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Synthesis of carbo- and heterocycles via palladium catalysed cascade allene insertion–nucleophile incorporation–Michael addition processes☆

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Abstract—Novel palladium catalysed two- and three-component thermal (conventional heating and microwave) cascade processes are described involving allenylation of an aryl iodide to generate a (π-allyl)palladium species, which are intercepted (inter- or intramolecularly) by a carbon or nitrogen nucleophile followed by intramolecular Michael addition to afford carbo- and heterocycles in good yields.
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1. Introduction

In recent years allenes have become useful building blocks in palladium catalysed processes.[2] We have demonstrated that they are powerful relay switches in our palladium catalysed cyclisation-anion capture cascades.[3] Reactions of aryl/vinyl palladium(II) intermediates with allenes lead to the formation of (π-allyl)palladium species, which undergo a wide range of transformations, including transmetallation,[6] or attack by nucleophiles[4] or electrophiles.[5] The versatility and power of relay switch components can be substantially enhanced by interfacing their palladium catalysed processes with 100% atom economic core organic reactions such as cycloadditions (1,3-dipolar and Diels–Alder reactions), aldol reactions and Michael addition reactions. We have developed a number of one-pot cascade protocols, which employ several types of 1,3-dipoles and palladium catalysed allenylation processes, including combinations with azomethine ylide/azomethine imine/azide/nitrone cycloaddition cascades[7,8] and cascade palladium catalysed tetramolecular queuing processes involving carbon monoxide and/or allene as relay switches followed by 1,3-dipolar cycloaddition, Diels–Alder reaction or Michael addition.[9,10] The above processes result in rapid access to molecules possessing a high degree of complexity, which would otherwise require tedious and/or technically demanding multi-step syntheses.

In this paper we explore the tactical combinations of palladium catalysed allenylation cascades with Michael addition processes as the key step.[1] Such processes can be classified into eight distinct classes depending on whether the formation of π-allyl species (from aryl iodide and allene), nucleophilic capture, and the Michael addition step are inter- or intramolecular (Table 1). Thus the immense synthetic power of the Michael addition[11] undergoes startling multiplication when linked to palladium catalysed multi-component processes.[12] In this paper we report palladium catalysed two- and three-component cascades.

Initially we explored a process in which a Michael acceptor is incorporated into the aryl iodide (Scheme 1), which might proceed via a class 2 (path **a**) or class 3 (path **b**) mechanism.

The key distinction between path **a** and path **b** is whether Michael addition precedes (path **b**) or follows (path **a**) the

Table 1. Synthetic strategies for allenylation/nucleophilic capture/Michael addition cascade

Class	π-Allyl formation	Nucleophilic capture	Michael addition
1	Intermolecular	Intermolecular	Intermolecular
2	Intermolecular	Intermolecular	Intramolecular
3	Intermolecular	Intramolecular	Intermolecular
4	Intermolecular	Intramolecular	Intramolecular
5	Intramolecular	Intermolecular	Intermolecular
6	Intramolecular	Intermolecular	Intramolecular
7	Intramolecular	Intramolecular	Intermolecular
8	Intramolecular	Intramolecular	Intramolecular

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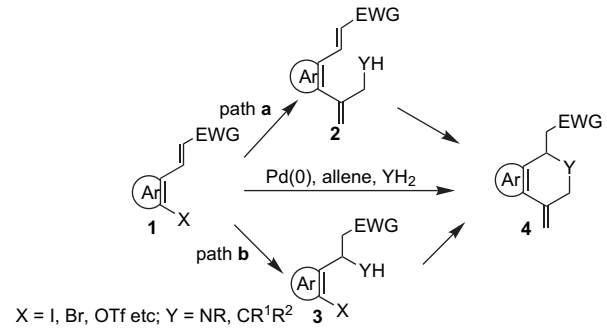
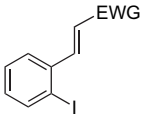


Scheme 1.

allenylation step. A series of dual aryl iodide/Michael acceptors **5a–e** were prepared in excellent yields from the commercially available 2-iodobenzaldehyde.



5 a. EWG = COPh (trans)
b. EWG = CN (2:1 cis:trans)
c. EWG = NO_2 (trans)
d. EWG = CO_2Me (1:5 cis:trans)
e. EWG = SO_2Ph (trans)

An initial solvent, base, catalyst screening was carried out using substrate **5a**, allene (1 bar) and benzylamine (2.00 mol equiv) (Table 2). The appearance of characteristic *exo*-methylene signals at δ 4.93 and 5.69 ppm in the ^{1}H NMR spectrum of **6a** indicated that allene had been successfully incorporated. The highest yield of product **6a** (Table 2, entry 1), was obtained in toluene. Varying the catalyst and base had little effect (entries 6–8) on the yield of **6a**. Substrates **5b–e** were then reacted with $Pd(OAc)_2$ (0.10 mol equiv), PPh_3 (0.20 mol equiv), amine (2.00 mol equiv) and allene (1 bar) in toluene at 80 °C for 18–36 h (Table 3) to afford tetrahydroisoquinolines in moderate to excellent yields.

The range of electron withdrawing groups examined, demonstrates the robustness of this process with respect to variations of the Michael acceptor. However **5c** (EWG=NO_2) requires a phosphine free catalyst system and palladacycle **13**[13] was found to be an excellent substitute. A possible explanation for this observation, is that PPh_3 undergoes conjugate addition to the α,β-unsaturated nitro group. The diastereoselectivity of the Michael addition has been briefly investigated. Thus using *R*-(+)-α-methylbenzylamine afforded **10** as a 1:1 mixture of diastereoisomers (Table 3, entry 5), whereas SAMP afforded **11** as a 2:1 diastereomeric mixture. Recently Desmaele have reported related processes in which π-allylpalladium(II) species are generated from allylic acetates.[14]

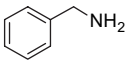
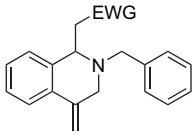
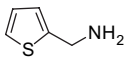
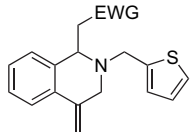
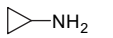
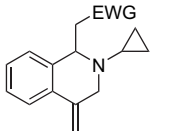
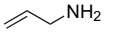
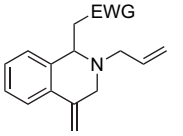
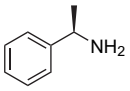
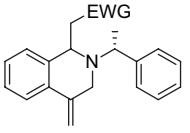
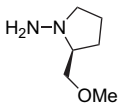
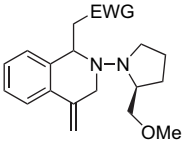
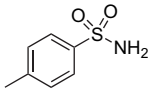
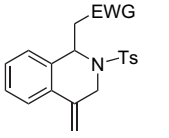
Microwave acceleration was briefly explored. A selection of compounds were synthesised under modified conditions, using microwave irradiation with the reaction time reduced to

Table 2. Optimisation of the palladium catalysed allene insertion–nucleophilic capture–Michael addition cascade[a,b]

Entry	Solvent	Catalyst	Time (h)	Yield[c] (%)
1	Toluene	$Pd(OAc)_2$	36	76
2	1,4-Dioxane	$Pd(OAc)_2$	36	32
3	DMF	$Pd(OAc)_2$	18	65
4	THF	$Pd(OAc)_2$	18	36
5	MeCN	$Pd(OAc)_2$	18	53
6	Toluene	$Pd(PPh_3)_4$	36	67
7	Toluene	Pd_2dba_3	36	71
8[d]	Toluene	$Pd(OAc)_2$	36	75

[a] Catalyst (0.10 mol equiv), PPh_3 (0.20 mol equiv), allene (1 bar), benzylamine (2.00 mol equiv) and K_2CO_3 (2.00 mol equiv).
[b] Reactions were carried out in a Schlenk tube at 80 °C.
[c] Isolated yield.
[d] Cs_2CO_3 (2.00 mol equiv) used as base.

Table 3. Three component cascade of 4-methylenetetrahydroisoquinolines[a]

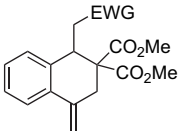
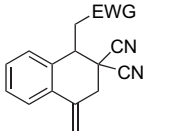
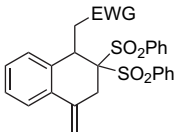
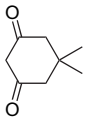
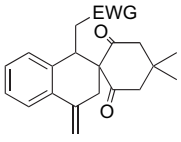
Entry	Aryl iodide	Nucleophile	Product	Yield[b] (%)
1	**5**			**6a** 76 (82)[e] **6b** 60 (78)[e] **6c** 66[c] **6d** 73 (69)[e] **6e** 60
2	**5**			**7a** 90 **7b** 58 **7c** 69[c] **7d** 87 **7e** 54
3	**5**			**8a** 80 (71)[e] **8b** 49 (74)[e] **8c** 68[c] **8d** 80 (70)[e] **8e** 69
4	**5a**			**9a** 62
5	**5a**,**d**,**e**			**10a** 72[d] **10d** 74[d] **10e** 72[d]
6	**5d**			**11d** 71[d]
7	**5a**,**b**,**d**			**12a** (78)[e] **12b** (68)[e] **12d** (87)[e]

[a] $Pd(OAc)_2$ (0.10 mol equiv), PPh_3 (0.20 mol equiv), K_2CO_3 (2.00 mol equiv), amine (2.00 mol equiv) and allene (1 bar) in toluene at 80 °C for 36 h.
[b] Isolated yield.
[c] Palladacycle **13** (0.05 mol equiv) was used instead of $Pd(OAc)_2$ and PPh_3 (18 h).
[d] Ratio of diastereoisomers (1:1).
[e] Pd_2dba_3 (0.025 mol equiv), TFP (0.10 mol equiv), K_2CO_3 (2.00 mol equiv), amine (1.20 mol equiv) and allene (0.2 bar) in toluene under microwave irradiation at 100 °C for 20 min.

20 min, in comparable yield (Table 3, entries 1 and 3) to thermal conditions. *p*-Toluenesulfonamide was also used as a nucleophile under microwave conditions to yield **12a**,**b** and **d** (Table 3, entry 7).

Successful utilisation of amines led us to investigate whether carbon pronucleophiles could be incorporated into the cascade. Thus exposure of **5a** to $Pd(OAc)_2$ (0.10 mol equiv), PPh_3 (0.20 mol equiv), dimethyl malonate (2.00 mol equiv), allene (1 bar) and Cs_2CO_3 (2.00 mol equiv) in MeCN at 50 °C furnished the carbocycle **14a** with a tetra-substituted carbon centre in 62% yield (Table 4, entry 1). This methodology was then extended to diethyl malonate, malononitrile and bisbenzenesulfonyl methane as pronucleophiles (Table 4, entries 1–3). Finally, on the carbocyclic theme, we employed dimedone as the pronucleophile to synthesise spirocyclic compounds **17a** and **17d** in 56–64% yields (Table 4, entry 4).

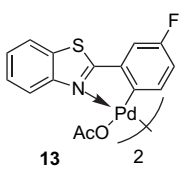
Table 4. Three component cascade synthesis of 4-methylenetetrahydronaphthalenes[a]

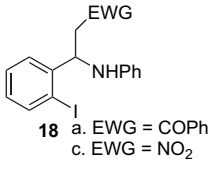
Entry	Aryl iodide	Nucleophile	Product	Yield[b] (%)
1	**5a**,**d**,**e**	$CH_2(CO_2Me)_2$		**14a** 62 **14d** 49[d] **14e** 47
2	**5d**	$CH_2(CN)_2$		**15d** 42
3	**5a**,**d**	$CH_2(SO_2Ph)_2$		**16a** 52[c] **16d** 60[d]
4	**5a**,**d**			**17a** 56 **17d** 64[d]

[a] $Pd(OAc)_2$ (0.10 mol equiv), PPh_3 (0.20 mol equiv), pronucleophile (2.00 mol equiv), allene (1 bar), Cs_2CO_3 (2.00 mol equiv) and MeCN at 50 °C for 18 h.
[b] Isolated yield.
[c] Experiment performed at 60 °C.
[d] Experiment performed at 110 °C in toluene.

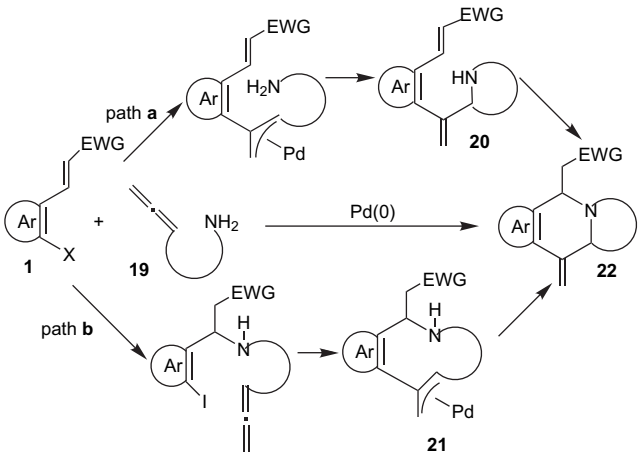
2. Mechanism

To distinguish between path **a** (class 2) and path **b** (class 3) (Scheme 1), the cascade was repeated in the absence of allene using benzylamine as the representative nucleophile. Importantly, the inclusion of $Pd(OAc)_2$ and PPh_3 was maintained due to the possibility of a Pd(II) species acting as a Lewis acid, potentially activating the Michael acceptor towards addition. Aryl iodides **5a** and **5c** afforded the Michael addition intermediates **18a** and **18c**. With less reactive Michael acceptors **5b**, **5d** and **5e** only starting material was observed in the ^1H NMR spectrum. These observations show that the choice of path **a** or path **b** is, perhaps, intimately connected with the type of Michael acceptor and suggests that when benzylamine is used, the least reactive Michael acceptors SO_2Ph, CN and CO_2Me react via path **a** (class 2) whilst the more reactive Michael acceptors NO_2 and COPh react via path **b** (class 3). Caution must be applied to this interpretation as the Michael addition is probably reversible and the relative rates of the Scheme 1 steps are not known. In all cases **6a**–**6e** were obtained when allene was added to the crude material and the mixture recycled through the standard cascade reaction conditions.





Next we briefly explored examples of Scheme 2 processes, which potentially could proceed via a class 4 process (path **a**) or class 7 process (path **b**) (Table 5). To study this we tethered the amine and allene in one component and aryl iodide and Michael acceptor in another component. Tethering two of the compounds used in the cascade reactions offsets diversity for a rapid increase in the molecular complexity of the product, through the formation of additional rings and stereocentres. Thus dual aryl iodide/Michael acceptor **1** reacts with dual allene–amine **19** in the presence of palladium(0) to afford tricyclic heterocycles **22** either via path **a** (class 4) or path **b** (class 7) (Scheme 2).

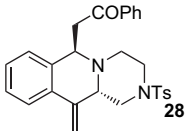
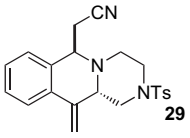
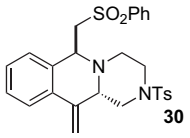


Scheme 2.

The aminoallene **27** was synthesised in four steps from the acetal **23** (Scheme 3).[15,16]

The key step was the use of Crabbe reaction to synthesise the allene **24**.[15] Reaction of **27** (2.00 mol equiv) with aryl iodide **5b** in the presence of $Pd(OAc)_2$ (0.10 mol equiv), PPh_3 (0.20 mol equiv) and K_2CO_3 (4.00 mol equiv) in toluene at 80 °C over 18 h afforded the desired tricyclic product **29** in 67% yield as a 1:2 mixture of *syn*/*anti* diastereoisomers (Table 5, entry 1). The stereochemistry of the major isomer of **29** was unequivocally established by an X-ray crystal structure (Fig. 1).[17] Utilisation of **27** as a key reactant militates

Table 5. Palladium catalysed synthesis of tetrahydroisoquinolines using **27**[a]

Entry	Aryl iodide	Allene/ nucleophile	Product	Yield[b] (%)
1	**5a**	**27**	 **28**	44 *anti* only
2	**5b**	**27**	 **29**	67 *anti*/*syn* 2:1
3	**5e**	**27**	 **30**	52 *anti*/*syn* 1:1

[a] $Pd(OAc)_2$ (0.1 mol equiv), PPh_3 (0.2 mol equiv), **27** (2 mol equiv) and K_2CO_3 (4.0 mol equiv) in toluene at 80 °C over 36 h.
[b] Isolated yield.

against path **b** as it involves formation of a nine-membered ring in **21** (Scheme 2). Two other aryl iodides **5a** and **5e** were also investigated in this cascade (Table 4, entries 1 and 3). When dual aryl iodide/Michael acceptor **5a** was employed in the cascade, only *anti*-isomer **28** was observed (Table 5, entry 1). This may be due to a retro Michael–Michael addition equilibration sequence to give the *anti*-isomer **28**.

An alternative three-component tethering strategy, which incorporates a further Michael addition reaction and employs a dual nucleophile–Michael acceptor **32**, shown in Scheme 5, which was synthesised in five steps from commercially available *trans*-β-muconic acid **31** (Scheme 4).[16] The additional Michael acceptor can in theory be attached to any one of the components utilised in the cascade (i.e., aryl iodide, allene or nucleophile).

Exposure of aryl iodide **5c** and amine salt **32** (3.00 mol equiv) to palladacycle **13** (0.05 mol equiv), K_2CO_3 (6.00 mol equiv)

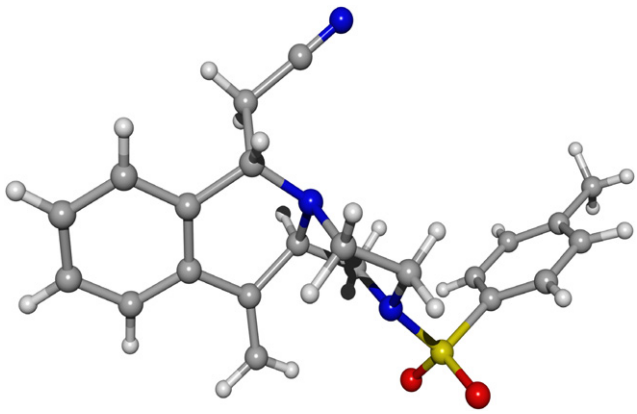
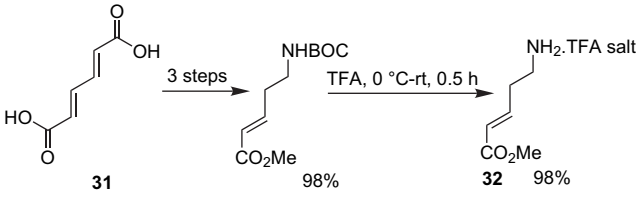


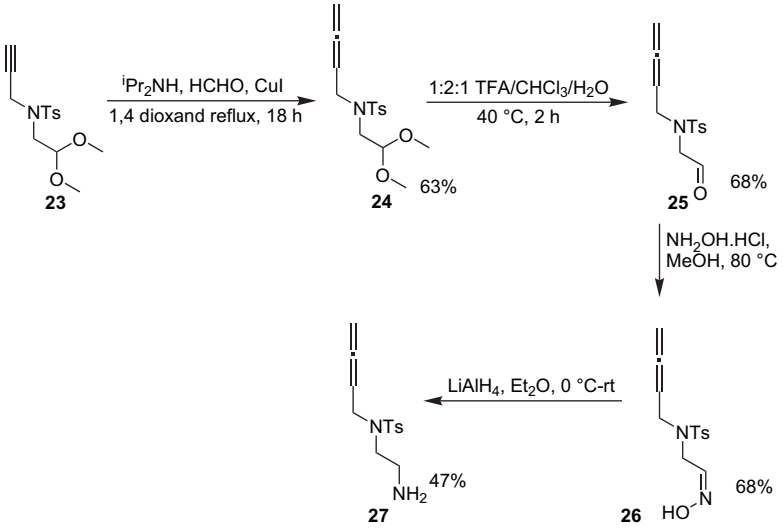
Figure 1. X-ray crystal structure of **29** (major isomer).



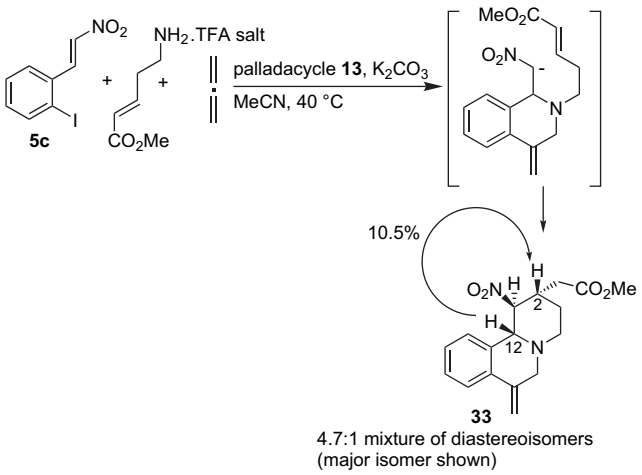
Scheme 4.

and allene (1 bar) in acetonitrile at 50 °C for 18 h, afforded the desired product **33** in 47% yield as a 4.7:1 mixture of diastereoisomers (Scheme 5). The stereochemistry of the major isomer was established from NOE studies. A positive enhancement of only H-(2) after irradiation of H-(12) was indicative of the stereochemistry shown in Scheme 5.

In summary, a novel 3-component palladium catalysed allene insertion–nucleophile incorporation–Michael addition cascade has been developed. This methodology is a powerful tool for the synthesis of novel tetrahydroisoquinolines and tetrahydronaphthalenes. The mechanism of this process is strongly influenced by the choice of Michael acceptor. When the amine and allene components are tethered, novel



Scheme 3.



Scheme 5.

tricyclic tetrahydroisoquinolines are afforded in moderate yields. Furthermore, an additional Michael addition reaction has been successfully incorporated into the cascade sequence, forming four bonds, three stereocentres and two rings in moderate yield. The importance, in certain cases, of phosphine free catalyst systems employing palladacycles as precursors of Pd(0) nanoparticles is described.

3. Experimental

3.1. General

Microwave reactions were carried out in a CEM Discover microwave reactor operating at 300 W. Melting points were determined on a Reichert hot-stage apparatus and are uncorrected. Mass spectral data were obtained from a VG Autospec instrument operating at 70 eV (EI and FAB) or ZD 2000 electrospray instrument (ES). Accurate molecular masses were obtained from the EPSRC Swansea Mass Spectroscopy service using perfluorotributylamine or polyethylenimine as an internal standard. Microanalyses were obtained using a Carbo Erba MOD11016 instrument. IR spectra were determined on a Nicolet Magna FT-IR 560 spectrometer. The IR samples were prepared as thin films by evaporation of a solution of the compound in DCM onto a germanium plate. Nuclear magnetic resonance spectra were recorded on Bruker DPX250, DPX300 and DPX500 instruments operating at 250, 300 and 500 MHz, respectively. The following abbreviations are used: s=singlet, d=doublet, t=triplet, q=quartet, q_i=quintet, m=multiplet, dd=doublet of doublets, ddd=double doublet of doublets, ddt=double doublet of triplets, br=broad. Solvents were dried according to established methods, unless purchased dry from Aldrich in sure-seal bottles. The term ether refers to diethyl ether and the term petrol refers to the 40–60 °C boiling point fraction of petroleum ether. All the compounds are named according to the IUPAC system and names were obtained using the ACD/*i*-Lab software version 4.5. Compound **5a** was prepared by the literature method.[19]

3.1.1. 3-(2-Iodophenyl)acrylonitrile (5b). A stirred mixture of 2-iodobenzaldehyde (2.32 g, 10.00 mmol) and methyl(triphenylphosporanylidene)cyanide (3.01 g, 10.00 mmol) in benzene (20 ml) was heated at 80 °C for 36 h. The solvent was then evaporated under reduced pressure and the residue partitioned between ether (20 ml) and water (20 ml). The two layers were separated and the aqueous layer was extracted with ether (2×10 ml). The combined organic extracts were washed with brine (10 ml), dried ($MgSO_4$) and the solvent evaporated under reduced pressure. The crude product was purified by column chromatography eluting with 2:3 v/v ether/petrol to afford the product (**5b**) (2.09 g, 82%) as a colourless oil, which comprised of a 2:1 mixture of *Z*/*E*-isomers. (Found: C, 42.50; H, 2.35; N, 5.40; I, 50.10; C_9H_6NI requires C, 42.40; H, 2.40; N, 5.40; I, 49.80%); *ν*/max (film) 3056, 2218, 1611, 1581, 1462 and 1432 cm^{-1}; *m*/*z* (%) (ES) 279 (MNa^+, 40), 219 (22) and 213 (18).

*E-(**5b**)*: δ_H (250 MHz, $CDCl_3$), 7.92 (1H, dd, *J* 8.2 and 0.9 Hz, ArH), 7.68 (1H, d, *J* 16.4 Hz, ArC*H*=CH), 7.49 (1H, dd, *J* 7.9 and 1.6 Hz, ArH), 7.39 (1H, d, *J* 7.9 and 0.9 Hz, ArH), 7.11 (1H, td, *J* 8.2 and 1.6 Hz, ArH), 5.79 (1H, d, *J* 16.4 Hz, ArCH=C*H*).

*Z-(**5b**)*: δ_H (250 MHz, $CDCl_3$), 7.96–7.92 (2H, m, 2×ArH), 7.46 (1H, t, *J* 8.2 Hz, ArH), 7.34 (1H, d, *J* 11.9 Hz, CH^1), 7.12 (1H, td, *J* 8.2 and 1.6 Hz, ArH), 5.57 (1H, d, *J* 11.9 Hz, CH^2).

3.1.2. 1-Iodo-2-[(*E*)-2-nitrovinyl]benzene (5c). A stirred mixture of 2-iodobenzaldehyde (1.00 g, 4.3 mmol, 1.0 mol equiv), nitromethane (0.23 ml, 4.30 mmol, 1.0 mol equiv) and anhydrous ammonium acetate (0.40 g, 5.20 mmol, 1.20 mol equiv) in glacial acetic acid (4 ml) was heated under reflux for 30 min. The solvent was then evaporated under reduced pressure. The crude product was purified by crystallisation from methanol to afford the product (**5c**) (0.72 g, 61%) as yellow prisms, mp 105–107 °C. (Found: C, 34.90; H, 2.15; N, 5.20; I, 46.20; $C_8H_6NO_2I$ requires C, 34.90; H, 2.20; N, 5.10; I, 46.10%); *ν*/max (Nujol mull) 1630, 1576, 1556, 1336 and 1284 cm^{-1}; δ_H (250 MHz, $CDCl_3$), 8.29 (1H, d, *J* 13.5 Hz, ArC*H*=CH), 7.97 (1H, dd, *J* 8.0 and 6.9 Hz, ArH), 7.54 (1H, dd, *J* 7.8 and 1.6 Hz, ArH), 7.49–7.40 (2H, m, 1×ArH+ ArCH=C*H*), 7.17 (1H, td, *J* 7.8 and 1.6 Hz, ArH); *m*/*z* (%) 275 (M^+, 13), 229 (86), 148 (48), 102 (100) and 75 (36).

3.1.3. Methyl 2-iodocinnamate (5d). A solution of 2-iodobenzaldehyde (2.11 g, 9.10 mmol) in dry dichloromethane (25 ml) was added in one portion to a stirred solution of carbomethoxymethylene triphenylphosphorane (3.56 g, 10.60 mmol) in dry dichloromethane (50 ml) at rt. The resulting mixture was stirred for 16 h and concentration in vacuo gave the crude product. Column chromatography eluting with 9:1 v/v petroleum ether/ether afforded the product (93%, 1:5 mixture of cis and trans isomers) as a light yellow oil. The ^1H NMR spectra of both isomers were assigned from the mixture of diastereoisomers.

trans-isomer: δ_H (250 MHz, $CDCl_3$), 7.92–6.96 (m, 5H, 4×ArH and ArCH=), 6.31 (d, 1H, *J* 15.9 Hz, =CHCO) and 3.82 (s, 3H, OMe).

cis-isomer: δ_H (250 MHz, $CDCl_3$), 7.92–6.96 (m, 5H, 4×ArH and ArCH=), 6.02 (d, 1H, *J* 11.8 Hz, =CHCO) and 3.64 (s, 3H, OMe).

3.1.4. (*E*)-2-(2-Iodophenyl)vinyl phenyl sulfone (5e). *n*-Butyllithium (3.44 ml, 5.50 mmol, 1.6 M solution in hexanes, 1.10 mol equiv) was added dropwise over 30 min, to a stirred solution of (phenylsulfonylmethyl)trimethylsilane (1.14 g, 5.00 mmol, 1.00 mol equiv) in ethylene glycol dimethyl ether (25 ml) under nitrogen at −78 °C. After 20 min at −78 °C, 2-iodobenzaldehyde (1.16 g, 5.00 mmol, 1.00 mol equiv) in ethylene glycol dimethyl ether (5.0 ml) was added dropwise over 10 min and the mixture allowed to reach rt. After 4 h at rt the mixture was quenched with saturated aqueous ammonium chloride (5 ml). The solvent was evaporated under reduced pressure and the residue partitioned between ether (20 ml) and water (20 ml). The two layers were separated and the aqueous layer was extracted with ether (2×10 ml). The combined organic extracts were washed with brine (20 ml), dried ($MgSO_4$) and the solvent evaporated under reduced pressure. The residue was purified by column chromatography eluting with 2:3 v/v ether/petrol, to afford the *E*-product (**5e**) (1.13 g, 61%) as a pale yellow amorphous solid, mp 62–64 °C. (Found: C, 45.40; H, 3.05; I, 34.10; $C_{12}H_{11}SO_2I$ requires C, 45.40; H, 3.00; I, 34.30%); *ν*/max (Nujol mull) 1608, 1580, 1209 1145 and 1083 cm^{-1}; δ_H (250 MHz, $CDCl_3$), 8.01–7.89 (4H, m, 3×ArH+ArC*H*=CH), 7.69–7.54 (3H, m, 3×ArH), 7.46 (1H, dd, *J* 7.8 and 1.7 Hz, ArH), 7.35 (1H, t, 7.6 Hz, ArH), 7.08 (1H, td, *J* 7.8 and 1.7 Hz, ArH), 6.75 (1H, d, *J* 15.3 Hz, ArCH=C*H*); *m*/*z* (%) (ES) 371 (MH^+, 22), 340 (18), 308 (48) and 243 (20).

3.2. General procedure for the three-component allenylation/amination/Michael addition cascade using (5a, 5b, 5d and 5e)

A mixture of aryl iodide (1.00 mmol, 1.00 mol equiv), amine (2.00 mmol, 2.00 mol equiv), potassium carbonate (276 mg, 2.00 mmol, 2.00 mol equiv), palladium acetate (22 mg, 0.10 mmol, 0.10 mol equiv), triphenylphosphine (52 mg, 0.20 mmol, 0.20 mol equiv) and toluene (10 ml) in a Schlenk tube was subjected to two freeze-pump-thaw cycles. Allene gas was then added (1 bar) and the reaction mixture was then heated at 80 °C for 36 h. After cooling to rt, excess allene gas was carefully vented, the reaction mixture filtered and the solids washed with ether (3×50 ml). The combined organic filtrates were dried ($MgSO_4$) filtered and the filtrate evaporated under reduced pressure. The residue was purified by column chromatography eluting with 2:3 v/v ether/petrol.

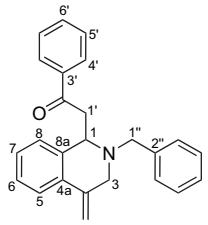
3.3. General procedure for the three-component allenylation/amination/Michael addition cascade using (5c)

As above but the reaction was run for 18 h at 80 °C.

3.4. General procedure for microwave-accelerated three-component allenylation/amination/Michael addition cascade

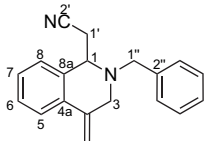
Aryl iodide (0.50 mmol, 1 equiv), nucleophile (0.60 mmol, 1.2 equiv), Pd_2dba_3 (0.0125 mmol, 2.50 mol %), tri-2-furylphosphine (0.05 mmol, 0.10 equiv, K_2CO_3 (1.0 mmol, 2.00 equiv) and toluene (2 ml) were combined in a 5 ml microwave tube with a magnetic stirrer bar. The tube was sealed with a septum and degassed via a needle through two freeze-pump-thaw cycles. Allene (0.2 bar) was charged to the tube via a needle, and the mixture was heated to 100 °C for 20 min. Upon cooling, $CHCl_3$ (2 ml) was added and the mixture was filtered, concentrated and purified by column chromatography to afford the product.

3.4.1. 2-(2-Benzyl-4-methylene-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenyl-ethanone (6a).



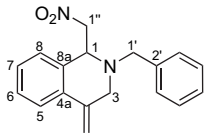
Prepared by the general procedure from (**5a**) (334 mg, 1.00 mmol) and benzylamine (214 mg, 2.00 mmol) gives the product (**6a**) (268 mg, 76%) as a yellow oil. (Found: C, 84.70; H, 6.60; N, 4.00; $C_{25}H_{23}NO$ requires C, 84.90; H, 6.55; N, 4.00%); *ν*/max (film) 3061, 1682, 1629, 1597 and 1448 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 7.95–7.91 (2H, m, 2×H$^{4'}$), 7.69 (1H, dt, *J* 9.3 and 3.6 Hz, 2×ArH$^{5'}$), 7.53 (1H, tt, *J* 7.4 and 1.3 Hz, ArH$^{6'}$), 7.45–7.4 (2H, m, ArH$^{5'}$), 7.25–7.11 (8H, m, 8×ArH), 5.69 (1H, t, *J* 1.0 Hz, =CH), 4.93 (1H, t, *J* 1.0 Hz, =CH), 4.57 (1H, dd, *J* 8.6 and 5.5 Hz, CH^1), 3.91 (1H, dt, *J* 15.5 and 1.8 Hz, CH^3), 3.64 (1H, d, *J* 13.1 Hz, CH$^{1''}$), 3.63 (1H, dd, *J* 15.5 and 8.6 Hz, CH$^{1'}$), 3.56 (1H, d, *J* 13.1 Hz, CH$^{1''}$), 3.25 (1H, d, *J* 15.5 Hz, CH^3), 3.17 (1H, dd, *J* 15.5 and 5.5 Hz, CH$^{1'}$); δ_C (126 MHz, $CDCl_3$), 198.5 (C$^{2'}$), 138.8 (C$^{2''}$), 137.4 (C$^{3'}$), 136.8 (C=), 136.2 (C^{8a}), 132.9 (C$^{6'}$), 132.3 (C^{4a}), 129.0, 128.6, 128.3, 128.2, 128.0, 127.8, 126.9, 126.8, 123.6 (C^5), 109.7 (=CH_2), 59.5 (C^1), 58.0 (C$^{1''}$), 49.5 (C^3), 45.3 (C$^{1'}$); *m*/*z* (%) (FAB) 353 (M^+, 11), 262 (16) and 234 (100).

3.4.2. (2-Benzyl-4-methylene-1,2,3,4-tetrahydroisoquinolin-1-yl)-acetonitrile (6b).



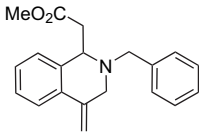
Prepared by the general procedure from (**5b**) (255 mg, 1.00 mmol) and benzylamine (214 mg, 2.00 mmol). Column chromatography afforded the product (**6b**) (165 mg, 60%) as a pale yellow oil. (Found: C, 83.00; H, 6.70; N, 10.40; $C_{19}H_{19}N_2$ requires C, 82.90; H, 6.95; N, 10.20%); *ν*/max (film) 3062, 2248, 1697, 1672, 1631 and 1598 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 7.72–7.69 (1H, m, CH^5), 7.39–7.37 (2H, m, 2×ArH), 7.35–7.31 (2H, m, 2×ArH), 7.30–7.26 (3H, m, 3×ArH), 7.10–7.07 (1H, m, ArH^8), 5.71 (1H, d, *J* 1.6 Hz, =CH), 5.02 (1H, d, *J* 1.6 Hz, =CH), 4.08 (1H, dd, *J* 9.2 and 5.6 Hz, CH^1), 3.86 (1H, dt, *J* 15.7 and 1.8 Hz, CH^3), 3.75 (1H, d, *J* 13.3 Hz, CH$^{1''}$), 3.64 (1H, d, *J* 13.3 Hz, CH$^{1''}$), 3.40 (1H, d, *J* 15.7, CH^3), 2.88 (1H, dd, *J* 16.9 and 9.2 Hz, CH$^{1'}$), 2.67 (1H, dd, *J* 16.9 and 5.6 Hz, CH$^{1'}$); δ_C (126 MHz, $CDCl_3$), 138.2 (C$^{2''}$), 136.0 (C^4), 133.1 (C^{8a}), 132.4 (C^{4a}), 129.0, 128.6 (C^8), 128.4, 127.8, 127.4, 124.0 (C^5), 118.2 (C$^{2'}$), 110.5 (=CH_2), 58.3 (C^1), 58.0 (C$^{1''}$), 50.0 (C^3), 24.7 (C$^{1'}$); *m*/*z* (%) (ES) 297 (MNa^+, 100).

3.4.3. 2-Benzyl-4-methylene-1-(nitromethyl)-1,2,3,4-tetrahydroisoquinoline (6c).



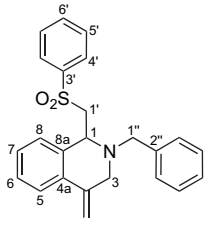
Prepared by the general procedure from (**5c**) (275 mg, 1.00 mmol) and benzylamine (214 mg, 2.00 mmol). Column chromatography afforded the product (**6c**) (182 mg, 62%) as a pale yellow oil. (Found HRMS: 295.1450; $C_{18}H_{18}N_2O_2$ (MH^+) requires 295.1446); ν/max (film) 3029, 1634, 1601, 1555, 1494 and 1483 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 7.73–7.71 (1H, m, ArH), 7.33–7.21 (7H, m, ArH), 7.12–7.09 (1H, m, ArH), 5.73 (1H, d, J 1.7 Hz, =CH), 5.02 (1H, d, J 1.7 Hz, =CH), 4.79 (1H, dd, J 11.9 and 11.2 Hz, $CH^{1''}$), 4.59 (1H, dd, J 11.2 and 4.5 Hz, CH^1), 4.49 (1H, dd, J 11.9 and 4.5 Hz, $CH^{1''}$), 3.89 (1H, dt, J 15.8 and 1.7 Hz, CH^3), 3.72 (1H, d, J 13.2 Hz, $CH^{1'}$), 3.61 (1H, d, J 13.2 Hz, $CH^{1'}$), 3.33 (1H, d, J 15.8 Hz, CH^3); δ_C (126 MHz, $CDCl_3$), 138.1 ($C^{2'}$), 135.6 (=C), 133.3 (C^{4a}), 130.2 (C^{8a}), 129.0, 128.7, 128.3, 128.1, 127.7, 127.4, 124.2 (C^8), 111.1 (=CH_2), 78.6 ($C^{1''}$), 60.4 (C^1), 57.8 ($C^{1'}$), 49.1 (C^3); m/z (%) (CI) 295 (MH^+, 4), 250 (29), 236 (100), 230 (28) and 144 (52).

3.4.4. Methyl (2-benzyl-4-methylene-1,2,3,4-tetrahydro-1-isoquinolinyl)-acetate (6d).



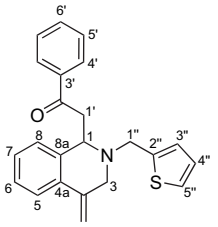
Prepared by the general procedure from (**5d**) (288 mg, 1.00 mmol) and benzylamine (214 mg, 2.00 mmol). Column chromatography afforded the product (**6d**) (73%) as a pale yellow oil. (Found: C, 77.90; H, 7.05; N, 4.70; $C_{20}H_{21}NO_2$ requires C, 78.15; H, 6.90; N, 4.55%); IR (film) 3028, 2949, 1739 and 1436 cm^{-1}; δ_H (250 MHz, $CDCl_3$), 7.70 (1H, dd, J 6.0 and 4.2 Hz, ArH), 7.34–7.22 (7H, m, 7×ArH), 7.09 (1H, dd, J 5.1 and 3.2 Hz, ArH), 5.70 (1H, d, J 1.5 Hz, CH_2=), 4.96 (1H, t, J 0.9 Hz, CH_2=), 4.30 (1H, dd, J 10.3 and 4.8 Hz, CH), 3.91 (1H, ddd, J 15.8, 1.5 and 0.9 Hz, CCH_2N), 3.69 (3H, s, CO_2Me), 3.67 and 3.57 (2×1H, AB, 2×d, J 13.2 Hz, NCH_2Ph), 3.28 (1H, dd, J 15.8 and 1.5 Hz, CCH_2N), 2.89 (1H, dd, J 14.5 and 10.3 Hz, CH_2CO), 2.65 (1H, dd, J 14.5 and 4.8 Hz, CH_2CO); m/z (EI) (%) 307 (M^+, 1), 234 (100) and 91 (95).

3.4.5. 1-Benzenesulfonylmethyl-4-methylene-2-benzyl-1,2,3,4-tetrahydroisoquinoline (6e).



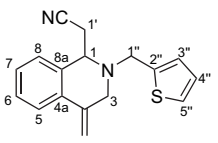
Prepared by the general procedure from (**5e**) (370 mg, 1.00 mmol) and benzylamine (214 mg, 2.00 mmol). Column chromatography afforded the product (**6e**) (212 mg, 60%) as a colourless oil. (Found: C, 74.10; H, 6.20; N, 3.80; $C_{24}H_{23}NO_2S$ requires C, 74.00; H, 5.95; N, 3.60%); ν/max (film) 3055, 1599, 1345, 1265 and 1165 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 7.96–7.94 (2H, m, $CH^{4'}$), 7.65–7.59 (2H, m, 2×ArH^5 and ArH^8), 7.53–7.49 (2H, m, 2×$ArH^{5'}$), 7.30–7.22 (5H, m, 5×ArH), 7.17–7.15 (2H, m, 2×ArH), 7.11–7.09 (1H, m, ArH), 7.66 (1H, d, J 1.5 Hz, =CH), 4.86 (1H, d, J 1.5 Hz, =CH), 4.49 (1H, dd, J 9.1 and 3.4 Hz, CH^1), 3.81 (1H, dd, J 15.0 and 9.1 Hz, $CH^{1'}$), 3.58 (2H, 2×d, J 13.2 Hz, 2×$CH^{1''}$), 3.47 (1H, d, J 15.9 Hz, CH^3), 3.32 (1H, dd, J 15.0 and 3.4 Hz, $CH^{1'}$), 3.06 (1H, d, J 15.9 Hz, CH^3); δ_C (126 MHz, $CDCl_3$), 140.5 ($C^{3'}$), 138.0 ($C^{2''}$), 135.7 (C^{4a}), 133.5 (=C), 133.4 (C^5), 132.3, 129.4, 129.1, 128.8, 128.2, 128.1, 127.7, 127.5, 127.2, 123.6 (C^8), 110.6 (CH_2), 61.5 ($C^{1'}$), 61.0 (C^1), 58.7 ($C^{1''}$), 48.0 (C^3); m/z (%) (FAB) 353 (M^+, 11), 262 (16) and 234 (100).

3.4.6. 2-(4-Methylene-2-thiophen-2-ylmethyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenyl-ethanone (7a).



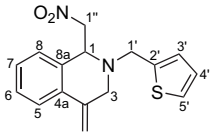
Prepared by the general procedure from (**5a**) (334 mg, 1.00 mmol) and 2-thiophenemethylamine (226 mg, 2.00 mmol). Column chromatography afforded the product (**7a**) (323 mg, 90%) as a pale yellow gum. (Found: C, 76.60; H, 5.80; N, 3.80; $C_{23}H_{21}NOS$ requires C, 76.90; H, 5.90; N, 3.90%); ν/max (film) 3064, 2917, 1682, 1597, 1481 and 1448 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 7.97–7.93 (2H, m, $ArH^{4'}$), 7.71–7.68 (1H, m, ArH^5), 7.55 (1H, t, 7.9, $ArH^{6'}$), 7.45 (2H, t, J 7.9 Hz, $ArH^{5'}$), 7.25–7.21 (2H, m, ArH^8 and ArH), 7.17–7.15 (2H, m, $ArH^{5''}$ and ArH), 6.86 (1H, dd, J 5.1 and 3.3 Hz, $ArH^{4''}$), 6.76 (1H, d, J 3.3 Hz, $CH^{3''}$), 5.7 (1H, s, =CH), 4.98 (1H, t, J 0.8 Hz, =CH), 4.63 (1H, t, J 7.2 Hz, CH^1), 3.94 (1H, d, J 15.6 Hz, CH^3), 3.86 (1H, d, J 13.8 Hz, $CH^{1''}$), 3.75 (1H, dd, J 13.8 Hz, $CH^{1''}$), 3.63 (1H, dd, J 15.5 and 7.2 Hz, $CH^{1'}$), 3.39 (1H, d, J 15.6 Hz, CH^3), 3.21 (1H, dd, J 15.5 and 7.2 Hz, $CH^{1'}$); δ_C (126 MHz, $CDCl_3$), 198.4 ($C^{2'}$), 143.0 ($C^{2''}$), 137.4 ($C^{3'}$), 136.5 (C=), 136.0 (C^{8a}), 132.9 ($C^{6'}$), 132.2 (C^{4a}), 128.5 ($C^{4'}$), 128.4 ($C^{(6\text{ or }7)}$), 128.3 ($C^{5'}$), 127.9 (C^8), 126.9 ($C^{5''}$), 126.2 ($C^{3''}$), 125.6 ($C^{4''}$), 125.0 ($C^{(6\text{ or }7)}$), 123.6 (C^5), 110.0 (=CH_2), 59.0 (C^1), 52.7 ($C^{1''}$), 49.8 (C^3), 45.6 ($C^{1'}$); m/z (%) (FAB) 360 (MH^+, 34), 262 (22) and 240 (100).

3.4.7. (4-Methylene-2-thiophen-2-ylmethyl-1,2,3,4-tetrahydroisoquinolin-1-yl)-acetonitrile (7b).



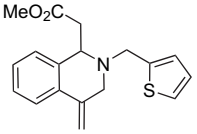
Prepared by the general procedure from (**5b**) (255 mg, 1.00 mmol) and 2-thiophenemethylamine (226 mg, 2.00 mmol). Column chromatography afforded the product (**7b**) (162 mg, 58%) as a colourless oil. (Found HRMS: 281.1111; $C_{17}H_{17}N_2S$ (MH^+) requires 281.1112); ν/max (film) 3069, 2249, 1632, 1570, 1484 and 1446 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 7.71–7.68 (1H, m, ArH^8), 7.31–7.25 (3H, m, ArH^6, ArH^7 and $ArH^{5''}$), 7.14–7.09 (1H, m, ArH^5), 6.95–6.90 (1H, m, $ArH^{4''}$), 6.90–6.89 (1H, m, $ArH^{3''}$), 5.71 (1H, d, J 1.8 Hz, =CH), 5.05 (1H, d, J 1.8 Hz, =CH), 4.14 (1H, dd, J 8.6 and 6.2 Hz, CH^1), 3.93 (1H, d, J 13.4 Hz, CH^3), 3.91 (1H, d, J 15.8 Hz, $CH^{1''}$), 3.83 (1H, d, J 13.4 Hz, CH^3), 3.51 (1H, d, 15.8 Hz, $CH^{1''}$), 2.90 (1H, dd, J 16.9 and 8.6 Hz, $CH^{1'}$), 2.71 (1H, dd, J 16.9 and 6.2 Hz, $CH^{1'}$); δ_C (126 MHz, $CDCl_3$), 142.2 ($C^{2''}$), 135.8 (C^4), 132.7 (C^{8a}), 132.3 (C^{4a}), 128.6 (C^7), 128.0, 127.9, 126.5 ($C^{4''}$), 126.0 ($C^{3''}$), 125.5, 124.0 (C^8), 118.1 ($C^{2'}$), 110.7 (=CH_2), 57.7 (C^1), 52.8 (C^3), 50.3 ($C^{1''}$), 24.8 ($C^{1'}$); m/z (%) (CI) 281 (MH^+, 100).

3.4.8. 4-Methylene-1-nitromethyl-2-thiophen-2-yl-methyl-1,2,3,4-tetrahydroisoquinoline (7c).



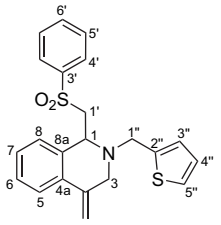
Prepared by the general procedure from (**5c**) (275 mg, 1.00 mmol) and 2-thiophenemethylamine (226 mg, 2.00 mmol). Column chromatography afforded the product (**7c**) (191 mg, 64%) as a pale yellow oil. (Found: C, 64.20; H, 5.30; N, 9.30; $C_{16}H_{15}N_2O_2S$ requires C, 64.20; H, 5.05; N, 9.40%); ν/max (film) 3055, 1553, 1483, 1447, 1424 and 1381 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 7.72–7.70 (1H, m, ArH^5), 7.33–7.28 (2H, m, ArH^6 and ArH^7), 7.24 (1H, dd, J 5.1 and 1.2 Hz, $ArH^{3'}$), 7.12–7.10 (1H, m, ArH^8), 6.92 (1H, dd, J 5.1 and 3.4 Hz, $ArH^{4'}$), 6.84–6.82 (1H, m, $ArH^{5'}$), 5.73 (1H, d, J 1.7 Hz, =CH), 5.07 (1H, d, J 1.9 Hz, =CH), 4.79 (1H, dd, J 10.9 and 11.8 Hz, $CH^{1''}$), 4.64 (1H, dd, J 10.9 and 4.5 Hz, CH^1), 4.50 (1H, dd, J 11.8 and 4.5 Hz, $CH^{1''}$), 3.93 (1H, dt, J 15.9 and 1.8 Hz, CH^3), 3.92 (1H, dd, J 13.9 and 0.8 Hz, CH^4), 3.78 (1H, d, J 13.9 Hz, CH^4), 3.46 (1H, d, J 15.9 Hz, CH^3); δ_C (126 MHz, $CDCl_3$), 142.0 ($C^{2'}$), 135.3 (C^4), 133.2 (C^{4a}), 130.0 (C^{8a}), 128.8 (C^6*C*^{7}), 128.1 ($C^{6 \text{ or } 7}$), 127.8 (C^8), 126.3 ($C^{3'}$), 126.0 ($C^{5'}$), 125.5 ($C^{4'}$), 124.2 (C^5), 111.3 (=CH_2), 78.7 ($C^{1''}$), 60.0 (C^1), 52.6 ($C^{1'}$), 49.5 (C^3); m/z (%) (FAB) 301 (MH^+, 44) and 240 (100).

3.4.9. Methyl [4-methylene-2-(2-thienylmethyl)-1,2,3,4-tetrahydro-1-isoquinolinyl]-acetate (7d).



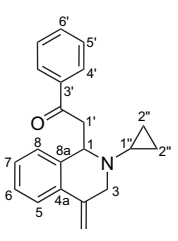
Prepared by the general procedure from (**5d**) (288 mg, 1.00 mmol) and 2-thiophenemethylamine (226 mg, 2.00 mmol). Column chromatography afforded product (**7d**) (87%) as a pale yellow liquid. (Found: C, 69.10; H, 6.05; N, 4.60; S, 10.30; $C_{18}H_{19}NO_2S$ requires: C, 69.00; H, 6.10; N, 4.45; S, 10.25%); IR (film) 3051, 2948, 1737 and 1436 cm^{-1}; δ_H (250 MHz, $CDCl_3$), 7.69–7.65 (1H, m, ArH), 7.28–7.20 (3H, m, 3×ArH), 7.11–7.07 (1H, m, ArH), 6.93–6.89 (1H, m, ArH), 6.82–6.80 (1H, m, ArH), 5.68 (1H, d, J 1.3 Hz, CH_2=), 4.98 (1H, t, J 0.9 Hz, CH_2=), 4.35 (1H, dd, J 10.3 and 5.2 Hz, CH), 3.91 (1H, ddd, J 15.8, 1.3 and 0.9 Hz, CCH_2N), 3.89 and 3.74 (2×1H, 2×d, J 14.9 Hz, NCH_2Ar), 3.73 (3H, s, CO_2Me), 3.38 (1H, dd, J 15.8 and 0.9 Hz, CCH_2N), 2.87 (1H, dd, J 14.5 and 10.3 Hz, CH_2CO) and 2.66 (1H, dd, J 14.5 and 5.2 Hz, CH_2CO); m/z (EI) (%) 313 (M^+, 1), 240 (89), 216 (44) and 97 (100).

3.4.10. 1-Benzenesulfonylmethyl-4-methylene-2-thiophen-2-ylmethyl-1,2,3,4-tetrahydroisoquinoline (7e).



Prepared by the general procedure from (**5e**) (370 mg, 1.00 mmol) and 2-thiophenemethylamine (226 mg, 2.00 mmol). Column chromatography afforded the product (**7e**) (213 mg, 54%) as a colourless oil. (Found HRMS: 418.0713; $C_{22}H_{21}NO_2S_2Na$ (MNa^+) requires 418.0706); ν/max (film) 3056, 1481, 1443 and 1426 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 8.01–7.98 (2H, m, $ArH^{4'}$), 7.64–7.60 (2H, m, $ArH^{5'}$), 7.55–7.51 (2H, m, ArH^5 and ArH), 7.28–7.22 (3H, m, ArH^7, ArH^6 and ArH), 7.14–7.11 (1H, m, ArH^8), 6.91 (1H, dd, J 5.1 and 3.4 Hz, $ArH^{4''}$), 6.80–6.79 (1H, m, ArH), 5.66 (1H, d, J 1.7 Hz, =CH), 4.89 (1H, d, J 1.8 Hz, =CH), 4.49 (1H, dd, J 8.9 and 3.7 Hz, CH^1), 3.81 (1H, d, J 13.5 Hz, $CH^{1''}$), 3.79 (1H, dd, J 15.0 and 9.0 Hz, $CH^{1'}$), 3.69 (1H, d, J 13.5 Hz, $CH^{1''}$), 3.42 (1H, d, J 16.0 Hz, CH^3), 3.34 (1H, dd, J 15.0 and 3.8 Hz, $CH^{1'}$), 3.16 (1H, d, J 16.0 Hz, CH^3); δ_C (126 MHz, $CDCl_3$), 141.2 ($C^{2''}$), 140.3 ($C^{3'}$), 135.4 (C^4), 133.4 ($C^{5'}$), 133.2 (C^{8a}), 132.2 (C^{4a}), 129.1, 128.8 ($C^{4'}$), 128.2, 127.8 ($C^{5'}$), 127.6, 126.8, 126.2 ($C^{4''}$), 125.4, 123.6, 110.8 (=CH_2), 61.5 ($C^{1'}$), 58.3 (C^1), 52.3 ($C^{1''}$), 48.1 (C^3); m/z (%) (FAB) 396 (MH^+, 29), 291 (68), 240 (22) and 97 (100).

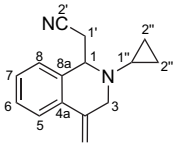
3.4.11. 2-(2-Cyclopropyl-4-methylene-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenyl-ethanone (8a).



Prepared by the general procedure from (**5a**) (334 mg, 1.00 mmol) and cyclopropylamine (114 mg, 2.00 mmol).

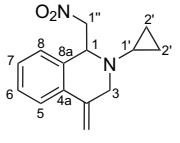
Column chromatography afforded the product (**8a**) (242 mg, 80%) as a pale yellow oil. (Found: C, 83.00; H, 6.75; N, 4.60; $C_{21}H_{21}NO$ requires C, 83.10; H, 7.00; N, 4.60%); ν/max (film) 3064, 2941 1682, 1633, 1597 and 1482 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 7.91 (1H, d, J 8.3 Hz, $ArH^{4'}$), 7.90 (1H, d, J 8.5 Hz, $ArH^{4'}$), 7.70–7.66 (1H, m, ArH^5), 7.54 (1H, tt, J 7.4 and 1.8 Hz, $ArH^{6'}$), 7.46 (2H, t, J 6.9 Hz, 2×$ArH^{5'}$), 7.25–7.16 (3H, m, ArH^6, ArH^7 and ArH^8), 5.66 (1H, s, =CH), 5.05 (1H, s, =CH), 4.72 (1H, dd, J 9.0 and 5.2 Hz, CH^1), 3.94 (1H, d, J 15.3 Hz, CH^3), 3.56 (1H, dd, J 15.7 and 9.0 Hz, $CH^{1'}$), 3.46 (1H, d 15.3 Hz, CH^3), 3.07 (1H, dd, J 15.7 and 5.2 Hz, $CH^{1'}$), 1.97–1.93 (1H, m, $CH^{1''}$), 1.25–1.19 (4H, m, 4×$CH^{2''}$); δ_C (126 MHz, $CDCl_3$), 198.7 ($C^{2'}$), 137.6, 137.6, 136.9 (C^4), 132.8 ($C^{6'}$), 132.3 (C^{4a}), 128.5 ($C^{5'}$), 128.2 ($C^{4'}$), 128.1, 127.8, 126.8, 123.7 ($C^{(5\ or\ 8)}$), 108.9 (=CH_2), 59.5 (C^1), 51.2 (C^3), 44.6 ($C^{1'}$), 34.6 ($C^{1''}$), 7.0 ($C^{2''}$), 6.9 ($C^{2''}$); m/z (%) (ES) 326 (MNa^+, 100).

3.4.12. (2-Cyclopropyl-4-methylene-1,2,3,4-tetrahydroisoquinolin-1-yl)-acetonitrile (8b).



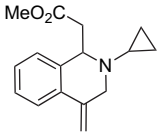
Prepared by the general procedure from (**5b**) (255 mg, 1.00 mmol) and cyclopropylamine (114 mg, 2.00 mmol). Column chromatography afforded the product (**8b**) (129 mg, 47%) as a pale yellow amorphous solid, mp 122–124 °C. (Found: C, 81.40; H, 7.40; N, 12.70; $C_{15}H_{16}N_2$ requires C, 80.30; H, 7.20; N, 12.50%); ν/max (Nujol mull) 2243, 1410, 1315 and 1252 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 7.69–7.67 (1H, m, ArH^5), 7.30 (2H, m, ArH^6, ArH^7), 7.19–7.15 (1H, m, ArH^8), 5.66 (1H, d, J 1.7 Hz, =CH), 5.10 (1H, t, J 1.0 Hz, =CH), 4.27 (1H, dd, J 9.2 and 5.4 Hz, CH^1), 3.80 (1H, dt, J 15.3 and 1.9 Hz, CH^3), 3.55 (1H, d, J 15.3 Hz, CH^3), 2.81 (1H, dd, J 16.8 and 9.2 Hz, $CH^{1'}$), 2.65 (1H, dd, J 16.8 and 5.4 Hz, $CH^{1'}$), 2.05–2.08 (1H, m, $CH^{1''}$), 0.65–0.60 (1H, m, $CH^{2''}$), 0.60–0.46 (3H, m, 3×$CH^{2''}$); δ_C (126 MHz, $CDCl_3$), 136.9 (C^4), 134.0 (C^{8a}), 132.6 (4^a), 128.4, 127.7, 127.6, 124.1 (C^5), 118.5 ($C^{2'}$), 109.8 (=CH_2), 59.8 (C^1), 50.9 (C^3), 34.7 ($C^{1''}$), 24.0 ($C^{1'}$), 7.5 ($C^{2''}$), 7.1 ($C^{2''}$); m/z (%) 224 (M^+, 55), 209 (29), 196 (37), 184 (100), 169 (43), 157 (40), 142 (48), 128 (76) and 115 (61).

3.4.13. 2-Cyclopropyl-4-methylene-1-nitromethyl-1,2,3,4-tetrahydroisoquinoline (8c).



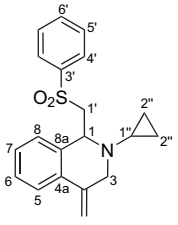
Prepared by the general procedure from (**5c**) (275 mg, 1.00 mmol) and cyclopropylamine (114 mg, 2.00 mmol). Column chromatography afforded the product (**8c**) (166 mg, 68%) as a pale yellow amorphous solid, mp 58–60 °C. (Found: C, 68.90; H, 6.60; N, 11.30; $C_{14}H_{16}N_2O_2$ requires C, 68.80; H, 6.55; N, 11.50%); ν/max (Nujol mull) 1547, 1334, 1252 and 1221 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 7.72–7.69 (1H, m, ArH^5), 7.31–7.28 (2H, m, ArH^6 and ArH^7), 7.18–7.14 (1H, m, ArH^8), 5.69 (1H, d, J 1.7 Hz, =CH), 5.12 (1H, d, J 1.9 Hz, =CH), 4.77 (1H, dd, J 11.3 and 4.2 Hz, CH^1), 4.69 (1H, t, J 11.8 Hz, $CH^{1'}$), 4.47 (1H, dd, J 11.9 and 4.2 Hz, $CH^{1'}$), 3.90 (1H, dt, J 15.6 and 1.9 Hz, CH^3), 3.52 (1H, d, J 15.6 Hz, CH^3), 2.07–2.03 (1H, m, $CH^{1''}$), 0.49–0.38 (4H, m, $CH^{2''}$); δ_C (126 MHz, $CDCl_3$), 136.3 (C^4), 133.4 (C^{4a}), 130.9 (C^{8a}), 128.5 (C^6), 127.9 (C^7), 127.7 (C^8), 124.2 (C^5), 110.3 (=CH_2), 78.7 ($C^{1'}$), 61.2 (C^1), 50.1 (C^3), 34.5 ($C^{1''}$), 7.4 ($C^{2''}$), 7.2 ($C^{2''}$); m/z (%) (FAB) 245 (MH^+, 41), 198 (100), 184 (85), 156 (57), 142 (31) and 129 (24).

3.4.14. Methyl (2-cyclopropyl-4-methylene-1,2,3,4-tetrahydro-1-isoquinolinyl)-acetate (8d).



Prepared by the general procedure from (**5d**) (288 mg, 1.00 mmol) and cyclopropylamine (114 mg, 2.00 mmol). Column chromatography afforded the product (**8d**) (80%) as a pale yellow oil. (Found: C, 74.45; H, 7.25; N, 5.70; $C_{16}H_{19}NO_2$ requires: C, 74.70; H, 7.45; N, 5.45%); IR (film) 3007, 2948, 1736 and 1436 cm^{-1}; δ_H (250 MHz, $CDCl_3$), 7.70–7.66 (1H, m, ArH), 7.28–7.19 (2H, m, 2×ArH), 7.15–7.11 (1H, m, ArH), 5.65 (1H, d, J 1.8 Hz, CH_2=), 5.05 (1H, t, J 0.9 Hz, CH_2=), 4.47 (1H, dd, J 10.3 and 5.1 Hz, PhCHN), 3.89 (1H, dd, J 15.4, 1.8 and 0.9 Hz, CCH_2N), 3.68 (3H, s, CO_2Me), 3.47 (1H, dd, J 15.4 and 0.9 Hz, CCH_2N), 2.80 (1H, dd, J 14.7 and 10.3 Hz, CH_2CO), 2.59 (1H, dd, J 14.7 and 5.1 Hz, CH_2CO), 1.98 (1H, m, NCH), 0.54–0.38 (4H, m, 2×$CH^{2''}$); δ_C (75 MHz, $CDCl_3$), 172.1, 137.4, 136.0, 132.4, 128.2, 127.6, 126.9, 123.7, 109.1, 59.8, 51.6, 50.8, 41.1, 34.5, 7.4, 7.1; m/z (EI) (%) 257 (M^+, 57), 184 (100), 141 (79) and 128 (60).

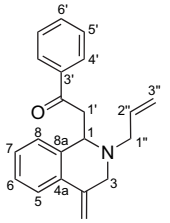
3.4.15. 1-Benzenesulfonylmethyl-2-cyclopropyl-4-methylene-1,2,3,4-tetrahydroisoquinoline (8e).



Prepared by the general procedure from (**5e**) (370 mg, 1.00 mmol) and cyclopropylamine (114 mg, 2.00 mmol). Column chromatography afforded the product (**8e**) (234 mg, 69%), which was crystallised from dichloromethane as colourless prisms, mp 126–128 °C. (Found: C, 70.70; H, 6.00; N, 3.90; $C_{20}H_{21}NO_2S$ requires C, 70.80; H, 6.25; N, 4.10%); ν/max (Nujol mull) 3055, 1483, 1446 and 1421 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 7.89–7.87 (2H, m,

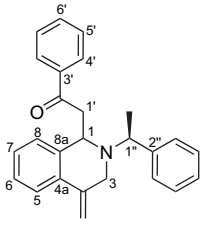
2×ArH), 7.62 (2H, tt, *J* 7.4 and 1.2 Hz, 2×CH), 7.52 (2H, tt, *J* 7.4 and 1.7 Hz, 2×ArH), 7.26 (1H, td, *J* 7.5 and 1.5 Hz, ArH), 7.22 (1H, td, *J* 7.6 and 1.8 Hz, ArH), 7.13 (1H, m, ArH), 5.60 (1H, d, *J* 2.0 Hz, =CH), 4.94 (1H, d, *J* 2.0 Hz, =CH), 4.62 (1H, dd, *J* 10.4 and 3.7 Hz, CH^1), 3.70 (1H, dd, *J* 15.2 and 10.4 Hz, $CH^{1''}$), 3.30 (1H, dt, *J* 16.0 and 2.0 Hz, CH^3), 3.28 (1H, dd, *J* 15.2 and 3.7 Hz, $CH^{1'}$), 3.03 (1H, d, *J* 16.0 Hz, CH^3), 1.91 (1H, sextet, *J* 3.6 Hz, $CH^{1''}$), 0.74 (1H, ddt, *J* 9.7, 6.1 and 3.8 Hz, $CH^{2''}$), 0.42–0.31 (2H, m, $CH^{2''}$), 0.22 (1H, ddt, *J* 9.6, 5.9 and 3.6 Hz, $CH^{2''}$); δ_C (126 MHz, $CDCl_3$), 140.9 ($C^{3'}$), 136.4 (C^{4a}), 133.6, 133.2, 132.4 (C^4), 128.7, 128.6, 128.1, 127.7, 127.4, 123.7, 109.7 (=CH_2), 60.3 ($C^{1''}$), 58.3 (C^1), 49.8 (C^3), 34.6 ($C^{1''}$), 6.72 ($C^{2''}$); *m*/*z* (%) (FAB) 340 (MH^+, 100), 198 (78) and 143 (23).

3.4.16. 2-(2-Allyl)-4-methylene-1,2,3,4-tetrahydroisoquinolin-1-yl-1-phenyl-ethanone (9a).



Prepared by the general procedure from (**5a**) (334 mg, 1.00 mmol) and allylamine (114 mg, 2.00 mmol). Column chromatography afforded the product (**9a**) (187 mg, 62%) as a yellow oil. (Found: C, 83.20; H, 6.75; N, 4.70; $C_{21}H_{21}NO$ requires C, 83.10; H, 7.00; N, 4.60%); *ν*/max (film) 3067, 2911, 1683, 1641, 1597 and 1582 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 7.95–7.92 (2H, m, 2×$ArH^{4'}$), 7.68–7.65 (1H, m, ArH^5), 7.54 (1H, tt, *J* 7.4 and 1.3 Hz, $ArH^{6'}$), 7.48–7.43 (2H, m, 2×$ArH^{5'}$), 7.22–7.19 (2H, m, ArH^6, ArH^7), 7.14–7.11 (1H, m, ArH^8), 5.75 (1H, ddt, *J* 16.3, 10.4 and 6.4 Hz, =$CH^{2''}$), 5.66 (1H, d, *J* 1.8 Hz, =CH), 5.07–5.02 (2H, m, 2×=$CH^{3''}$), 5.0 (1H, t, *J* 1.0 Hz, =CH), 4.6 (1H, dd, *J* 7.9 and 5.6 Hz, CH^1), 3.94 (1H, dt, *J* 15.4 and 1.9 Hz, CH^3), 3.61 (1H, dd, *J* 16.0 and 8.1 Hz, $CH^{1'}$), 3.42 (1H, d, *J* 15.5 Hz, CH^3), 3.16 (1H, dd, *J* 16.0 and 5.6 Hz, $CH^{1'}$), 3.14 (1H, ddt, *J* 13.6, 6.2 and 1.4 Hz, $CH^{1''}$), 3.05 (1H, dt, *J* 13.6, 6.7 and 1.2 Hz, $CH^{1''}$); δ_C (126 MHz, $CDCl_3$), 198.5 ($C^{2'}$), 137.5 ($C^{3'}$), 136.9 (C^4), 136.3 (C^{8a}), 135.9 ($C^{2''}$), 132.9 ($C^{6'}$), 132.2 (C^{4a}), 128.6 ($C^{5'}$), 128.3, 128.2, 127.9, 126.8, 123.5, 117.4 ($C^{3''}$), 109.3 (=CH_2), 57.8 (C^1), 57.0 ($C^{1''}$), 50.7 (C^3), 44.9 ($C^{1'}$); *m*/*z* (%) (FAB) 304 (MH^+, 31), 262 (13), 184 (100) and 105 (33).

3.4.17. 2-((*R*)-1-Phenylethyl-4-methylene-1,2,3,4-tetrahydroisoquinolin-1-yl)-1-phenyl-ethanone (10a).



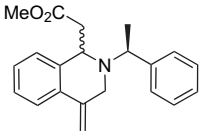
Prepared by the general procedure from (**5a**) (334 mg, 1.00 mmol) and (*R*)-(+)-α-methylbenzylamine (242 mg, 2.00 mmol). Column chromatography afforded the product (**10a**) (264 mg, 72%) as a pale yellow oil which comprised of a 1:1 mixture of diastereoisomers. (Found: C, 84.70; H, 6.70; N, 3.90; $C_{26}H_{25}NOS$ requires C, 85.00; H, 6.85; N, 3.80%); *ν*/max (film) 3060, 1681, 1598, 1491 and 1448 cm^{-1}; *m*/*z* (%) (FAB) 368 (MH^+, 31), 248 (97), 144 (33) and 105 (100).

The two diastereoisomers were separated by column chromatography eluting with 2:3 v/v ether/petrol containing triethylamine (10%).

Diasteroisomer ***A***: δ_H (250 MHz, $CDCl_3$), 8.00 (2H, 2×d, *J* 8.5 Hz, 2×ArH), 7.72–7.65 (1H, m, ArH), 7.61–7.44 (3H, m, 3×ArH), 7.28–7.17 (6H, m, 6×ArH), 7.16–7.08 (2H, m, 2×ArH), 5.63 (1H, s, =CH), 5.00 (1H, dd, *J* 8.6 and 5.3 Hz, CH), 4.72 (1H, s, =CH), 3.81 (1H, d, *J* 15.7 Hz, CH), 3.68 (1H, dd, *J* 15.1 and 8.6 Hz, CH), 3.56 (1H, q, *J* 6.6 Hz, CH), 3.18 (1H, dd, *J* 15.1 and 5.3 Hz, CH), 3.11 (1H, d, *J* 15.7 Hz, CH), 1.14 (3H, d, *J* 6.6 Hz, Me).

Diastereoisomer ***B***: δ_H (250 MHz, $CDCl_3$), 7.75 (2H, 2×d, *J* 8.5 Hz, 2×ArH), 7.64 (1H, dd, *J* 9.1 and 1.6 Hz, ArH), 7.46 (1H, t, *J* 7.2 Hz, ArH), 7.32 (2H, t, *J* 7.5 Hz, 2×ArH), 7.15–6.87 (8H, m, 8×ArH), 5.64 (1H, s, =CH), 4.97 (1H, s, =CH), 4.33 (1H, t, *J* 7.2 Hz, CH), 3.99 (1H, d, *J* 16.0 Hz, CH), 3.79 (1H, d, *J* 16.0 Hz, CH), 3.46 (1H, q, *J* 6.6 Hz, CH), 3.76 (1H, dd, *J* 14.4 and 7.2 Hz, CH), 3.09 (1H, dd, *J* 14.5 and 7.2 Hz, CH), 1.21 (3H, d, *J* 6.6 Hz, Me).

3.4.18. Methyl [4-methylene-2-(1-phenylethyl)-1,2,3,4-tetrahydro-1-isoquinolinyl]-acetate (10d).

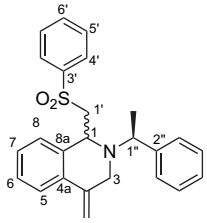


Prepared from (**5a**) (288 mg, 1.00 mmol) and *R*-(+)-α-methylbenzylamine (242 mg, 2.00 mmol). Column chromatography afforded product isomer **A** (34%) and isomer **B** (40%).

Isomer ***A***: Pale yellow oil. $[\alpha]_D$ −70.2 (0.114 g/100 ml). (Found: C, 78.20; H, 7.05; N, 4.50; $C_{21}H_{23}NO_2$ requires C, 78.45; H, 7.20; N, 4.35%); IR (film) 3027, 2973, 1736 and 1436 cm^{-1}; δ_H (250 MHz, $CDCl_3$), 7.69–7.64 (1H, m, ArH), 7.32–7.18 (7H, m, 7×ArH), 7.16–7.12 (1H, m, ArH), 5.61 (1H, d, *J* 1.8 Hz, CH_2=), 4.77 (1H, dd, *J* 10.5 and 5.2 Hz, N*CH*CH_2), 4.72 (1H, t, *J* 1.0 Hz, CH_2=), 3.77 (1H, ddd, *J* 16.1, 1.8 and 1.1 Hz, CCH_2N), 3.78 (3H, s, CO_2Me), 3.60 (1H, q, *J* 6.5 Hz, CH), 3.13 (1H, dd, *J* 16.1 and 1.0 Hz, CCH_2N), 2.93 (1H, dd, *J* 14.3 and 10.5 Hz, CH_2CO), 2.70 (1H, dd, *J* 14.3 and 5.2 Hz, CH_2CO), 1.27 (3H, d, *J* 6.5 Hz, Me); *m*/*z* (%) (EI) 321 (M^+, 1), 248 (89), 216 (41), 144 (78), 115 (50), 105 (100) and 77 (49).

Isomer ***B***: Pale yellow oil, which crystallised from ether/petroleum ether as pale yellow prisms, mp 54–55 °C. $[\alpha]_D$ +86.2 (0.116 g/100 ml). (Found: C, 78.15; H, 7.25; N, 4.40; $C_{21}H_{23}NO_2$ requires C, 78.45; H, 7.20; N, 4.50%); IR (film) 3030, 2977, 1739 and 1436 cm^{-1}; δ_H (250 MHz, $CDCl_3$), 7.00 (1H, dd, *J* 7.3 and 2.0 Hz, ArH), 7.32–7.14 (7H, m, 7×ArH), 6.91 (1H, dt, *J* 2.0 and 0.5 Hz, ArH), 5.69 (1H, s, CH_2=), 5.01 (1H, s, CH_2=), 4.13 (1H, dd, *J* 10.0 and 5.4 Hz, N*CH*CH_2), 4.00 and 3.75 (2×1H, AB, 2×d, *J* 16.3 Hz, CCH_2N), 3.63 (3H, s, CO_2Me), 3.54 (1H, q, *J* 6.4 Hz, CH), 2.43 (1H, dd, *J* 14.0 and 10.0 Hz, CH_2CO), 2.25 (1H, dd, *J* 14.0 and 5.4 Hz, CH_2CO) and 1.27 (3H, d, *J* 6.5 Hz, Me); *m/z* (%) (ES) 344 (M^++Na, 1) and 322 (72).

3.4.19. 1-Benzenesulfonylmethyl-4-methylene-2-((*R*)-1-phenylethyl)-1,2,3,4-tetrahydroisoquinoline (10e).

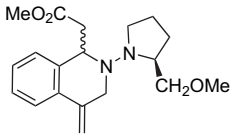


Prepared by the general procedure from (**5e**) (370 mg, 1.00 mmol) and (*R*)-(+)-α-methylbenzylamine (242 mg, 2.00 mmol). Column chromatography afforded the product (**10e**) (290 mg, 72%), which comprised of a separable 1:1 mixture of diastereoisomers.

Diastereoisomer ***A***: crystallised from ethanol/water as colourless needles (145 mg, 36%), mp 184–186 °C. $[\alpha]_D$ +62.2 (0.051 g/50 ml). (Found: C, 73.30; H, 6.40; N, 3.70; $C_{25}H_{25}NO_2S$ requires C, 74.40; H, 6.25; N, 3.50%); *ν*/max (Nujol mull) 1305, 1147 and 1085 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 8.05–8.03 (2H, m, ArH), 7.69–7.63 (2H, m, ArH), 7.60–7.52 (2H, m, ArH), 7.30–7.15 (4H, m, ArH), 7.09 (1H, m, ArH), 5.60 (1H, d, *J* 1.7 Hz, =CH), 4.98 (1H, dd, *J* 9.2 and 3.2 Hz, CH^1), 4.65 (1H, d, *J* 1.8 Hz, =CH), 3.94 (1H, dd, *J* 14.9 and 9.2 Hz, $CH^{1'}$), 3.51 (1H, q, *J* 6.5 Hz, $CH^{1''}$), 3.43 (1H, d, *J* 16.6 Hz, CH^3), 3.35 (1H, dd, *J* 14.9 and 3.2 Hz, $CH^{1'}$), 2.97 (1H, d, *J* 16.6 Hz, CH^3), 1.28 (3H, d, *J* 6.5 Hz, Me); δ_C (126 MHz, $CDCl_3$), 144.9 ($C^{2''}$), 140.9 ($C^{3'}$), 135.7, 133.3, 133.0, 132.7, 129.1, 128.8, 128.2, 127.9, 127.7, 127.6, 127.5, 126.9, 123.5, 110.1 (=CH_2), 61.1 ($C^{1'}$), 58.8 ($C^{1''}$), 53.8 (C^1), 47.9 (C^3), 21.8 ($C^{2'}$); *m/z* (%) (FAB) 404 (MH^+, 100), 298 (34), 248 (79), 144 (26) and 105 (43).

Diastereoisomer ***B***: crystallised from ethanol water as colourless needles (147 mg, 36%), mp 172–174 °C. $[\alpha]_D$ −88.4 (0.051 g/50 ml). (Found: C, 73.30; H, 6.40; N, 3.70; $C_{25}H_{25}NO_2S$ requires C, 74.20; H, 6.40; N, 3.60%); *ν*/max (Nujol mull) 1304, 1146 and 1084 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 7.79–7.77 (2H, m, ArH), 7.65–7.59 (2H, m, ArH), 7.51–7.46 (2H, m, ArH), 7.33–7.26 (3H, m, ArH), 7.23–7.20 (3H, m, ArH), 7.19–7.12 (1H, m, ArH), 6.70 (1H, d, *J* 7.01, ArH), 5.67 (1H, s, =CH), 5.0 (1H, s, =CH), 4.36 (1H, dd, *J* 7.7 and 4.5 Hz, CH^1), 3.72 (1H, dd, *J* 14.8 and 7.7 Hz, $CH^{1'}$), 3.64–3.60 (2H, m, CH_2^3), 3.55 (1H, q, *J* 6.5 Hz, $CH^{1''}$), 3.17 (1H, dd, *J* 14.8 and 4.5 Hz, $CH^{1'}$), 1.32 (3H, d, *J* 6.5 Hz, Me); δ_C (126 MHz, $CDCl_3$), 143.8 ($C^{2''}$), 140.4 ($C^{2'}$), 136.5, 134.4, 133.4, 132.4, 129.0, 128.6, 128.4, 128.3, 128.1, 127.7, 127.4, 127.3, 123.4, 109.3 (=CH_2), 61.1 ($C^{1'}$), 60.0 ($C^{1''}$), 55.2 (C^1), 47.5 (C^3), 21.0 ($C^{2'}$); *m/z* (%) (ES) 404 (MH^+, 100).

3.4.20. Methyl {2-[2-(methyoxymethyl)-1-pyrrolidinyl]-4-methylene-1,2,3,4-tetrahydro-1-isoquinolinyl}acetate (11d).



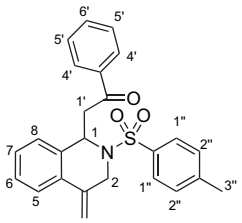
Prepared from (**5d**) (288 mg, 1.00 mmol) and SAMP (268 μl, 2.00 mmol). Column chromatography afforded product **11d** major (53%) and product **11d** minor (25%).

11d *major*: Pale yellow oil. $[\alpha]_D$ +58.8 (0.102 g/100 ml). (Found: C, 68.80; H, 7.85; N, 8.30; $C_{19}H_{26}N_2O_3$ requires C, 69.05; H, 7.95; N, 8.50%); IR (film) 2949, 1733 and 1436 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 7.62 (1H, dd, *J* 7.9 and 1.2 Hz, ArH), 7.25–7.18 (3H, m, 3×ArH), 5.53 (1H, s, CH_2=), 5.02 (1H, s, CH_2=), 4.50 (1H, t, *J* 5.8 Hz CCHN), 3.69 (3H, s, CO_2Me), 3.66 (2H, m, CCH_2N and CH_2O), 3.39 (1H, d, *J* 11.9 Hz, CCH_2N), 3.33 (3H, s, OMe), 3.20 (1H, t, *J* 8.8 Hz, CH_2O), 2.99 (1H, m, OCH_2CHN), 2.99 and 2.61 (2×1H, 2×m, CH_2), 2.76 (2H, d, *J* 5.8 Hz, CH_2CO), 1.86 and 1.68 (2×1H, 2×m, CH_2), 1.60–1.47 (2H, m, CH_2); δ_C (125 MHz, $CDCl_3$) 172.9 (CO), 140.9 (C_q), 137.9 (C_q), 133.0 (C_q), 128.5 (CH), 126.6 (CH), 126.5 (CH), 124.0 (CH), 107.3 (CH_2), 75.9 (CH_2), 61.0 (CH), 59.0 (Me), 58.9 (CH), 51.3 (Me), 48.4 (CH_2), 41.7 (CH_2), 41.3 (CH_2), 27.1 (CH_2), 21.5 (CH_2); *m/z* (%) (EI) 330 (M^+, 56), 285 (100), 257 (100), 156 (55), 142 (73), 128 (56), 115 (55), 85 (45) and 70 (45).

11d *minor*: Pale yellow oil. $[\alpha]_D$ −146.7 (0.150 g/100 ml). (Found: C, 68.80; H, 8.05; N, 8.45; $C_{19}H_{26}N_2O_2$ requires C, 69.05; H, 7.95; N, 8.50%); IR (film) 2950, 1735 and 1436 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 7.65 (1H, dd, *J* 7.7 and 1.4 Hz, ArH), 7.26–7.19 (2H, m, 2×ArH), 7.13 (1H, dd, *J* 7.5 and 1.5 Hz, ArH), 5.55 (1H, d, *J* 1.6 Hz, CH_2=), 5.07 (1H, t, *J* 0.9 Hz, CH_2=), 4.52 (1H, dd, *J* 10.5 and 4.5 Hz, CCHN), 4.02 (1H, ddd, *J* 15.2, 1.6 and 0.9 Hz, CCH_2N), 3.72 (3H, s, CO_2Me), 3.59 (1H, dd, *J* 15.2 and 0.9 Hz, CCH_2N), 3.45 (1H, dd, *J* 3.3 and 9.0 Hz, CH_2O), 3.36 (3H, s, OMe), 3.26 (1H, dd, *J* 9.0 and 7.0 Hz, CH_2O), 2.96 (1H, m, OCH_2CHN), 2.78 (1H, dd, *J* 14.6 and 10.5 Hz, CH_2CO), 2.74 and 2.33 (2×1H, 2×m, CH_2), 2.66 (1H, dd, *J* 14.6 and 4.5 Hz, CH_2CO), 1.73 (1H, m, CH_2), 1.58–1.49 (3H, m, CH_2); δ_C (125 MHz, $CDCl_3$) 172.0 (CO), 139.1 (C_q), 137.3 (C_q), 133.4 (C_q), 128.3 (CH), 126.7 (CH), 126.4 (CH), 123.7 (CH), 108.1 (CH_2), 75.4 (CH_2), 59.9 (CH), 59.1 (Me), 54.7 (CH), 53.2 (CH_2), 51.5 (Me), 48.6 (CH_2), 42.4 (CH_2), 25.2 (CH_2), 21.4 (CH_2); *m/z* (%) (EI) 330 (M^+, 27), 285

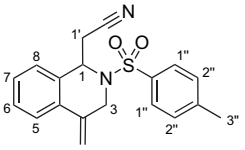
(82), 257 (100), 156 (61), 142 (91), 128 (71), 85 (45) and 70 (45).

3.4.21. 2-{4-Methylene-2-[(4-methylphenyl)sulfonyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}-1-phenyl-ethanone (12a).



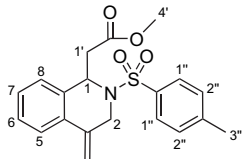
Prepared by the general procedure from **5a** (0.144 g, 0.50 mmol), *p*-toluenesulfonamide (0.083 g, 0.60 mmol), Pd_2dba_3 (0.011 g, 0.0125 mmol), tri-2-furylphosphine (0.012 g, 0.05 mmol), K_2CO_3 (0.138 g, 1.00 mmol), allene (0.2 bar) and toluene (2 ml). Column chromatography eluting with 3:1 hexane/ether afforded the product (**12a**) as colourless needles (0.163 g, 78%), mp 94–96 °C. HRMS: 440.1302, $C_{25}H_{23}NO_3SNa$ requires: 440.1291; ν/max (film) 1682, 1345 and 1159 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 7.89 (2H, d, *J* 7.3 Hz, $ArH^{1''}$), 7.55 (1H, t, *J* 7.3 Hz, $ArH^{4'}$), 7.42–7.49 (4H, m, $ArH^{1''}$, $ArH^{5'}$), 7.35 (1H, d, *J* 7.0 Hz, ArH^5), 7.06–7.14 (3H, m, ArH^6, ArH^7 and ArH^8), 6.97 (2H, d, *J* 7.7 Hz, $ArH^{2''}$), 5.73 (1H, dd, *J* 6.9 and 5.8 Hz, CH^1), 5.48 (1H, s, =CH), 5.07 (1H, s, =CH), 4.59 (1H, d, *J* 16.6 Hz, CH^2), 4.29 (1H, d, *J* 16.6 Hz, CH^2), 3.54 (1H, dd, *J* 16.2 and 5.8 Hz, $CH^{1'}$), 3.38 (1H, dd, *J* 16.2 and 6.9 Hz, $CH^{1'}$), 2.24 (3H, s, $CH^{3''}$); δ_C (75 MHz, $CDCl_3$): 196.3, 143.0, 136.7, 136.0, 135.8, 135.2, 133.3, 131.1, 129.0, 128.7, 128.2, 127.4, 127.3, 127.0, 124.0, 110.0, 53.3, 46.0, 45.6, 29.7, 21.4; *m*/*z* (%) (ES) 440 (MNa^+, 10) and 298 (100).

3.4.22. {4-Methylene-2-[(4-methylphenyl)sulfonyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}acetonitrile (12b).



Prepared by the general procedure from **5b** (0.128 g, 0.50 mmol), *p*-toluenesulfonamide (0.083 g, 0.60 mmol), Pd_2dba_3 (0.011 g, 0.0125 mmol), tri-2-furylphosphine (0.012 g, 0.05 mmol), K_2CO_3 (0.138 g, 1.00 mmol), allene (0.2 bar) and toluene (2 ml). Column chromatography eluting with 9:1 hexane/ethyl acetate afforded the product (**12b**) as colourless needles (0.115 g, 68%), mp 132–134 °C. (Found: C, 67.15; H, 5.35; N, 8.45; S, 9.20; $C_{19}H_{18}N_2SO_2$ requires C, 67.43; H, 5.36; N, 8.28; S, 9.47%); ν/max (film) 1597, 1346, 1161 and 1090 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 7.55 (2H, d, *J* 8.1 Hz, $ArH^{1''}$), 7.43 (1H, d, *J* 7.7 Hz, ArH^8), 7.26 (1H, t, *J* 7.3 Hz, ArH^6), 7.21 (1H, dd, *J* 7.7 and 7.3 Hz, ArH^7), 7.15 (1H, d, *J* 7.3 Hz, ArH^5), 7.07 (2H, d, *J* 8.1 Hz, $ArH^{2''}$), 5.50 (1H, s, =CH), 5.28 (1H, dd, *J* 6.8 and 6.4 Hz, CH^1), 5.08 (1H, s, =CH), 4.49 (1H, d, *J* 6.3 Hz, CH^3), 4.25 (1H, d, *J* 16.3, CH^3), 2.96 (1H, dd, *J* 16.7 and 6.4 Hz, $CH^{1'}$), 2.89 (1H, dd, *J* 16.7 and 6.8 Hz, $CH^{1'}$), 2.31 (3H, s, $CH^{3''}$); δ_C (75 MHz, $CDCl_3$): 143.7, 135.6, 134.8, 131.7, 131.6, 129.4, 128.6, 128.4, 127.4, 126.9, 124.5, 116.7, 111.2, 53.5, 45.7, 25.9, 21.5; *m*/*z* (%) (ES) 339 (MH^+, 30), 184 (38) and 143 (100).

3.4.23. Methyl {4-methylene-2-[(4-methylphenyl)sulfonyl]-1,2,3,4-tetrahydroisoquinolin-1-yl}acetate (12d).



Prepared by the general procedure from **5d** (0.144 g, 0.50 mmol), *p*-toluenesulfonamide (0.083 g, 0.60 mmol), Pd_2dba_3 (0.011 g, 0.0125 mmol), tri-2-furylphosphine (0.012 g, 0.05 mmol), K_2CO_3 (0.138 g, 1.00 mmol), allene (0.2 bar) and toluene (2 ml). Column chromatography eluting with 3:1 hexane/ether afforded the product (**12d**) as colourless needles (0.161 g, 87%), mp 179–181 °C. HRMS: 372.1284, $C_{20}H_{22}NO_4S$ requires: 372.1275); ν/max (film) 1475, 1398, 1171 and 1038 cm^{-1}; δ_H (500 MHz, $CDCl_3$): 7.46 (2H, d, *J* 8.0 Hz, $ArH^{1''}$), 7.32 (1H, d, *J* 7.7 Hz, ArH^5), 7.15 (d, *J* 6.8 Hz, ArH^8), 7.05–7.10 (2H, m, ArH^6 and ArH^7), 5.46 (1H, dd, *J* 8.6 and 6.2 Hz, CH^1), 5.45 (1H, s, =CH), 5.02 (1H, s, =CH), 4.57 (1H, d, *J* 17.0 Hz, CH^2), 4.24 (1H, d, *J* 17.0 Hz, CH^2), 3.73 (3H, s, $CH^{4'}$), 2.86 (1H, dd, *J* 14.7 and 8.6 Hz, $CH^{1'}$), 2.73 (1H, dd, *J* 14.7 and 6.2 Hz, $CH^{1'}$), 2.25 (3H, s, $CH^{3''}$); δ_C (75 MHz, $CDCl_3$), 170.6, 143.5, 136.5, 135.6, 134.5, 131.4, 129.4, 128.7, 127.9, 127.8, 127.0, 124.4, 110.4, 54.9, 52.5, 45.7, 42.0, 21.8; *m*/*z* (%) 765 ($2MNa^+$, 11), 372 (MNa^+, 19), 298 (62), 217 (56) and 143 (100).

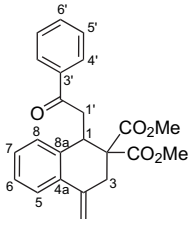
3.5. General procedure for the three-component allenylation/nucleophilic capture/Michael addition cascade using carbon nucleophiles, and (5a and 5e)

A Schlenk tube was charged with aryl iodide (1.00 mmol), carbon pronucleophile(2.00 mmol), cesium carbonate (276 mg, 2.00 mmol, 2.00 mol equiv), palladium acetate (22 mg, 0.10 mmol, 0.10 mol equiv), triphenylphosphine (52 mg, 0.20 mmol, 0.20 mol equiv) and acetonitrile (20 ml) and subjected to two freeze-pump-thaw cycles. Allene gas (1 bar) was then added and the reaction mixture heated at 50–60 °C for 18 h. After cooling to rt, excess allene gas was vented, the mixture filtered and the solids washed with ether (3×50 ml). The organic extracts were combined, dried ($MgSO_4$), filtered and the filtrate evaporated under reduced pressure. The residue was purified by column chromatography eluting with 2:3 v/v ether/petrol.

3.6. General procedure for the three-component allenylation/nucleophilic capture/Michael addition cascade using carbon nucleophiles, and (5d)

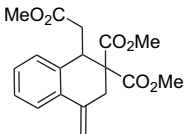
Reaction conditions as above except the process was run in toluene for 18 h at 110 °C and 1.20 mmol of pronucleophile was used.

3.6.1. Dimethyl 4-methylene-1-(2-oxo-2-phenylethyl)-3,4-dihydronaphthalene-2,2(1*H*)-dicarboxylate (14a).



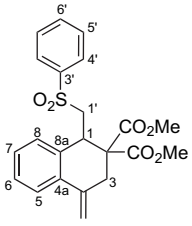
Prepared by the general procedure from (**5a**) (334 mg, 1.00 mmol) and dimethyl malonate (260 mg, 2.00 mmol). Column chromatography afforded the product (**14a**) (234 mg, 62%) as a colourless oil, which crystallised from ethanol/water as colourless prisms, mp 79–81 °C. (Found: C, 73.00; H, 5.85; $C_{23}H_{22}O_5$ requires C, 72.90; H, 5.80%); ν/max (Nujol mull) 1743, 1719, 1683, 1580, 1299 and 1278 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 7.89 (2H, 2×d, *J* 8.5 and 8.3 Hz, 2×ArH), 7.59–7.57 (1H, m, ArH), 7.53 (1H, tt, *J* 7.4 and 1.3 Hz, ArH), 7.44–7.40 (2H, m, 2×ArH), 7.19–7.12 (3H, m, 3×ArH), 5.64 (1H, t, *J* 0.9 Hz, =CH), 5.13 (1H, t, *J* 0.9 Hz, =CH), 4.59 (1H, dd, *J* 6.7 and 5.4 Hz, CH^1), 3.67 (3H, s, Me), 3.57 (3H, s, Me), 3.38 (1H, dd, *J* 17.5 and 5.4 Hz, $CH^{1'}$), 3.29 (1H, dd, *J* 15.8 and 0.9 Hz, CH^3), 3.20 (1H, d, *J* 15.8 and 0.9 Hz, CH^3), 3.12 (1H, d, *J* 17.5 and 6.7 Hz, $CH^{1'}$); δ_C (126 MHz, $CDCl_3$), 197.3 (C^{8a}), 170.9 (C=O), 170.3 (C=O), 138.6, 138.3, 136.9, 133.1, 132.3, 129.2, 128.6, 128.5, 128.1, 126.9 (C^4), 124.0 (=CH_2), 111.5, 57.7, 52.9 (Me), 52.8 (Me), 42.9 ($C^{1'}$), 38.7 (C^1), 34.0 (C^3); *m/z* (%) (ES) 401 (MNa^+, 100).

3.6.2. Dimethyl 1-(2-methoxy-2-oxo-ethyl)-4-methylene-3,4-dihydro-2,2(1*H*)-naphthalenedicarboxylate (14d).



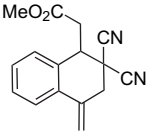
Prepared by the general procedure from (**5d**) (288 mg, 1.00 mmol) and dimethyl malonate (127 μl, 1.20 mmol). Column chromatography afforded the product (**14d**) (64%) as a pale yellow gum. (Found: C, 65.30; H, 6.30; $C_{18}H_{20}O_6$ requires C, 65.05; H, 6.10%); IR (film) 3035, 2954, 1736 and 1436 cm^{-1}; δ_H (250 MHz, $CDCl_3$), 7.60–7.56 (1H, m, ArH), 7.23–7.16 (3H, m, 3×ArH), 5.62 (1H, d, *J* 2.2 Hz, CH_2=), 5.11 (1H, d, *J* 0.8 Hz, CH_2=), 4.23 (1H, dd, *J* 8.0 and 5.3 Hz, CH), 3.74 (3H, s, CO_2Me), 3.64 and 3.55 (2×3H, 2×s, 2×CCO_2Me), 3.24 (1H, d, *J* 16.0 Hz, CCH_2C=), 3.05 (1H, ddd, *J* 16.0, 2.2 and 0.8 Hz, CCH_2C=), 2.60 (1H, dd, *J* 15.9 and 5.3 Hz, CH_2CO), 2.45 (1H, dd, *J* 15.9 and 8.0 Hz, CH_2CO); *m/z* (%) (EI) 332 (M^+, 4), 241 (63), 213 (84), 199 (100) and 141 (65).

3.6.3. 1-Benzenesulfonylmethyl-4-methylene-3,4-dihydro-1*H*-naphthalene-2,2-dicarboxylic acid dimethyl ester (14e).



Prepared by the general procedure from (**5e**) (370 mg, 1.00 mmol) and dimethyl malonate (260 mg, 2.00 mmol). Column chromatography afforded the product (**14e**) (195 mg, 47%) as a colourless oil, which crystallised from ethanol/water as colourless needles, mp 114–116 °C. (Found: C, 63.70; H, 5.10; $C_{22}H_{22}O_6S$ requires C, 63.80; H, 5.35%); ν/max (Nujol mull) 1730, 1336, 1295, 1276 and 1243 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 7.89–7.87 (2H, m, 2×ArH), 7.63 (1H, tt, *J* 2.5 and 1.2 Hz, ArH), 7.56–7.50 (3H, m, 3×ArH), 7.33 (1H, dd, *J* 7.9 and 1.5 Hz, ArH), 7.21 (1H, td, *J* 7.4 and 1.5 Hz, ArH), 7.16 (1H, td, *J* 7.7 and 1.5 Hz, ArH), 5.57 (1H, s, =CH), 5.08 (1H, s, =CH), 4.35 (1H, t, *J* 4.5 Hz, CH^1), 3.76 (3H, s, Me), 3.70 (1H, dd, *J* 14.8 and 4.5 Hz, $CH^{1'}$), 3.59 (3H, s, Me), 3.26 (1H, dd, 14.8 and 4.5 Hz, $CH^{1'}$), 3.23 (1H, dd, *J* 15.8 and 1.9 Hz, CH^3), 2.95 (1H, dt, *J* 15.8 and 1.9 Hz, CH^3); δ_C (126 MHz, $CDCl_3$), 170.2 (C=O), 169.7 (C=O), 139.9, 137.7, 136.5, 133.7, 132.3, 129.3, 129.2, 128.8, 128.0, 127.5, 124.1, 112.0 (=CH_2), 59.0 ($C^{1'}$), 58.2 (C^2), 53.2 (Me), 53.0 (Me), 37.8 (C^1), 34.5 (C^3); *m/z* (%) (CI) 437 (MNa^+, 100), 415 (85) and 355 (27).

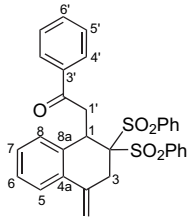
3.6.4. Methyl (2,2-dicyano-4-methylene-1,2,3,4-tetrahydro-1-naphthalenyl)-acetate (15d).



Prepared by the general procedure from (**5d**) (288 mg, 1.00 mmol) and malononitrile (79 mg, 1.20 mmol). Column chromatography afforded the product (**15d**) (42%) as a colourless oil. (Found: C, 72.30; H, 5.60; N, 10.35; $C_{16}H_{14}N_2O_2$ requires C, 72.15; H, 5.30; N, 10.50%); IR (film) 3029, 2954, 1735 and 1437 cm^{-1}; δ_H (250 MHz, $CDCl_3$), 7.72–7.68 (1H, m, ArH), 7.36–7.27 (2H, m, 2×ArH), 7.23–7.18 (1H, m, ArH), 5.87 (1H, d, *J* 1.4 Hz, CH_2=), 5.29 (1H, d, *J* 1.4 Hz, CH_2=), 4.12 (1H, dd, *J* 8.5 and 4.1 Hz, CH), 3.77 (3H, s, CO_2Me), 3.25 (2H, t, *J* 1.4 Hz, CCH_2C=), 3.02 (1H, dd, *J* 16.4 and 4.1 Hz, CH_2CO), 2.75 (1H, dd,

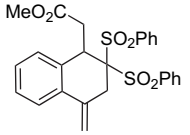
J 16.4 and 8.5 Hz, CH_2CO); *m/z* (%) (EI) 266 (M^+, 8), 240 (81), 179 (100), 166 (66) and 128 (60).

3.6.5. 2-(2,2-Bis-benzenesulfonyl-4-methylene-1,2,3,4-tetrahydronaphthalen-1-yl)-1-phenyl-ethanone (16a).



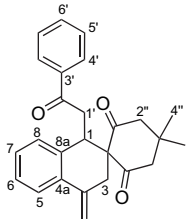
Prepared by the general procedure from (**5a**) (334 mg, 1.00 mmol) and bis(phenylsulfonyl)methane (592 mg, 2.00 mmol). Column chromatography afforded the product (**16a**) (141 mg, 52%) as a colourless oil, which crystallised from ethanol/water as colourless needles, mp 152–154 °C. (Found: C, 68.40; H, 4.75; $C_{31}H_{26}O_5S_2$ requires C, 68.60; H, 4.85%); *ν*/max (Nujol mull) 1683, 1334, 1154 and 1075 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 8.21 (2H, d, *J* 7.9 Hz, 2×ArH), 8.12 (2H, d, *J* 7.4 Hz, 2×ArH), 8.06 (2H, d, *J* 9.1, 2×ArH), 7.70 (1H, t, *J* 7.4 Hz, ArH), 7.63 (1H, t, *J* 7.4 Hz, ArH), 7.59–7.45 (8H, m, 8×ArH), 7.15–7.11 (2H, m, 2×ArH), 6.83–6.81 (1H, m, ArH), 5.59 (1H, d, *J* 1.8 Hz, =CH), 4.94 (1H, d, *J* 19.3 Hz, $CH^{1'}$), 4.87 (1H, d, *J* 8.1 Hz, $CH^{1'}$), 4.61 (1H, s, =CH), 3.98 (1H, dd, *J* 19.3 and 8.1 Hz, CH^1), 3.03 (1H, d, *J* 15.7 Hz, CH^3), 2.96 (1H, d, *J* 15.7 Hz, CH^3); δ_C (126 MHz, $CDCl_3$), 198.4 ($C^{2'}$), 137.7, 136.5, 136.5, 136.4, 135.6, 134.7, 134.6, 133.5, 132.7, 132.1, 131.6, 129.1, 129.0, 128.7, 128.5, 128.1, 126.5, 126.5, 123.5, 112.7 ($=CH_2$), 90.2 (C^2), 42.0 (C^1), 37.0 ($C^{1'}$), 36.6 (C^3); *m/z* (%) (ES) 565 (MNa^+, 100), 543 (42), 371 (63), 338 (69) and 331 (42).

3.6.6. Methyl (4-methylene-2,2-bis(phenylsulfonyl)-1,2,3,4-tetrahydro-1-naphthalenyl)-acetate (16d).



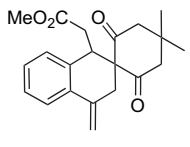
Prepared by the general procedure from (**5d**) (288 mg, 1.00 mmol) and bis(phenylsulfonyl)methane (356 mg, 1.20 mmol). Column chromatography afforded the product (**16d**) (60%) as a white powder, which crystallised from ethyl acetate/petroleum ether as colourless prisms, mp 139–140 °C. (Found: C, 62.80; H, 4.95; S, 12.80; $C_{26}H_{23}O_6S_2$ requires C, 63.00; H, 4.70; S, 12.95%); IR (film) 3065, 2952, 1733, 1447, 1329 and 1155 cm^{-1}; δ_H (250 MHz, $CDCl_3$), 8.15–8.04 (4H, m, ArH), 7.71–7.61 (2H, m, ArH), 7.57–7.48 (4H, m, ArH), 7.38 (1H, dd, *J* 7.7 and 1.4 Hz, ArH), 7.24 (1H, d, *J* 6.0 Hz, ArH), 7.22–7.13 (1H, m, ArH), 6.99 (1H, d, *J* 7.8 Hz, ArH), 5.53 (1H, s, CH_2=), 4.64 (1H, s, CH_2=), 4.45 (1H, d, *J* 9.0 Hz, CH_2CO), 4.26 (1H, d, *J* 18.1 Hz, CH_2CO), 3.82 (3H, s, CO_2Me), 3.20 (1H, dd, *J* 18.1 and 9.0 Hz, CH), 3.02 (2H, s, CCH_2C=); *m/z* (%) (EI) 355 (M^+-HSO_2Ph, 23), 323 (70), 294 (55), 281 (70), 215 (76), 154 (48), 141 (76), 77 (100) and 51 (52).

3.6.7. 3″,3″-Dimethyl-4-methylene-1-(2-oxo-2-phenyl-ethyl)-3,4-dihydro-1*H*-naphthalene-spiro[2,2]cyclohexane-1″,1″-dione (17a).



Prepared by the general procedure from (**5a**) (334 mg, 1.00 mmol) and dimedone (280 mg, 2.00 mmol). Column chromatography afforded the product (**17a**) (216 mg, 56%) as a pale yellow amorphous solid, mp 57–59 °C. (Found HRMS: 387.1955; $C_{26}H_{26}O_3$ (MH^+) requires 387.1960); *ν*/max (Nujol mull) 1727, 1693, 1596 and 1579 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 7.77–7.75 (2H, m, ArH), 7.58 (1H, dd, *J* 7.8 and 0.8 Hz, ArH), 7.50 (1H, t, *J* 7.3 Hz, ArH), 7.38 (2H, t, *J* 7.8 Hz, 2×ArH), 7.17 (1H, td, *J* 8.8 and 1.3 Hz, ArH), 7.12 (1H, d, *J* 7.3 Hz, ArH), 7.08 (1H, td, *J* 7.3 and 1.3 Hz, ArH), 5.69 (1H, t, *J* 1.6 Hz, =CH), 5.25 (1H, t, *J* 1.6 Hz, =CH), 4.46–4.44 (1H, m, CH^1), 3.30 (1H, dt, *J* 17.7 and 1.6 Hz, CH^3), 3.18 (1H, dd, *J* 17.7 and 8.1 Hz, $CH^{1'}$), 3.15 (1H, d, *J* 14.3 Hz, $CH^{2''}$), 3.04 (1H, d, *J* 13.6 Hz, $CH^{2''}$), 2.94 (1H, td, *J* 17.7 and 3.4 Hz, $CH^{1'}$ and CH^3), 2.44 (1H, dd, *J* 14.3 and 2.5 Hz, $CH^{2''}$), 2.24 (1H, dd, *J* 13.6 and 2.5 Hz, $CH^{2''}$), 1.22 (3H, s, $Me^{4'}$), 0.81 (3H, s, $Me^{4'}$); δ_C (126 MHz, $CDCl_3$), 207.7 ($C^{1'}$), 206.4 ($C^{1'}$), 197.3 ($C^{2'}$), 139.49, 136.6, 135.1, 134.7, 133.4, 128.6, 128.2, 128.1, 128.0, 127.9, 124.8, 111.3 ($=CH_2$), 69.4 (C^2), 51.8 ($C^{2''}$), 50.8 ($C^{2''}$), 42.8 (C^1), 41.2 ($C^{1'}$), 31.0 ($C^{3''}$), 30.4 ($C^{4''}$), 28.2 (C^3), 26.9 ($C^{4''}$); *m/z* (%) (CI) 387 (MH^+, 10), 369 (22), 236 (41), 219 (100) and 96 (37).

3.6.8. Methyl (4,4-dimethyl-4′-methylene-2,6-dioxo-3′,4′-dihydro-1′*H*-spiro[cyclohexane-1,2′-naphthalen]-1′-yl)-acetate (17d).



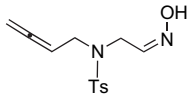
Prepared from (**5d**) (288 mg, 1.00 mmol) and dimedone (168 mg, 1.20 mmol). Column chromatography afforded the product (**17d**) (64%) as a pale yellow oil. (Found: C, 73.85; H, 7.4; $C_{21}H_{24}O_4$ requires C, 74.1; H, 7.1%); IR (film) 2955, 1729, 1695 and 1436 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 7.58 (1H, dd, *J* 1.2 and 1.2 Hz, ArH), 7.23–7.20 (1H, m, ArH), 7.16–7.12 (1H, m, ArH), 7.09 (1H, dd, *J* 7.7

and 7.7 Hz, ArH), 5.56 and 5.19 (2×1H, 2×t, *J* 1.9 Hz, CH_2=), 4.06 (1H, m, CH), 3.59 (3H, s, CO_2Me), 3.17 (1H, dt, *J* 17.4 and 1.9 Hz, CCH_2C=), 3.08 (1H, dd, *J* 14.2 and 0.5 Hz, CCH_2CO), 2.94 (1H, d, *J* 13.6 Hz, CCH_2CO), 2.89 (1H, dt, *J* 17.4 and 1.9 Hz, CCH_2C=), 2.47 (1H, dd, *J* 14.2 and 2.5 Hz, CCH_2CO), 2.38 (2H, m, CH_2CO_2Me), 2.22 (1H, dd, *J* 13.6 and 2.5 Hz, CCH_2CO), 1.20 and 0.80 (2×3H, 2×s, Me); *m*/*z* (%) (ES) 363 (M^++Na, 100).

3.6.9. *N*-Buta-2,3-dien-1-yl-*N*-(2,2-dimethoxyethyl)-4-methylbenzenesulfonamide (24). Prepared by the literature method.[16]

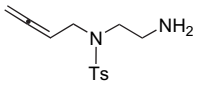
3.6.10. *N*-Buta-2,3-dienyl-*N*-(2-oxoethyl)-4-methylbenzene-4-sulfonamide (25). Prepared by the literature method.[16]

3.6.11. *N*-Buta-2,3-dienyl-*N*-(2-(*Z*)-hydroxyimino-ethyl)-4-methylbenzenesulfonamide (26).



A solution of sodium acetate trihydrate (4.20 g, 30 mmol, 3.00 mol equiv) and hydroxylamine hydrochloride (1.38 g, 20.00 mmol, 2.00 mol equiv) in water (10 ml) was added dropwise over 30 min at rt to a stirred solution of (**22**) (2.65 g, 10.00 mmol, 1.00 mol equiv) in methanol (20 ml). The reaction mixture was then heated at 80 °C for 20 min and allowed to stand at rt for 1 h. The solution was partitioned between water (20 ml) and dichloromethane (20 ml). The layers were separated and the aqueous layer extracted with dichloromethane (2×10 ml). The combined organic extracts were carefully evaporated under reduced pressure. The residue was purified by column chromatography eluting with 1:1 v/v ether/petrol to give *Z*-(**26**) (1.91 g, 68%) as a colourless oil, which crystallised from ethanol/water as colourless needles, mp 108–110 °C. (Found HRMS: 281.0960; $C_{13}H_{16}N_2O_3S$ (MH^+) requires 281.0961); *ν*/max (Nujol mull) 3203, 1957, 1599, 1338 and 1159 cm^{-1}; δ_H (250 MHz, $CDCl_3$), 7.71 (2H, d, *J* 8.2 Hz, 2×ArH), 7.62 (1H, br s, OH), 7.33 (2H, d, *J* 8.2 Hz, 2×ArH), 6.79 (1H, t, *J* 4.4 Hz, CH), 4.98 (1H, pentet, *J* 6.9 Hz, =CH), 4.77–4.71 (2H, m, CH_2), 4.10 (2H, d, *J* 4.4 Hz, CH_2), 3.84 (2H, dt, *J* 6.9 and 2.2 Hz, CH_2), 2.44 (3H, s, Me); *m*/*z* (%) 280 (M^+, 4), 257 (57), 104 (100) and 77 (47).

3.6.12. *N*-(2-Amino-ethyl)-*N*-buta-2,3-dienyl-4-methylbenzenesulfonamide (27).

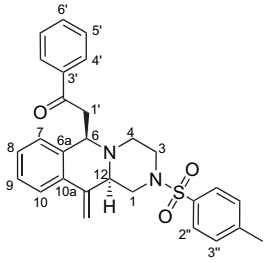


A solution of (**26**) (2.0 g, 7.10 mmol, 1.00 mol equiv) in ether (4 ml) was added dropwise over 30 min to a stirred suspension of lithium aluminium hydride (0.49 g, 12.90 mmol, 1.80 mol equiv) in ether (20 ml) at 0 °C. The reaction mixture was allowed to reach rt, stirred at rt for 3 h, and quenched by the sequential dropwise addition of water (0.5 ml), aqueous sodium hydroxide (15%, 0.5 ml) and water (3 ml). The precipitate was filtered and the solids washed with ether (4×10 ml). The combined organic filtrates were dried ($MgSO_4$) filtered and the filtrate evaporated under reduced pressure to afford the product (**27**) (0.89 g, 47%) as a pale yellow oil, which was used without further purification. (Found HRMS: 267.1167; $C_{13}H_{18}N_2O_2S$ (MH^+) requires 267.1168); *ν*/max (film) 3368, 2924, 1955, 1597, 1494 and 1450 cm^{-1}; δ_H (250 MHz, $CDCl_3$), 7.70 (2H, d, *J* 8.3 Hz, 2×ArH), 7.30 (2H, d, *J* 8.3 Hz, 2×ArH), 4.92 (1H, pentet, *J* 6.8 Hz, =CH), 4.74–4.70 (2H, m, CH_2), 3.85 (2H, dt, *J* 7.1 and 2.5 Hz, CH_2), 3.21 (2H, t, *J* 6.3 Hz, CH_2), 2.87 (2H, t, *J* 6.3 Hz, CH_2), 2.43 (3H, s, Me), 1.33 (2H, br s, NH_2).

3.7. General procedure for the three-component allenylation/anion-capture/Michael addition cascade using (27)

A stirred mixture of aryl iodide (0.50 mmol), (**27**) (266 mg, 1.00 mmol, 2.00 mol equiv), potassium carbonate (138 mg, 1.00 mmol, 2.00 mol equiv), palladium acetate (11 mg, 0.05 mmol, 0.05 mol equiv) and triphenylphosphine (26 mg, 0.10 mmol, 0.10 mol equiv) in acetonitrile (10 ml) was heated at 55 °C for 18 h. The mixture was cooled to rt, filtered and the solids washed with ether (2×10 ml). The combined organic filtrates were evaporated under reduced pressure and the organic residue was partitioned between ether (25 ml) and saturated aqueous ammonium chloride (25 ml). The two layers were separated and the organic layer washed with brine (25 ml), dried ($MgSO_4$), filtered and the filtrate evaporated under reduced pressure. The residue was purified by column chromatography eluting with ether/petrol mixtures.

3.7.1. 2-[11-Methylene-2-(4-methyl-phenyl-sulfonyl)-1,3,4,6,6a,10a,11,12-octahydro-2*H*-pyrazino[1,2-*b*]isoquinolin-6-yl]-1-phenyl-ethanone (28).

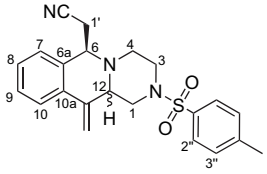


Prepared by the general procedure from (**5a**) (167 mg, 0.50 mmol). Column chromatography afforded the *anti*-product (**28**) (111 mg, 47%) as a colourless amorphous solid, mp 132–134 °C. (Found HRMS: 473.1894; $C_{28}H_{28}N_2O_3S$ (MH^+) requires 473.1894); *ν*/max (Nujol mull) 1680, 1593, 1578 and 1165 cm^{-1}; *anti*-(**28**): δ_H (500 MHz, $CDCl_3$), 7.79 (2H, d, *J* 7.1 Hz, 2×ArH$^{4'}$), 7.61 (2H, d, *J* 8.2 Hz, 2×ArH$^{2''}$), 7.51–7.49 (2H, m, 2×ArH), 7.39 (2H,

t, *J* 8.0 Hz, 2×ArH), 7.28 (2H, d, *J* 8.2 Hz, 2×ArH$^{3''}$), 7.18 (1H, td, *J* 7.5 and 1.6 Hz, ArH), 7.13–7.05 (2H, m, ArH^{7} and ArH), 5.81 (1H, d, *J* 2.0 Hz, =CH), 5.38 (1H, d, *J* 2.0 Hz, =CH), 4.49 (1H, dd, *J* 7.3 and 5.7 Hz, CH^{6}), 3.79–3.77 (1H, m, CH^{12}), 3.51 (1H, br d, CH^{1}), 3.41 (1H, dd, *J* 15.9 and 5.7 Hz, CH$^{1'}$), 3.35 (1H, br d, CH^{3}), 3.06 (1H, dd, *J* 15.9 and 7.3 Hz, CH$^{1'}$), 2.93 (1H, dd, *J* 8.2 and 4.6 Hz, CH^{4}), 2.75–2.43 (3H, m, CH^{4}, CH^{3} and CH^{1}), 2.39 (3H, s, Me); δ_C (126 MHz, $CDCl_3$), 198.6 (C$^{2'}$), 143.7, 138.9, 138.2 (C$^{3'}$), 137.3, 133.2 (C$^{6'}$), 132.4, 132.0 (C^{10a}), 129.7 (C$^{2''}$), 128.6, 128.0, 127.9, 127.8, 127.5, 126.6, 124.4, 112.1 (CH_2), 59.8 (C^{6}), 55.6 (C^{12}), 50.7 (C^{1}), 49.7 (C^{4}), 45.7 (C^{3}), 39.2 (C$^{1'}$), 21.5 (Me); *m*/*z* (%) (ES) 473 (MH$^+$, 100), 353 (17) and 270 (36).

Irradiated proton	Enhancement (%)						
	6	12	4 2.93 ppm	1 3.51 ppm	1′ 3.41 ppm	1′ 3.06 ppm	=CH_2
6	—	0	4.0	—	1.6	1.3	—
12	0	—	—	4.0	4.6	2.1	1.6
4 2.93 ppm	10.1	—	—	—	—	—	—
1 3.51 ppm	—	8.0	—	—	—	—	4.1
1′ 3.41 ppm	2.4	5.5	—	—	—	22.8	—
1′ 3.06 ppm	2.9	3.1	—	—	21.3	—	—

3.7.2. (+/−) 11-Methylene-2-(4-methyl-phenyl-sulfonyl)-1,3,4,6,6a,10a,11a,12-octahydro-2*H*-pyrazino[1,2-*b*]isoquinolin-6-yl-acetonitrile (29).



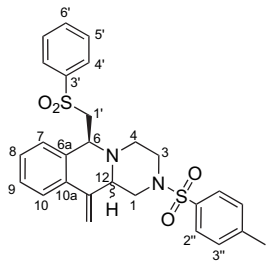
Prepared by the general procedure from (**5b**) (128 mg, 0.5 mmol). Column chromatography eluting with 2:3 v/v ether petrol afforded the product (**29**) (132 mg, 67%) as a 2:1 mixture of *anti*/*syn* diastereoisomers. (Found: C, 67.10; H, 5.80; N, 10.50; $C_{22}H_{23}N_3O_2S$ requires C, 67.20; H, 5.90; N, 10.70%); *ν*/max (Nujol mull) 2720, 1347, 1303 and 1165 cm^{-1}; *m*/*z* (%) (ES) 394 (MH$^+$, 100).

anti-(**29**): crystallised from the mixture as colourless needles from ethanol/water, mp 124–126 °C; δ_H (500 MHz, $CDCl_3$), 7.65–7.62 (2H, m, ArH$^{2''}$), 7.60 (1H, dd, *J* 7.7 and 1.5 Hz, ArH^{10}), 7.47–7.24 (4H, m, 2×ArH$^{3''}$ and 2×ArH), 7.13 (1H, dd, *J* 7.4 and 1.6 Hz, ArH^{7}), 5.86 (1H, d, *J* 2.0 Hz, =CH), 5.43 (1H, d, *J* 1.8 Hz, =CH), 4.00 (1H, t, *J* 7.1 Hz, CH^{6}), 3.72–3.70 (1H, m, CH^{12}), 3.48 (1H, br d, CH^{1}), 3.26 (1H, br s, CH^{3}), 3.01 (1H, br s, CH^{1}), 2.97–2.93 (1H, m, CH^{4}), 2.89–2.88 (1H, br t, CH^{3}), 2.84–2.81 (1H, m, CH^{4}), 2.77 (1H, dd, *J* 16.6 and 7.1 Hz, CH$^{1'}$), 2.48 (1H, dd, *J* 16.6 and 7.1 Hz, CH$^{1'}$), 2.42 (3H, s, Me); δ_C (126 MHz, $CDCl_3$), 143.9, 137.2, 134.4, 132.4, 132.0, 129.8, 128.5, 128.2, 127.8, 126.8, 124.7, 117.9, 113.3 (=CH_2), 60.8 (C^{6}), 54.2 (C^{12}), 50.0 (C^{1}), 49.4 (C^{3}), 45.8 (C^{4}), 21.5 (Me), 20.3 (C$^{1'}$).

Irradiated proton	Enhancement (%)									
	6	12	4 2.97–2.93 ppm	4 2.84–2.81 ppm	1 3.48 ppm	1 3.01 ppm	1′ 2.77 ppm	1′ 2.48 ppm	=CH_2	7
6	—	0	4.3	4.8	—	—	1.8	2.2	—	10
12	0	—	—	—	4.4	—	4.3	2.8	1.5	—
4 2.97–2.93 ppm	9.2	—	—	10.6	—	—	—	—	—	—
1 3.48 ppm	—	10	—	—	—	8.1	—	—	4.3	—
1 3.01 ppm	—	3.7	—	—	7.4	—	—	—	3.7	—
1′ 2.77 ppm	3.8	5.4	—	—	—	—	—	23.2	—	—
1′ 2.48 ppm	3.7	3.9	—	—	—	—	22.9	—	—	—

syn-(**29**): δ_H (500 MHz, $CDCl_3$, 6:1 enriched sample), 7.69 (2H, d, *J* 8.3 Hz, 2×ArH$^{2''}$), 7.49 (1H, d, *J* 6.9 Hz, ArH), 7.36 (2H, dd, *J* 8.3 Hz, 2×ArH$^{3''}$), 7.31–7.28 (2H, m, 2×ArH), 7.09 (1H, d, *J* 6.9 Hz, ArH), 5.60 (1H, s, =CH), 5.03 (1H, s, =CH), 4.00–3.92 (2H, m, CH^{6} and CH^{1}), 3.69–3.61 (1H, br s, CH^{4}), 3.23 (1H, br d, CH^{12}), 3.13 (1H, br d, CH^{3}), 2.76 (1H, td, *J* 10.9 and 2.8 Hz, CH^{3}), 2.68 (1H, dd, *J* 16.7 and 4.8 Hz, CH$^{1'}$), 2.62 (2H, br d, CH^{1} and CH^{4}), 2.56 (1H, dd, *J* 16.7 and 5.8 Hz, CH$^{1'}$), 2.46 (3H, s, Me); δ_C (126 MHz, $CDCl_3$, 6:1 enriched sample), 144.0, 140.3, 134.7, 133.4, 132.5, 129.9, 128.7, 127.9, 127.8, 126.0, 125.0, 117.6, 109.2 (=CH_2), 60.8 (C^{6}), 57.3 (C^{12}), 50.2 (C^{3}), 48.9 (C^{1}), 46.1 (C^{4}), 21.6 (Me), 20.3 (C$^{1'}$).

3.7.3. 6-Benzenesulfonylmethyl-11-methylene-2-(4-methyl-phenyl-sulfonyl)-1,3,4,6,6a,10a,11,12-octahydro-2*H*-pryazino[1,2-*b*]isoquinoline (30).



Prepared by the general procedure from (**5e**) (185 mg, 0.5 mmol). Column chromatography afforded the product

(**30**) (132 mg, 52%) as a colourless oil, which comprised of an inseparable 1:1 mixture of *syn*/*anti* diastereoisomers. (Found HRMS: 509.1568; $C_{27}H_{28}N_2O_4S_2$ (MH^+) requires 509.1569); *ν*/max (Nujol mull) 1336, 1298, 1169 and 1126 cm^{-1};

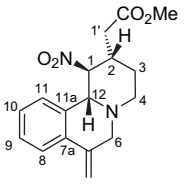
anti-(**30**): δ_H (500 MHz, $CDCl_3$, 9:1 enriched sample), 7.80 (2H, d, *J* 6.8 Hz, 2×ArH), 7.59 (2H, d, *J* 8.1 Hz, 2×$ArH^{2''}$), 7.58–7.56 (1H, m, ArH^{10}), 7.40 (2H, d, *J* 8.1 Hz, 2×$ArH^{3''}$), 7.28–7.21 (5H, m, 5×ArH), 7.09 (1H, dd, *J* 5.6 and 3.5 Hz, ArH^7), 5.87 (1H, s, =CH), 5.40 (1H, s, =CH), 4.35 (1H, dd, *J* 9.0 and 4.2 Hz, CH^6), 3.67 (1H, dd, *J* 14.9 and 9.0 Hz, $CH^{1'}$), 3.39 (2H, br s, CH^{12} and CH^1), 3.19 (1H, dd, *J* 14.9 and 4.2 Hz, $CH^{1'}$), 3.15–3.13 (1H, br s, CH^3), 2.85–2.80 (1H, m, CH^4), 2.58–2.52 (2H, m, CH^4 and CH^3), 2.51 (3H, s, Me), 2.04 (1H, br s, CH^1); δ_C (126 MHz, $CDCl_3$), 143.7, 140.9 ($C^{3'}$), 135.6 (C^{11}), 133.0, 132.5, 132.4, 129.7, 128.8, 128.4, 127.9, 127.8, 127.6, 127.0 (C^7), 126.5, 124.4 (C^{10}), 113.4 (=CH_2), 59.1 (C^6), 58.4 ($C^{1'}$), 51.8 (C^{12}), 48.0 (C^4), 47.3 (C^1), 45.3 (C^3), 21.6 (Me).

Irradiated proton	Enhancement (%)									
	6	12	4 2.83 ppm	4 2.584 –2.52 ppm	1 3.39 ppm	1 2.04 ppm	1′ 3.67 ppm	1′ 2.48 ppm	=CH_2	7
6	—	—	—	—	—	—	—	—	—	6.7
12	—	—	—	—	4.4	—	4.3	2.8	1.5	—
4 2.83 ppm	9.2	—	—	10.6	—	—	—	—	—	—
4 2.584–2.52 ppm	—	—	—	—	—	—	—	—	—	—
1 3.39 ppm	—	10	—	—	—	8.1	3.9	—	3.7	—
1 2.04 ppm	—	—	—	—	25.7	—	—	—	—	—
1′ 3.67 ppm	—	2.5	—	—	—	—	—	23.1	—	—
1′ 2.48 ppm	4.6	—	—	—	—	—	22.0	—	—	7.2

syn-(**30**): δ_H (500 MHz, $CDCl_3$, 4:1 enriched sample), 7.84 (2H, d, *J* 7.7 Hz, 2×ArH), 7.65 (2H, d, *J* 8.1 Hz, 2×$ArH^{2''}$), 7.47 (1H, t, *J* 7.4 Hz, ArH), 7.39 (2H, d, *J* 8.1 Hz, 2×$ArH^{3''}$), 7.29–7.22 (6H, m, 6×ArH), 5.64 (1H, br s, =CH), 5.05 (1H, br s, =CH), 4.43 (1H, br s, CH^1), 3.55–3.43 (3H, m, CH), 3.31 (1H, br s, CH), 3.05 (1H, br s, CH), 2.78–2.63 (1H, br s, CH), 2.61–2.38 (6H, m, 3×CH and Me).

3.7.4. (*E*)-3-Methyoxycarbonyl-allyl-ammonium trifluoroacetate (32). (*E*)-4-*tert*-Butoxycarbonylamino-but-2-enoic acid ethyl ester (**31**) (1.15 g, 5.0 mmol)[18] was dissolved in trifluoroacetic acid (10 ml) at 0 °C and allowed to warm to rt over 30 min. The organic solvent was evaporated under reduced pressure to give the amine salt **32** (1.19 g, 0.98 mmol) as a pale yellow oil, which was used without further purification. *ν*/max (film) 3131, 1783, 1209 and 1165 cm^{-1}; δ_H (250 MHz, $CDCl_3$), 6.86 (1H, dt, *J* 15.7 and 7.2 Hz, CH), 6.02 (1H, d, *J* 15.7 Hz, CH), 3.76 (3H, s, Me), 3.39–3.19 (2H, m, CH_2), 2.67 (2H, q, *J* 7.2 Hz, CH_2); *m*/*z* (%) (FAB) 130 (MH^+, 100).

3.7.5. (+/−) (7-Methylene-1-nitro-1,3,4,6,7,11b-hexahydro-2*H*-pyrido[2,1-*a*]isoquinolin-2-yl)-acetic acid methyl ester (33). A mixture of (**5c**) (1.00 mmol, 1.00 mol equiv), (**32**) (3.00 mmol, 3.00 mol equiv), potassium carbonate (1.38 g, 10.00 mmol, 10.00 mol equiv), palladacycle (**13**) (20 mg, 0.05 mmol, 0.05 mol equiv) and acetonitrile (10 ml) in a Schlenk tube was subjected to two freeze-pump-thaw cycles and then allene gas (1 bar) was added and the reaction mixture heated at 50 °C for 18 h. After cooling to rt, excess allene gas was vented, the crude reaction mixture filtered and the solids washed with ether (3×50 ml). The organic filtrates were combined, dried ($MgSO_4$), filtered and the filtrate evaporated under reduced pressure. The residue was purified by column chromatography eluting with 7:3 v/v ether/petrol to afford the product (**33**) (148 mg, 47%) as a 4.7:1 mixture of separable diastereoisomers.



Irradiated proton	Enhancement (%)								
	H^{12}	H^1	$H^{1'}$	H^2	H^{3l}	H^{3ii}	H^{6i}	H^{6ii}	H^7
H^{12}	—	—	0	10.5	—	—	—	—	—
H^1	0	—	2.8	0	—	—	—	5.9	—
H^2	9.8	1.6	4.2	—	—	—	—	—	—
H^{3i}	—	3.2	3.1	—	—	—	5.4	—	—
H^{3ii}	—	—	—	7.4	19.3	—	—	—	—
H^{6i}	—	11.5	—	—	5.1	—	—	23.3	—
H^{6ii}	—	—	—	—	—	—	27.8	—	5.4

Major diastereoisomer: obtained as colourless thick oil. (Found: C, 64.40; H, 6.50; N, 8.70; $C_{17}H_{20}N_2O_4$ requires C, 64.50; H, 6.35; N, 8.60%); *ν*/max (Nujol mull) 1724, 1633, 1542, 1287 and 1170 cm^{-1}; δ_H (500 MHz, $CDCl_3$), 7.73 (1H, d, *J* 8.0 Hz, ArH^8), 7.27 (1H, t, *J* 7.5 Hz, ArH^9), 7.16 (1H, t, *J* 7.5 Hz, ArH^{10}), 6.88 (1H, d, *J* 7.8 Hz, ArH^{11}), 5.66 (1H, s, =CH), 5.05 (1H, s, =CH), 4.79 (1H, t, *J* 10.2 Hz, CH^1), 4.30 (1H, d, *J* 10.2 Hz, CH^{12}), 3.91 (1H, d, *J* 14.1 Hz, CH^6), 3.68 (3H, s, OMe), 3.43 (1H, d, *J* 14.1 Hz, CH^6), 3.24 (1H, td, *J* 14.1 and 3.1 Hz, CH^4), 3.15 (1H, dd, *J* 14.1 and 4.1 Hz, CH^4), 2.87–2.79 (1H, m, CH^2), 2.40 (1H, dd, *J* 16.2 and 3.4 Hz, $CH^{1'}$), 2.27 (1H, dd, *J* 16.2 and 8.4 Hz, $CH^{1'}$), 1.85 (1H, ddd, *J* 13.8, 4.1 and 3.1, CH^3), 1.73 (1H, br d, *J* 13.8 Hz, CH^3); δ_C (126 MHz, $CDCl_3$), 171.2 (C=O), 138.4 (C^7), 132.6, (C^{11a}), 131.3 (C^{7a}), 128.4 (C^9), 128.2 (C^{10}), 127.0 (C^{11}), 124.1 (C^8), 108.7 (=CH_2), 88.4 (C^1), 63.2 (C^{12}), 52.3 (C^4), 51.8 (Me), 51.4 (C^6), 38.2 (C^2), 36.4 ($C^{1'}$), 23.5 (C^3); *m*/*z* (%) (FAB) 317 (MH^+, 100), 270 (50), 196 (45) and 143 (22).

Minor diastereoisomer: (undetermined stereochemistry due to overlapping peaks): obtained as colourless thick oil.

(Found: C, 64.40; H, 6.35; N, 8.70; $C_{17}H_{20}N_2O_4$ requires C, 64.50; H, 6.35; N, 8.60%); ν/max (Nujol mull) 1721, 1629, 1282 and 1165 cm^{-1}; δ_H (250 MHz, $CDCl_3$), 7.67–7.61 (1H, m, ArH), 7.34–7.19 (3H, m, 3×ArH), 5.58–5.54 (2H, m, =CH and CH^2), 5.06 (1H, s, =CH), 3.77–3.71 (4H, m, CH^{12} and Me), 3.55 (1H, d, J 12.6 Hz, CH^4), 3.21 (1H, dq, J 11.6 and 2.5 Hz, CH), 3.14 (1H, d, J 12.6 Hz, CH^4), 2.60–2.40 (4H, m, CH^2, $CH_2^{1'}$), 2.19 (1H, ddd, J 16.7, 11.6 and 3.1 Hz, CH^3), 1.71–1.62 (1H, m, CH^3).

Acknowledgements

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