmol) were stirred in methanol (10 cm^3) at 20 °C for 4 h, the mixture was evaporated under reduced pressure, and the residue was suspended in hydrochloric acid (3 mol dm^{-3}; 20 cm^3) and extracted with diethyl ether (3 × 20 cm^3). The extracts were washed with brine (20 cm^3), dried ($MeSO_4$), and evaporated under reduced pressure to give the half-acid ester (85 mg), which was stirred with oxalyl dichloride (4 cm^3) in dichloromethane (20 cm^3) at 20 °C for 2 h. The solvents were evaporated off under reduced pressure, and the residue was dissolved in diethyl ether (20 cm^3) and purged with ammonia at 20 °C for 2 h. The mixture was filtered through silica gel, the filter was washed with dichloromethane (50 cm^3), and the filtrate and washings were evaporated under reduced pressure to give the *amido ester* **21** (70 mg, 80%), R_f [light petroleum–EtOAc (4:1)] 0.21; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3470, 3250, 2900, 2850, 1700 ($ArCO_2Me$ and amide I), 1670 (amide II), 1595, 1095, 1070, 955 and 900; $\delta_H(CDCl_3)$ 7.74–7.21 (4 H, m), 5.27 (2 H, br s, NH_2), 3.93 (3 H, s, OMe) and 3.08–1.18 (14 H, m) (Found: M^+, 313.1692. $C_{19}H_{23}NO_3$ requires M, 313.1678); *m/z* 313 (1.5%, M^+), 298 (70, M − Me), 281 (90, M − MeOH) and 238 (100, M − CO_2Me − NH_2).

2-(2′-*Carbamoylphenyl*)*tricyclo*[3.3.1.1^{3,7}]*decane*-2-*carboxylic Acid* **22**.—Ammonia was bubbled through a stirred solution of the anhydride **20** (0.80 g, 2.80 mmol) in THF (50 cm^3) at 0 °C for 1 h, and the solution was then refluxed for 1 h. The solvent was evaporated off under reduced pressure and the residue was triturated successively with hydrochloric acid (50 cm^3; 3 mol dm^{-3}) and water (50 cm^3). The residue was dried (P_2O_5) to give the *amido acid* **22** (0.61 g, 73%) as plates, m.p. 185–187 °C (from EtOAc); ν_{max}(Nujol)/cm^{-1} 3350, 3200, 2905, 2840, 2600, 1740 (sat. CO_2H), 1700 (amide I), 1650 (amide II), 1570, 1450, 1370 and 1230; $\delta_H[(CD_3)_2SO]$ 7.56–7.23 (6 H, m), 3.34 (1 H, br s, NH or OH), 3.00 (2 H, br s), 2.23 (1 H, br d) and 1.90–1.39 (11 H, m) (Found: M^+, 299.1534. $C_{18}H_{21}NO_3$ requires M, 299.1521); *m/z* 299 (0.2%, M^+), 281 (6, M − H_2O), 256 (100, M − CONH) and 238 (100, M − CO_2H − H_2O). Hofmann reaction[36] and pyrolysis (250 °C/0.1 mmHg) gave none of the oxindole.

Attempted Hofmann Reaction on the Amido Ester **21**.—Bromine was added to the amido ester (67 mg, 0.21 mmol) in methanolic sodium methoxide (5 cm^3; 1 mol dm^{-3}) until the colour of bromine just persisted, and the mixture was kept for 10 min. Aq. sodium hydroxide (3 cm^3; 2 mol dm^{-3}) was then added and the mixture was refluxed for 3 days. The solution was neutralised (Universal indicator paper) with hydrochloric acid (3 mol dm^{-3}), and evaporated under reduced pressure. The resulting salts were heated (250 °C/0.05 mmHg) for 1 h, in order to dehydrate any amino acids formed. The residue was dissolved in water (50 cm^3) and extracted with diethyl ether (3 × 25 cm^3), and the extracts were washed with brine (30 cm^3), dried ($MgSO_4$), and evaporated under reduced pressure. Chromatography [TLC; light petroleum–EtOAc (7:3)] gave the isoquinolinedione **19** (8 mg, 14%), identical (TLC, NMR, IR and MS) with the compound described above. No oxindole was detected.

Attempted Hofmann Reaction on the Imide **19**.—A similar reaction carried out on the imide **19** gave the anhydride **20** (70%), and under the conditions of Jönsson and Moses,[19] no reaction took place.

Tricyclo[3.3.1.1^{3,7}]*decane*-2-*spiro*-1′-3′-*hydroxyiminoindane*-2′-*one* **23**.—Following a standard method,[37] the diketone **17** (0.22 g, 0.827 mmol) gave the *oxime* **23** (185 mg, 80%) as needles, m.p. 190 °C (decomp.) (from aq. EtOH); R_f [$CHCl_3$–MeOH (9:1)] 0.60; ν_{max}(Nujol)/cm^{-1} 3510, 3250, 2880, 1725 (sat. C=O), 1580, 1080, 950 and 920; $\delta_H(CDCl_3)$ 8.51 (1 H, d, *J* 7.5, 4′-H), 8.09 (1 H, d, *J* 7.5), 7.55–7.35 (2 H, m), 4.55 (1 H, br s, OH), 2.91–2.58 (4 H, 2 × br d) and 2.17–1.24 (10 H, m), with signals also at 7.95 (d, *J* 7.5) and 7.75 (d, *J* 7.5) suggesting the presence of *ca.* 10% of another oxime (Found: M^+, 281.1403. $C_{18}H_{19}NO_2$ requires M, 281.1416); *m/z* 281 (32%, M^+), 264 (100) and 236 (70).

1,2-*Dihydro*-3-*oxoisoindole*-1-*spiro*-2′-*tricyclo*[3.3.1.1^{3,7}]-*decane* **24**.—The α-ketooxime **23** (185 mg, 0.658 mmol) was added to cold PPA (10.1 g) and the mixture was heated rapidly to 130 °C, with evolution of a gas. After 20 min the mixture was poured onto ice (100 g) and extracted with dichloromethane (3 × 40 cm^3). The extracts were washed with brine (30 ml), dried ($MgSO_4$), and evaporated under reduced pressure. Chromatography [TLC; $CHCl_3$–MeOH (19:1)] gave the *isooxindole* **24** (56 mg, 34%), R_f [$CHCl_3$–MeOH (19:1)] 0.40; $\nu_{max}(CH_2Cl_2)/cm^{-1}$ 3365 (NH), 3180, 2890, 1700 (C=O), 1595, 1350 and 890; $\delta_H(CDCl_3)$, 8.09 (1 H, dd, *J* 7.6 and 1.1, 4′-H), 7.88–7.25 (3 H, m), 6.64 (1 H, br s, NH), 3.18 (1 H, br s), 2.70 (1 H, br s) and 2.41–1.38 (12 H, m); $\delta_C(CDCl_3)$ 164.98 (C=O),

140.10 (C), 132.27 (CH), 129.11 (C), 128.16 (3 × CH), 126.34, 124.28, 52.00 (C), 47.24 (CH), 43.74 (5 × CH_2), 39.47, 37.55, 36.13, 29.80, 29.10 (3 × CH), 29.80, 28.78 and 28.62 (Found: M^+, 253.1448. $C_{17}H_{19}NO$ requires M, 253.1467).

2-(α-*Nitrobenzylidene*)*tricyclo*[3.3.1.1^{3,7}]*decane* **26**.—A solution of nitromethyleneadamantane **25**[20] (100 mg, 0.52 mmol) in THF (3 cm^3) was added dropwise during 10 min to a stirred solution of phenyllithium [0.29 cm^3 of a 1.9 mol dm^{-3} solution in cyclohexane–Et_2O (70:30)] under nitrogen at −78 °C. After 40 min the red-brown solution was quenched by the addition of acetic acid (2.5 cm^3) in dichloromethane (7.5 cm^3), allowed to warm to room temperature during 15 min, then poured into a mixture of dichloromethane (30 cm^3) and water (50 cm^3). The mixture was extracted with dichloromethane, the extracts were washed several times with water, dried ($MgSO_4$), and evaporated, and the residue was chromatographed [TLC; hexane–Et_2O (15:1)] to give what seems likely to be the contra-Michael product, nitroalkene **26**, or conceivably the homoadamantene isomer, 4-nitro-5-phenyltricyclo[4.3.1.1^{3,8}]undec-4-ene (26.6 mg, 19%) as plates, m.p. 108.5–109.5 °C (from hexane) (Found: C, 75.9; H, 7.1; N, 5.0. $C_{17}H_{19}NO_2$ requires C, 75.8; H, 7.1; N, 5.2%); R_f [hexane–Et_2O (10:1)] 0.28; $\nu_{max}(CCl_4)/cm^{-1}$ 1.495 (NO_2) and 1355 (NO_2); $\delta_H(CDCl_3)$ 7.47–7.32 (5 H, m, Ph), 3.02 (1 H, br s, CHC=C *cis* to NO_2 or 3-H), 2.57 (1 H, br s, CH=C *trans* to NO_2 or 6-H) and 1.99–1.61 (12 H, m, CH and CH_2); $\delta_C(CDCl_3)$ 148.7, 131.8, 129.2, 129.5, 128.7, 127.8, 39.0, 38.9, 27.5, 36.3, 33.9 and 33.8; *m/z* 269 (8%, M^+), 239 (11, M − NO) and 223 (100, M − NO_2); and recovered nitromethyleneadamantane **25** (22.5 mg, 23%).

Triphenylaluminium.—Following the procedure of Eisch and Kaska,[38] diphenylmercury (7.34 g, 20.7 mmol, pretreated with hydrazine hydrate[39]) and aluminium turnings (3.78 g, 140 mmol, freshly cut into short lengths) in xylene (30 cm^3) were degassed and heated to reflux (140 °C) under nitrogen for 2–3 h. Droplets of mercury appeared after *ca.* 10 min at reflux. On cooling to room temperature triphenylaluminium crystallised as needles, and was redissolved on heating to 100 °C. Attempts to transfer the triphenylaluminium solution by syringe led to decomposition, and all subsequent transfers were done with double-tipped needles into degassed solvents. The triphenylaluminium could be kept under nitrogen for 1–2 days, but in most cases was prepared directly before use.

2-*Nitromethyl*-2-*phenyltricyclo*[3.3.1.1^{3,7}]*decane* **27**.—Following the procedure of Pecunioso and Menicagli,[21] a degassed solution of nitromethyleneadamantane **25** (1.0 g, 5.18 mmol) in hexane (50 cm^3) was added slowly by double-tipped needle during 10 min to a suspension of triphenylaluminium [25 cm^3 of a *ca.* 0.36 mol dm^{-3} solution in xylene, freshly prepared from diphenylmercury (7.71 g, 21.7 mmol) and aluminium turnings (2.45 g, 90.7 mmol), 9 mmol] in degassed hexane (15 cm^3) under nitrogen at 0 °C, immediately giving an orange suspension. The colour faded to yellow as the addition was completed, and the mixture was stirred at 0 °C for 80 min. Diethyl ether (30 cm^3) was added, giving a pale yellow solution, which was quenched by the addition of cold (0 °C), dil. hydrochloric acid (150 cm^3; 0.1 mol dm^{-3}). The mixture was extracted with diethyl ether, and the extracts were washed with brine, dried ($MgSO_4$), and evaporated to give a pale yellow solid (1.46 g). Dry-column flash chromatography[32] [hexane–Et_2O (25:1)] to remove the last of the xylene gave the *nitroalkane* **27** (1.27 g, 91%) as needles, m.p. 126–128.5 °C (from hexane) (Found: C, 74.6; H, 7.7; N, 5.1. $C_{17}H_{21}NO_2$ requires C, 75.2; H, 7.8; N, 5.2%); R_f [hexane–Et_2O (10:1)] 0.22; $\nu_{max}(CHCl_3)/cm^{-1}$ 1545 (NO_2) and 1375 (NO_2); $\delta_H(CDCl_3)$ 7.45–7.20 (5 H, m, Ph), 4.72 (2 H, s, CH_2NO_2), 2.67 (2 H, br s, 2 × CH α to CPh) and 2.21–1.50 (12 H, m, CH and CH_2) (Found: M^+, 271.1581. $C_{17}H_{21}NO_2$ requires M, 271.1572); *m/z* 271 (14%, M^+), 241 (9, M − NO), 225 (14, M − NO_2) and 211 (100, M − CH_2NO_2). Repetition of the reaction in the presence of diethyl ether (1 mol equiv. per Ph_3Al), and heating at 60 °C for 1 h,[21] gave only recovered nitromethyleneadamantane **25** and no trace of the phenyl addition product.

Cyclisation of 2-Nitroethylbenzene to Oxindole.—Sodium methoxide (0.62 cm^3 of a 1.70 mol dm^{-3} solution in methanol, 1.05 mmol) was added to 2-nitroethylbenzene[40] (100 mg, 0.66 mmol) in diethyl ether (5 cm^3) and the mixture was stirred at room temperature for 30 min. The solvent was evaporated off and the residue was suspended in dichloromethane (10 cm^3) at 0 °C. The solid dissolved on addition of trifluoroacetic anhydride (0.28 cm^3, 1.98 mmol) and the solution was kept for 5 min. Iron(III) chloride (0.32 g, 1.98 mmol) was added in a single portion, and the brown-black mixture was stirred at 0 °C for 5 h, then quenched and worked up with water. Chromatography of the crude product (54 mg) [TLC; hexane–Et_2O (2:1)] gave recovered 2-nitroethylbenzene (19 mg, 19%) and oxindole (2 mg, *ca.* 2%), identical (TLC, ^1H NMR) with an authentic sample. The recovery of oxindole was inefficient: the crude product was a mixture of starting material and oxindole in the ratio *ca.* 2:1 (^1H NMR).

2-*Phenyltricyclo*[3.3.1.1^{3,7}]*decane*-2-*carbonitrile Oxide* **28**.—Sodium methoxide (1.37 cm^3 of a 0.59 mol dm^{-3} solution in methanol, 0.81 mmol) was added to a solution of the nitromethyl(phenyl)adamantane **27** (200 mg, 0.74 mmol) in diethyl ether (20 cm^3), the mixture was stirred at room temperature for 40 min, and the solvent was evaporated off. The residue was suspended in dichloromethane (10 cm^3), acetyl chloride (0.10 cm^3, 1.5 mmol) was added, and the solution was stirred at room temperature for 40 min. A cloudy precipitate appeared within several minutes. The reaction mixture was quenched with brine and extracted with dichloromethane, the extracts were dried ($MgSO_4$), and the solvent was evaporated off. The residue was separated by dry-column flash chromatography,[32] [hexane–Et_2O (12:1)] to give the *nitrile oxide* **28** (124 mg, 66%) as prisms, m.p. 149–151.5 °C [from light petroleum (b.p. 40–60 °C)] (Found: C, 80.4; H, 7.55; N, 5.6. $C_{17}H_{19}NO$ requires C, 80.6; H, 7.55; N, 5.6%); R_f [hexane–Et_2O (3:1)] 0.35; $\nu_{max}(CCl_4)/cm^{-1}$ 2275 (CNO); $\delta_H(CDCl_3)$ 7.45–7.24 (5 H, m, Ph), 2.76 (2 H, br s, 2 × CH α to CPH), 2.35–2.28 (2 H, m, 2 × CH) and 2.04–1.59 (10 H, m, CH and CH_2); $\delta_C(CDCl_3)$ 139.3 (*ipso*-C), 129.1 and 126.0 (*o*-, *m*-C), 127.6 (*p*-C), 47.4 (C-2), 37.2 (C-6), 35.5 (CNO), 34.1 (C-1 and -3), 31.5 (C-4, -9, -8 and -10), 26.7 and 26.4 (C-5 and -7); *m/z* 237 (6%, M − O), 225 (3, M − CO) and 223 (100, M − NO); recovered nitromethyl(phenyl)adamantane (14 mg, 6%), and a mixture, R_f [hexane–Et_2O (1:3)] 0.26, of the *O*-acetyl hydroxamate (*ca.* 14 mg, 6%) (see below), and a product (*ca.* 7 mg, 4%), tentatively identified as the corresponding isocyanate, $\nu_{max}(CHCl_3)/cm^{-1}$ 2250 (NCO); *m/z* 253, 225 and 211.

O-*Acetyl* 2-*Phenyltricyclo*[3.3.1.1^{3,7}]*decane*-2-*carbohydroxamate*.—Following the procedure of Dignam *et al.*,[41] the nitrile oxide[28] (124 mg, 0.49 mmol), acetic acid (0.28 cm^3, 4.9 mmol), and sodium acetate (8 mg, 0.10 mmol) in diethyl ether (15 cm^3) were stirred at room temperature for 17 h, diluted with water (50 cm^3), and extracted with ethyl acetate. The extracts were washed with brine, dried ($MgSO_4$), and evaporated (< 40 °C), and the residue was dried *in vacuo* over potassium hydroxide, to give the O-*acetyl hydroxamate* (131 mg, 85%) as needles, m.p. 145 °C (decomp.) (from EtOAc; < 60 °C); R_f [hexane–Et_2O

(1:3)] 0.26; $\nu_{max}(CHCl_3)/cm^{-1}$ 3350 (NH), 1790 (C=O) and 1695 (C=O); $\delta_H(CDCl_3)$ 9.20 (1 H, s, NH), 7.48 (2 H, dd, *J* 7.3 and 1.4, *o*-Ph), 7.35 (2 H, t, *J* 7.5, *m*-Ph), 7.26–7.20 (1 H, m, *p*-Ph), 2.96 (2 H, br s, 2 × CH α to CPh), 2.26–2.15 (2 H, m, 2 × CH), 2.09 (3 H, s, COMe) and 1.94–1.60 (10 H, m, CH and CH_2); $\delta_C(CDCl_3)$ 173.7 (CO), 169.0 (CO), 141.4 (*ipso*-C), 128.9 and 126.6 (*o*-, *m*-C), 126.9 (*p*-C), 55.7 (C-2), 37.4 (C-6), 34.7 and 32.6 (C-4, -9, -8 and -10), 31.6 (C-1 and -3), 27.2 and 26.5 (C-5 and -7) and 18.3 (Me) (Found: M^+ − HOAc, 253.1462. $C_{17}H_{19}NO$ requires *m/z* 253.1466); *m/z* 253 (8%, M − HOAc) and 211 (100, $C_{16}H_{19}$). The reaction was repeated (a) with conc. sulphuric acid [42] (3 drops) in place of the sodium acetate to give, after 3 h at room temperature, the *O*-acetyl hydroxamate (100%), and (b) with acetic anhydride [42] (100 mol equiv., freshly distilled) in diethyl ether at reflux for 4 h, to give the *O*-acetyl hydroxamate (100%).

Attempted Cyclisation of O-*Acetyl* 2-*Phenyltricyclo*[3.3.1.1^{3,7}]*decane*-2-*carbohydroxamate*.—Following the method of Cherest and Lusinchi,[25] acetic acid (9 mm^3, 0.16 mmol) and iron(III) chloride (52 mg, 0.32 mmol) were added to a solution of the *O*-acetyl hydroxamate (50 mg, 0.16 mmol) in dichloromethane (8 cm^3) and the mixture was stirred vigorously at room temperature for 17 h. Aqueous work-up gave the hydroxamic acid (37 mg, 85%) as an orange oil, identical (TLC, IR, ^1H NMR) with the sample prepared below. A similar reaction in the absence of acetic acid gave the oxindole **8** (*ca.* 1 mg, <1%) as a pale yellow oil (Found: M^+, 253.1465. $C_{17}H_{19}NO$ requires M, 253.1467), identical (TLC) with an authentic sample, Other variations were no more successful.

2-*Phenyltricyclo*[3.3.1.1^{3,7}]*decane*-2-*carbohydroxamic Acid*.—The nitrile oxide **28** (82 mg, 0.32 mmol), acetone (5 cm^3), and dil. sulphuric acid (2 mol dm^{-3}; 3 cm^3) were heated at 75 °C for 22 h. The acetone was evaporated off, and the residue was diluted with water and extracted with diethyl ether. The extracts were washed with brine, dried ($MgSO_4$), and evaporated to give the *title hydroxamic acid* (49 mg, 56%) as needles, m.p. 163–164 °C (from hexane–Et_2O); R_f [hexane–Et_2O (1:5)] 0.20 (streaks); $\nu_{max}(CHCl_3)/cm^{-1}$ 3440 and 3220 (OH and NH) and 1650 (C=O); $\delta_H(CDCl_3)$ 8.2 (1 H, br s, OH or NH), 7.9 (1 H, br s, NH or OH), 7.42 (2 H, d, *J* 7.3, *o*-Ph), 7.33 (2 H, d, *J* 7.5, *m*-Ph), 7.23 (1 H, t, *J* 7.1, *p*-Ph), 2.87 (2 H, s, 2 × CH α to CPh), 2.10–2.04 (2 H, m, 2 × CH) and 1.90–1.57 (10 H, m, CH and CH_2) (Found: M^+ − NHOH, 239.1435. $C_{17}H_{19}NO$ requires *m/z*, 239.1436); *m/z* 239 (35%, M − NHOH) and 211 (100, $C_{16}H_{19}$).

O-*Methyl* 2-*Phenyltricyclo*[3.3.1.1^{3,7}]*decane*-2-*carbohydroxamate* **29**.—The hydroxamic acid (44 mg, 0.16 mmol), iodomethane (0.10 cm^3, 1.6 mmol), and sodium carbonate (36 mg, 0.34 mmol) were stirred in methanol (15 cm^3) at room temperature for 70 h. The methanol was evaporated off, and the residue was diluted with water, acidified with dil. hydrochloric acid (3 mol dm^{-3}), and extracted with dichloromethane. The extracts were washed successively with aq. sodium thiosulphate and brine, dried ($MgSO_4$), and evaporated to give the O-*methyl hydroxamate* **29** (43 mg, 93%) as needles, m.p. 210.5–211.5 °C (from hexane–Et_2O) (Found: C, 75.4; H, 8.2; N, 4.7%; M, 285.1724. $C_{18}H_{23}NO_2$ requires C, 75.8; H, 8.1; N, 4.9%); M, 285.1729); R_f [hexane–Et_2O (1:5)] 0.24; $\nu_{max}(CHCl_3)/cm^{-1}$ 3420 (NH) and 1685 (C=O); $\delta_H(CDCl_3)$ 8.42 (1 H, s, NH), 7.44 (2 H, d, *J* 7.4, *o*-Ph), 7.32 (2 H, t, *J* 7.6, *m*-Ph), 7.19 (1 H, t, *J* 7.2, *p*-Ph), 3.51 (3 H, s, OMe), 2.88 (2 H, br s, 2 × CH α to CPh), 2.15 (2 H, br d, *J* 12.6, 2 × CH), 1.92–1.68 (8 H, m, CH and CH_2) and 1.60 (2 H, br d, *J* 12.6, 2 × CH); *m/z* 285 (0.3%, M^+), 254 (1, M − OMe), 239 (2, M − NHOMe) and 211 (100, $C_{16}H_{19}$).

The synthesis was repeated, starting from the nitro compound **27** (309 mg, 1.14 mmol), using identical conditions to those described above but without purification of the crude products, to give the *O*-methyl hydroxamate **29** (223 mg, 69%).

2,3-*Dihydro*-1-*methoxy*-2-*oxoindole*-3-*spiro*-2′-*tricyclo*[3.3.1.1^{3,7}]*decane* **30**.—t-Butyl hypochlorite (26 mm^3, 0.23 mmol) was added to a solution of the *O*-methyl hydroxamate **29** (63 mg, 0.22 mmol) in dichloromethane (8 cm^3) and the mixture was stirred at room temperature in the dark for 16 h, after which time all the starting material had been consumed (TLC). The solvent was evaporated off and the residue, taken up in nitromethane (3 cm^3), was added to a refluxing suspension of zinc acetate (202 mg, 1.10 mmol, powdered and dried at 175 °C for 4 h [43]) in nitromethane (3 cm^3). After 10 min the mixture was filtered through Celite, and the filter was washed with ethyl acetate. The solvent was evaporated off, the residue was dissolved in dichloromethane and filtered through silica, and the solvent was evaporated off to give the *methoxyoxindole* **30** (53 mg, 85%) as prisms, m.p. 148–151 °C (from hexane) (Found: C, 76.1; H, 7.3; N, 4.8%; M, 283.1570. $C_{18}H_{21}NO_2$ requires C, 76.3; H, 7.5; N, 4.9%; M, 283.1572); R_f [hexane–Et_2O (1:5)] 0.67; $\nu_{max}(CHCl_3)/cm^{-1}$ 1710 (C=O); $\delta_H(CDCl_3)$ 7.78 (1 H, d, *J* 7.7, ArH *o* to C), 7.29 (1 H, dt, *J* 1.0 and 7.7, ArH *p* to C), 7.03 (1 H, dt, *J* 1.3 and 7.7, ArH *p* to N), 6.98 (1 H, d, *J* 7.7, ArH *o* to N), 3.98 (3 H, s, OMe), 3.04 (2 H, br d, *J* 13, 2 × CH α to CAr), 2.54 (2 H, br d, *J* 13, 2 × CH), 2.10–1.67 (8 H, m, CH and CH_2) and 1.56 (2 H, br d, *J* 13, 2 × CH); $\delta_C(CDCl_3)$ 174.1 (CO), 139.7 and 130.2 (C *ipso* to N, C), 128.3, 127.7, 121.7 and 106.8 (4 × Ar-C), 63.1 (OMe), 52.3 (C-2), 39.5 (C-6), 33.6 (C-1 and -3), 33.4 and 31.8 (C-4, -9, and -8 and -10), 27.1 and 26.9 (C-5 and -7); *m/z* 283 (44%, M^+), 255 (55, M − CO) and 224 (100, M − MeOCO).

5-*Chloro*-2,3-*dihydro*-1-*methoxy*-2-*oxoindole*-3-*spiro*-2′-*tricyclo*[3.3.1.1^{3,7}]*decane* **31**.—t-Butyl hypochlorite (0.06 cm^3, 0.52 mmol) was added to a solution of the *O*-methyl hydroxamate **29** (124 mg, 0.43 mmol) in dichloromethane (10 cm^3) and the mixture was stirred at room temperature for 50 min, giving incomplete chlorination (TLC). More t-butyl hypochlorite (0.06 cm^3, 0.52 mmol) was added and the mixture was kept at 40 °C for 70 min, after which time all the starting material had been consumed (TLC). The solvent was evaporated off, and a solution of silver(I) carbonate (240 mg, 0.87 mmol) in trifluoroacetic acid (3 cm^3) was added to the residue at 0 °C, immediately giving a yellow precipitate. After 15 min at room temperature the reaction was worked up as described above, and the product was chromatographed [TLC; hexane–Et_2O (1:2)] to give an inseparable mixture, R_f [hexane–Et_2O (1:5)] 0.67, of the methoxyoxindole **30** (50 mg, 41%), identical (TLC, IR, ^1H NMR, MX) with the pure sample prepared above, and the *chloro*(*methoxy*)*oxindole* **31** (19 mg, 14%), $\nu_{max}(CHCl_3)/cm^{-1}$ 1710 (C=O); $\delta_H(CDCl_3)$ (by subtraction of the ^1H NMR spectrum of the pure methoxyoxindole **30** from that of the mixture) 7.75 (1 H, d, *J* 1.9, ArH *o* to C), 7.36–7.26 (1 H, m, ArH *p* to C), 6.90 (1 H, d, *J* 8.2, ArH *o* to N), 3.97 (3 H, s, OMe), 3.08–3.01 (2 H, m, 2 × CH α to CAr), 2.57–2.40 (2 H, m, 2 × CH) and 2.09–1.50 (10 H, m, CH and CH_2) [Found: $M^+(^{35}Cl)$, 317.1200. $C_{18}H_{20}ClNO_2$ requires $M(^{35}Cl)$, 317.1183]; *m/z* (for ^{35}Cl) 317 (9%, M^+), 289 (14, M − CO) 258 (16, M − MeOCO).

The Spirooxindole **8**.—Sodium amalgam (6%; powdered; 0.4 g, 1 mmol) was stirred with the methoxyoxindole **30** (14.2 mg, 0.052 mmol) in a mixture of methanol (2 cm^3) and diethyl ether (2 cm^3) under nitrogen at 0 °C for 50 min. Starting material was still detectable (TLC), so more sodium amalgam (0.4 g) was added and the mixture was stirred for a further 30

min. The mixture was filtered through Celite and then through silica, the filters were washed with diethyl ether, the solvent was evaporated off, and the residue was chromatographed (TLC; hexane–Et_2O) to give the oxindole **8** (12.4 mg, '102%'), R_f [hexane–Et_2O (1:5)] 0.36, identical (TLC, ^1H NMR) with an authentic sample.[3]

Reduction of a Mixture of the Methoxyoxindole **30** *and the Chloro(methoxy)oxindole* **31**.—A similar reduction to that described above, but on the mixture of oxindoles (32 mg), and in the presence of disodium hydrogen phosphate (75 mg), which is reported to speed up the reduction (but which made little difference here) gave, after chromatography [TLC; hexane–Et_2O (2:1), eluting six times], the adamantanespirooxindole **8** (18.6 mg), identical (TLC, ^1H NMR) with an authentic sample, and *5-chloro-2,3-dihydro-2-oxoindole-3-spiro-2′-tricyclo*[3.3.1.1^{3,7}]*decane* (6.6 mg), R_f [hexane–Et_2O (1:5)] 0.30; $\nu_{max}(CHCl_3)/cm^{-1}$ 3430 (NH), 1700 (C=O) and 1620 (C=O); $\delta_H(CDCl_3)$ 8.22 (1 H, br s, NH), 7.73 (1 H, d, *J* 1.9, ArH *o* to C), 7.19 (1 H, dd, *J* 8.2 and 1.9, ArH *p* to C), 6.80 (1 H, d, *J* 8.2, ArH *o* to N), 3.02 (2 H, br d, *J* 13, 2 × CH α to CAr), 2.50 (2 H, br d, *J* 11, 2 × CH), 2.12–1.71 (8 H, m, CH and CH_2) and 1.56 (2 H, br d, *J* 13, 2 × CH) [Found: M^+(^{35}C), 287.1093. $C_{17}H_{18}ClNO$ requires M(^{35}Cl), 287.1077]; *m/z* (for ^{35}Cl) 287 (100%, M^+) and 167 (45). The total yield of oxindoles from the *N*-methoxyoxindoles was *ca.* 88%.

4-Nitromethylene-2-oxatricyclo[3.3.1.1^{3,7}]*decane* **33**.—The oxaadamantanone **30**[5] (200 mg, 1.31 mmol) and 1,2-diaminoethane (2 mg, 0.03 mmol) in nitromethane (10 cm^3) were refluxed under nitrogen for 3 h. More 1,2-diaminoethane (3 mg) was added and reflux was continued for a further 3 h. The solvent was removed and the residue was flash chromatographed [hexane Et_2O (5:1)] to give the *nitromethyleneoxaadamantane* **33** (193 mg, 75%) (55:45 *trans*:*cis*) as a pale yellow oil, R_f [hexane–Et_2O (1:2)] 0.41; $\nu_{max}(CCl_4)/cm^{-1}$ 1640 and 1345 (NO_2); $\delta_H(CDCl_3)$ 6.94 (0.6 H, s, *trans*-$CHNO_2$), 6.88 (0.4 H, s, *cis*-$CHNO_2$), 5.59 (0.4 H, d, *J* 4.4, *cis*-3-H), 4.17–4.06 (2.2 H, m, 1-H, *trans*-3-H, and *trans*-5-H), 2.67–2.65 (0.4 H, m, *cis*-5-H) and 2.40–1.72 (9 H, m, CH and CH_2); $\delta_C(CDCl_3)$ 157.1, 156.4 (*trans*:*cis*-C-4), 129.7, 128.9 (*trans,cis*-CNO_2), 71.7, 68.0, 67.3, 66.4 (*trans,cis*-C-1 and -3), 38.7, 38.3, 38.2, 37.9, 37.1, 36.9, 34.65 and 34.61 (*trans,cis*-C-6, -8, -9 and -10), 36.1, 30.9 (*trans,cis*-C-5) and 25.7 and 25.6 (*trans,cis*-C-7) (Found: M^+, 195.0901. $C_{10}H_{13}NO_3$ requires M, 195.0895); *m/z* 195 (8%, M^+), 178 (29, M − OH), 151 (95, M − H_2NO_2), 79 (100, C_6H_7); and recovered oxaadamantanone **32** (36 mg, 18%).

4-Nitromethyl-4-phenyl-2-oxatricyclo[3.3.3.1^{3,7}]*decane* **34**.—The nitromethyleneoxaadamantane **33** (110 mg, 0.56 mmol) was added to triphenylaluminium, as described above for the adamantane series. Chromatography [TLC; hexane–Et_2O (3:1) then (2:1)] gave the *nitroalkane* **34** (25 mg, 16%) (11:1 mixture of isomers at C-4), R_f [hexane–Et_2O (1:2)] 0.35; $\nu_{max}(CHCl_3)/cm^{-1}$ 1550 (NO_2) and 1380 (NO_2); $\delta_H(CDCl_3)$ 7.41–7.21 (5 H, m, Ph), 4.92 (0.9 H, d, *J* 11.5, $CH_AH_BNO_2$ major isomer), 4.86 (1 H, br s, 3-H), 4.77 (0.1 H, d, *J* 10.9, $CH_AH_BNO_2$ minor isomer), 4.60 (0.1 H, d, *J* 10.9, $CH_AH_BNO_2$ minor isomer), 4.58 (0.9 H, d, *J* 11.5, $CH_AH_BNO_2$ major isomer), 3.92–3.90 (1 H, m, 1-H), 2.59 (1 H, br s, CH) and 2.34–1.41 (9 H, CH and CH_2); $\delta_C(CDCl_3)$ (for the major isomer only) 140.4 (*ipso*-C), 128.6 and 127.2 (*o*- and *m*-C), 127.0 (*p*-C), 83.6 (CH_2NO_2), 66.3 and 67.7 (C-1 and -3), 46.3 (C-4), 36.7, 32.2, 31.5 and 31.0 (C-6, -8, -9 and -10), 33.8 (C-5) and 25.2 (C-7) (Found: M^+, 273.1364. $C_{16}H_{19}NO_3$ requires M, 273.1365); *m/z* 273 (3%, M^+) and 227 (100, M − NO_2), and recovered nitromethyleneoxaadamantane **33** (62 mg, 56%) (6:4 *trans*:*cis* mixture). The reaction was repeated with cooling during the addition of the nitromethyleneadamantane, so that the external temperature fell from −10 to −65 °C during the addition, was kept at −65 to −45 °C for 3.5 h, and was then brought to 0 °C for a further 3.5 h. Work-up and separation as described above gave recovered nitromethyleneoxaadamantane **33** (5%) and the phenyl-addition product **34** (35%) (90:1 mixture of isomers at C-4 by ^{1}HNMR). Crystallisation gave needles, m.p. 190–192 °C (from hexane) (Found: C, 70.1; H, 6.75; N, 5.3. $C_{16}H_{19}NO_3$ requires C, 70.3; H, 7.0; N, 5.1%). A COSY spectrum taken at 400 MHz in [$^2H_5$]pyridine allowed the assignment of downfield signals at δ 3.8 and 5.1 to the protons on C-1 and C-3, respectively, since the former was coupled to two methylene groups, whereas the latter was coupled only to one. The signal from the proton on C-3 at δ 5.1 was coupled to the AB system from the protons on C-10 at δ 2.38 and 2.19, and by W-coupling to the proton on C-5 at δ 2.58. The latter signal was, in turn, coupled to signals at δ 2.19 and 1.82 and at δ 1.88 and 1.29. Since the latter pair were coupled to the proton on C-1, they can be assigned to the protons on C-9, and the signals at δ 2.19 and 1.82 can therefore be assigned to the protons on C-6. Irradiation at either δ 2.38 or δ 2.19 gave 1% NOE enhancement in the doublet at δ 5.32, the downfield signal from the diastereotopic pair of protons adjacent to the NO_2 group, with no effect on the signals of the phenyl group.

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