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Graphical Abstract

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Radical cyclisation studies of β-nitroamines from the nitro-Mannich reaction

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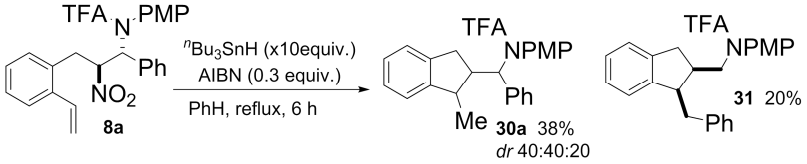

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Radical cyclisation studies of β-nitroamines from the nitro-Mannich reaction

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ABSTRACT

A range of novel β-nitroacetamides with an alkenyl- or alkynyl tether were synthesized using the deprotonative or conjugate addition nitro-Mannich reaction. They were subjected to radical denitration-cyclisation with a 10 equivalent excess of tributyltin hydride, catalytic AIBN in refluxing benzene to explore the structural and electronic requirements for efficient cyclisation. Cyclisations of the β-nitroacetamides were successful in most cases, undergoing 5-*exo*-trig cyclisation to give the desired cyclopentyl or indanyl structures. Radical 1,4-translocation of a phenyl group was observed in several cases. Diastereoselectivity was low, with 2 or 3 of 4 possible diastereoisomers observed in most cases. Further purification by crystallisation allowed the isolation of some as single diastereoisomers. It was found that higher yields were obtained by increasing the substitution or reducing the degrees of freedom of the tether between the nitro group and the radical acceptor.

1. Introduction

The nitro-Mannich (or aza-Henry) reactions is a versatile method for the synthesis of β-nitroamines.[1] The nitro function has been transformed into many other functional groups such as carboxylic acids in α-amino acids (via Nef reaction), vicinal diamines (via nitro reduction) and peptides.[2-4] A less common transformation is reduction of the nitro group to a carbon-centred radical followed by addition of a hydrogen[5] or formation of a carbon-carbon bond.[6] The deprotonative[3a,7] or conjugate addition[8] nitro Mannich reactions are useful routes to stereodefined β-nitroamines that can be used for the synthesis of an array of amino heterocycles.[9] We were interested to investigate the synthesis of carbocyclic structures through the radical denitration of the secondary nitro function in β-nitroamines onto a tethered alkene or alkyne. The radical denitration cyclisation of a β-nitroamine has been reported by Kamimura in 2006.[10] A β-nitroformamide underwent cyclisation on treatment with an unspecified quantity of $^{n}Bu_3SnH$ and AIBN in toluene to afford the corresponding pyrrolidine in very good yield (Figure 1). Only two of a possible four diastereoisomers were observed, with a *dr* of 60:40, but with unknown stereochemistry.

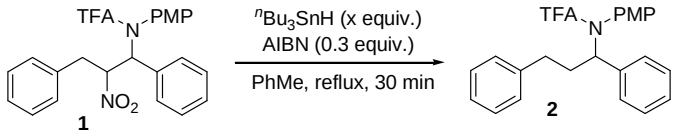
Figure 1. Radical denitration-cyclisation of a β-nitroformamide by Kamimura

2. Results and discussion

2.1. Preliminary results

The radical denitration of β-nitroacetamides and subsequent replacement of the nitro group with hydrogen, or carbon-carbon bond formation, required the synthesis of novel β-nitroacetamides by the nitro-Mannich reaction. In order to probe the feasibility of radical denitration of these compounds, β-nitroacetamide **1**, previously generated by us *via* the conjugate hydride addition nitro-Mannich reaction,[8b] was subjected to preliminary investigation. Methods described for radical denitration, including the use of MeSNa,[11] KOH/ethylene glycol,[12] 1-benzyl-1,4-dihydronicotinamide,[13a,b] NaTeH[14] and tri-^{n}butyltinhydride,[5b,15] are mainly limited to the denitration of tertiary nitro compounds[11,12,14,16] or nitro compounds activated by an adjacent stabilising group (COR, CO_2R, CN, Ar).[13] Ono showed that $^{n}Bu_3SnH$ could be used for the denitration of unactivated secondary nitro compounds[17] under harsh conditions (toluene, reflux, 5 equiv. $^{n}Bu_3SnH$). A search of the literature showed a focus on $^{n}Bu_3SnH$ as the method of choice for radical denitration of secondary nitro compounds, with high variation in yield depending on structure.[18] Furthermore $^{n}Bu_3SnH$ has previously been used in radical denitration reactions of β-nitroamine derivatives and was thus picked as the reagent for radical denitration in this work.[13c,16,18b,d-h] Initial reaction of **1** with $^{n}Bu_3SnH$ (1.2 equiv.) and AIBN (0.3 equiv.) in toluene at reflux resulted in trace amounts of a possible denitration product **2** (Scheme 1). As expected, increasing the equivalents of $^{n}Bu_3SnH$ resulted in higher yield, although disappointingly, the reported denitration conditions for secondary nitro compounds (5 equiv.) resulted in only 17% yield. Pleasingly, a further increase

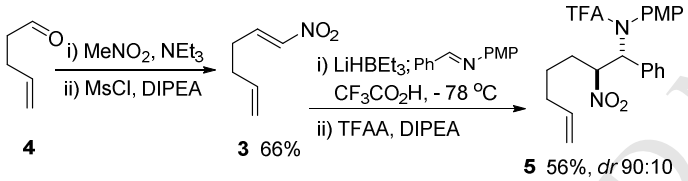
in the equivalents of $^{n}Bu_3SnH$ used (10 eq. 0.7 eq AIBN) resulted in the isolation of acetamide **2** in very good (79 %) yield (Scheme 1). With these results in hand, application to the more interesting and useful addition of the intermediate radical formed to alkenes was investigated.



x	yield
1.2	<1%
2	4%
5	17%
10 (0.7 equiv AIBN)	79%

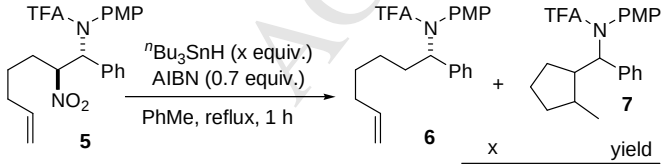
Scheme 1. TFA=CF_3CO, PMP=$CH_3OC_6H_5$, AIBN=$NC(CH_3)_2CN$=$NC(CH_3)_2CN$

The investigation of the addition reactions of radicals formed *via* denitration of β-nitroacetamides was initiated with the formation of the simplest precursor based on the 5-hexen-1-yl radical template. Formation of nitroalkene **3** from aldehyde **4** was achieved by a Henry reaction with nitromethane in good yield (Scheme 2). Formation of β-nitroacetamide **5** was achieved with a conjugate addition nitro-Mannich reaction of nitroalkene **3** with Superhydride ($LiHBEt_3$), trapping of the nitronate with imine and TFA protection. Although the nitro-Mannich reaction proceeded with good diastereoslectivity, the loss of stereochemical integrity that takes place upon formation of the radical negates any need for specificity in the nitro-Mannich reaction.



Scheme 2. DIPEA=$^{i}Pr_2EtN$, TFAA=$(CF_3CO)_2O$

Radical denitration-cyclisation was attempted using 5 and 10 equivalents of $^{n}Bu_3SnH$. While 5-hexen-1-yl radical cyclisations are known to be extremely fast, at higher concentrations of $^{n}Bu_3SnH$ the rate of reduction increases. However the use of less $^{n}Bu_3SnH$ resulted in a complex mixture of starting material, possible cyclopentane diastereoisomers and decomposition products resulting from elimination of the TFA-NH-PMP group (Scheme 3), which is known to occur at high temperatures.[12] Use of the optimized conditions for protodenitration (10 equiv. $^{n}Bu_3SnH$, 0.7 equiv. AIBN) resulted in the isolation of an inseperable mixture of the protodenitrated product **6** with the desired cyclized product **7** in a 2:1 ratio in 60% yield.



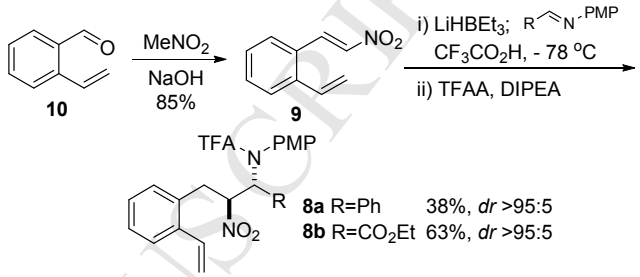
x	yield
5	-
10	**6**:**7**, 2:1, 60%

Scheme 3.

We envisaged that a lower boiling point solvent such as benzene might reduce the amount of thermal decomposition products. It was hoped that the addition of substituents on the tether may increase the rate of cyclisation over that of reduction by holding the reactive centres in closer proximity.[19] Also the rate of cyclisation might be increased by modification of the β-nitroacetamide to incorporate electron stabilizing groups on the terminus of the alkene tether.

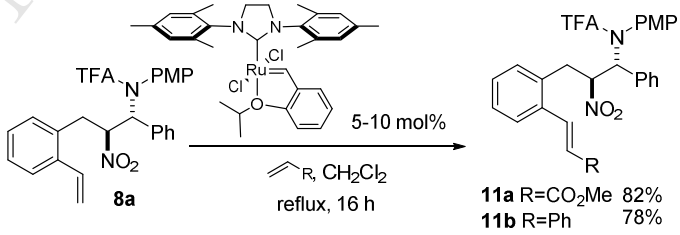
2.2. Synthesis β-nitroacetamide cyclisation precursors.

The first series of cyclisation precursors were derived from nitro coupling partners containing unsaturated substituents. The first of these was the styrl-tether derivatives **8**. This series was derived from nitroalkene **9**, which was synthesised from 2-vinylbenzaldehyde[20] **10** by a Henry reaction with nitro methane in good 85% yield (Scheme 4).[8b,9d] A reductive conjugate addition nitro-Mannich reaction[8b,c] with imines derived from benzaldehyde or glyoxal gave β-nitroacetamides **8a** and **8b** in 38% and 63% yield respectively, both with diastereoselectivity >95:5.



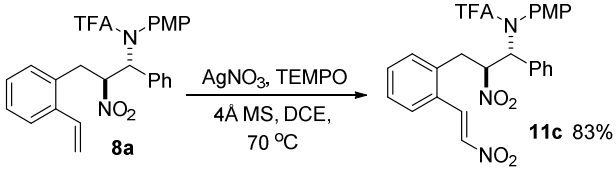
Scheme 4.

Late stage functionalisation of the terminal alkene of **8a** was an attractive option to prepare more functionalised substrates and was achieved through olefin metathesis. We were hoping to prepare an array of electron rich and electron poor styryl tethers, but after some optimisation only methyl acrylate and styrene led to products **11** (Scheme 4).[21] The *E*-alkenes were formed exclusively as expected (**11a** *J*=16.0 Hz and **11b** *J*=15.7 Hz).



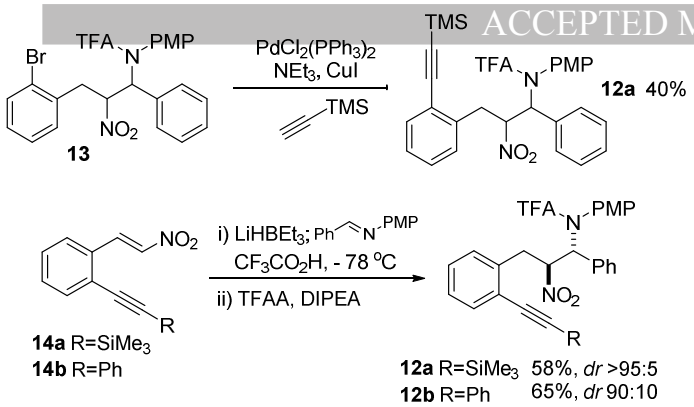
Scheme 5.

Conversion of terminal alkene **8a** to the corresponding nitroalkene **11c** was achieved using the $AgNO_3$/TEMPO methodology described by Maity[22] which we had used on sensitive substrates before (Scheme 6).[9h,i]



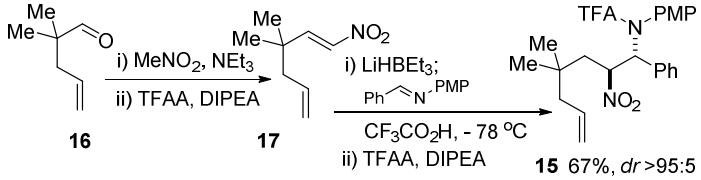
Scheme 6.

The synthesis of alkynyl analogues **12a** was attempted by Sonogashira coupling of **13** (Scheme 7). Although successful (40%) the product could not be separated from residual starting material or scaled up. The corresponding alkynyl nitro styrene derivatives **14a**[23] and **14b**[24] are known and were used in a reductive conjugate addition nitro-Mannich reaction with PMP protected benzaldehyde imine. Protection of the product as the trifluoroacetamide gave the β-nitroacetamides **12a,b** in good yield and diastereoselectivity (Scheme 7).



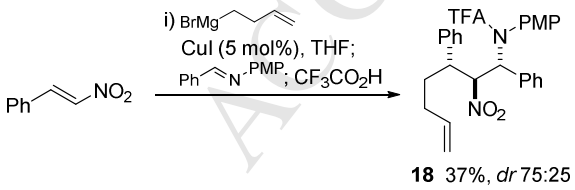
Scheme 7.

Non-planar tethers could potentially be made more prone to cyclisation by the Thorpe Ingold effect through the incorporation of geminal substituents. Formation of the gem-dimethyl substrate **15** of the hexenyl tether was found to be viable from commercially available aldehyde **16** which underwent standard nitroalkene formation *via* a Henry reaction to give **17** in 52% yield. Reductive conjugate addition nitro-Mannich reaction with PMP protected benzaldehyde imine and protection as the trifluoroacetamide gave the β-nitroacetamide **15** in 67% yield essentially as the single *anti*-diastereoisomer (Scheme 8).[8b]



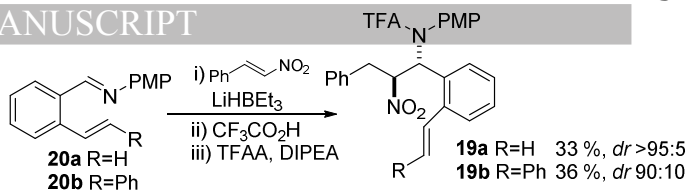
Scheme 8.

Mono-substitution of the hexenyl tether was achieved by using a copper catalyzed 1,4-conjugate addition nitro-Mannich reaction previously described by us.[8a] Our original protocol used dialkyl zinc reagents as carbon nucleophiles, but the cuprate generated from the Grignard of 4-bromobut-1-ene performed reasonably well to give **18** in 37% yield with a *dr* 75:25 (Scheme 9). The crude reaction mixture had a *dr* 50:25:25, which changed upon trifluoro acetate protection to *dr* 75:25. From our previous work we know that the major product from homogeneous reactions is normally the *syn* (from conjugate addition), *anti* (from nitro-Mannich) -diastereoisomer. We found that the *syn*, *syn*-diastereoisomer is normally resistant to trifluoro acetate protection and so the minor diastereoisomer was tentatively assigned as *anti*, *syn*-**18**.[8a]



Scheme 9.

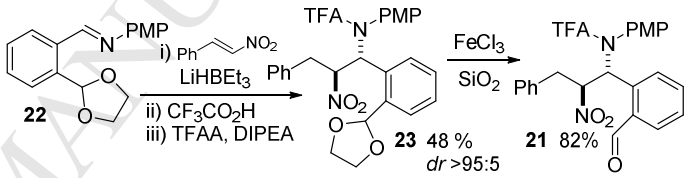
An alternative series of cyclisation precursors were derived from imines containing unsaturated substituents. A styrene derivative **19a** could be derived from known imine **20a**.[25] A reductive conjugate addition reaction with nitrostyrene and **20a** gave β-nitroacetamide **19a** in 33% yield essentially as a single *anti*-diastereoisomer (Scheme 10).



Scheme 10.

Late stage functionalization of the alkene in **19a** was also attempted by olefin metathesis as for substrate **8a** (scheme 5). Surprisingly under identical conditions and attempted optimisations, no cross coupling could be detected with methyl acrylate. Cross coupling with styrene led to product formation (40%), but the product was inseparable from styrene. Alternatively stilbene **19b** was prepared from another nitro-Mannich reaction using imine **20b** (scheme 10) in 36% yield as 90:10 diastereomeric ratio in favour of the *anti*-diastereoisomer.

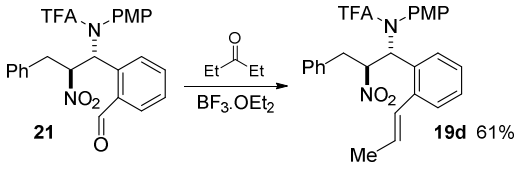
It was envisaged that further electronically different analogues of **19** could be made from the aldehyde **21** by Wittig reaction. The generation of acetal protected imine **22** was straightforward from the known aldehyde.[26] Reductive conjugate addition nitro-Mannich reaction of nitrostyrene with **22** gave β-nitroacetamide **23** in 48% yield essentially as the single *anti*-diastereoisomer. (Scheme 11). The aldehyde was unmasked in 82% yield using $FeCl_3$.[27]



Scheme 11.

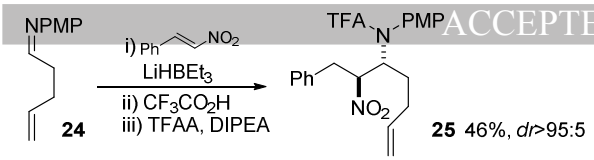
Aldehyde **21** degraded upon treatment with the Horner-Wadsworth-Emmons reagent derived from diethylcyanophosphonate, giving TFA-NH-PMP. This suggested that the anion is basic enough to deprotonate the C*H*NO_2 proton. The less basic Wittig reagent (carboethoxymethylene)triphenylphosphorane (pKa 8.5 (H_2O)[28]) gave a mixture of products **19c** (R=CO_2Me, 85:10:5) in 31% yield, but could not be definitively assigned. The mixture would make the analysis of any radical cyclisations complex, so this reaction was not optimized further.

Although not providing an electronically different alkene, aldehyde **21** underwent an interesting BF_3 initiated aldol-Grob fragmentation with 3-pentanone, which had been previously reported by Kabalka, to give alkene derivative **19d** (Scheme 12).[29]



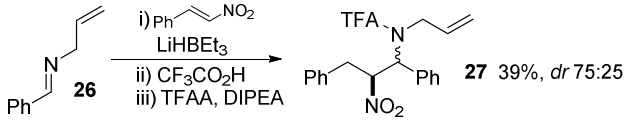
Scheme 12.

A non planar tether derived from crude imine **24** (from the known aldehyde) was synthesized by a reductive conjugate addition reaction with nitrostyrene to give β-nitroacetamide **25** in 46% yield essentially as a single *anti*-diastereoisomer (Scheme 13).



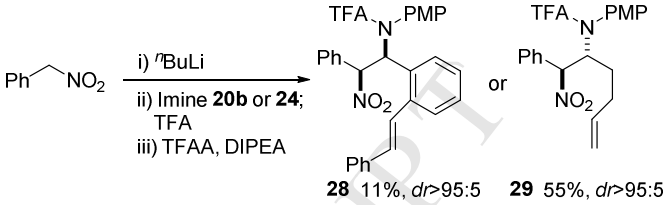
Scheme 13.

The amino-tethered alkene was prepared from the corresponding known *N*-allyl imine **26**.[30] Combination of *N*-allylamine and benzaldehyde in the presence of the dehydrating reagent $MgSO_4$ followed by filtration gave the crude imine which was coupled directly with the nitronate anion from the conjugate hydride reduction of nitrostyrene (Scheme 14). After protection as the trifluoroacetamide the β-nitroacetamide **27** was isolated in 39% yield with a slightly reduced *dr* 75:25. We were unable to define the major diastereoisomer from the spectral data.



Scheme 14.

The final series of cyclisation precursors were those possessing an activated nitro substituent that upon radical denitration would give a more stabilized benzylic radical. We were able to synthesise two from the corresponding unsaturated imines **20b** and **24**. A standard nitro-Mannich reaction with nitro toluene gave **28** and **29** (Scheme 15). The isolation of planar tethered **28** was by recrystallization from a complex mixture of diastereoisomers in 11% yield. The *syn*-diastereoselectivity was assigned from a single crystal X-ray determination. The corresponding styryl imine **20a** led to a complex reaction mixture from which we could not isolate any clean nitro-Mannich product. The simpler non-planar imine **24** gave **29** in 55% yield as the single *anti*-diastereoisomer.

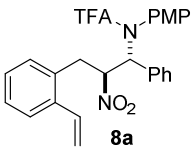
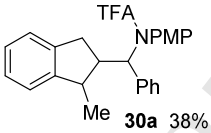
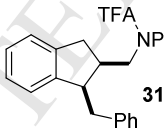
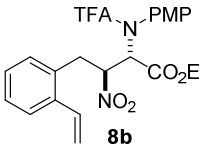
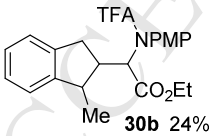
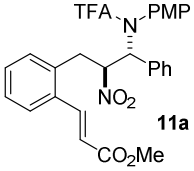
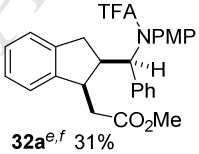
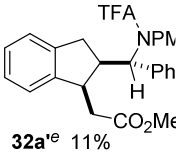
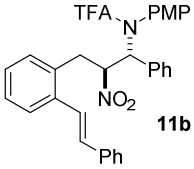
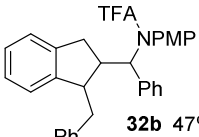
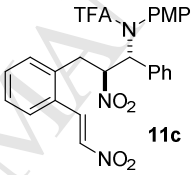
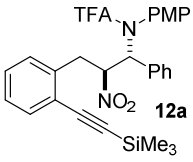
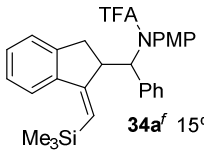
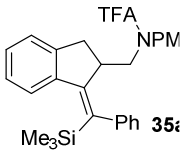
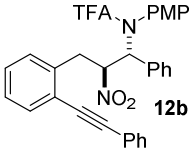
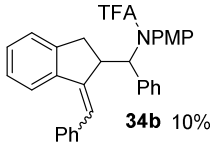
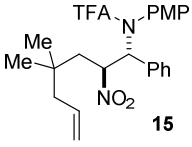
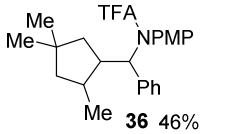
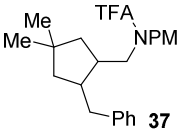
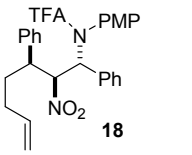
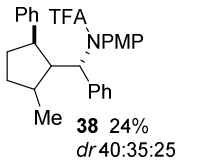
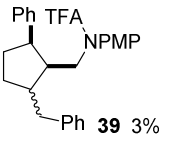


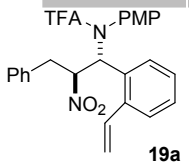
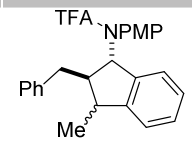
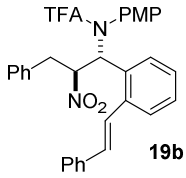
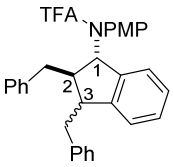
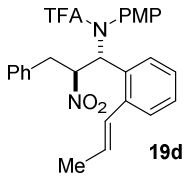
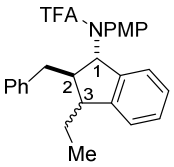
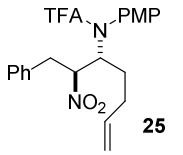
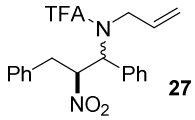
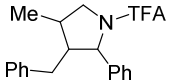
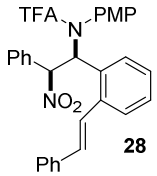
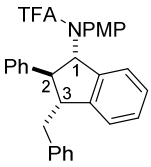
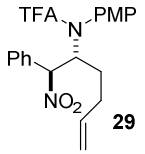
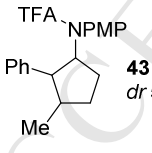
Scheme 15.

2.3. Results of radical denitration cyclisation.

Using the optimized conditions determined for the rearrangement of **5** (Scheme 3) the β-nitroacetamide cyclisation precursors were treated with 10 equiv. $^{n}Bu_3SnH$ in refluxing benzene and the product mixtures purified by flash column chromatography and recrystallization where possible. The structures were elucidated by a combination of NMR experiments and X-ray crystallography (Table).

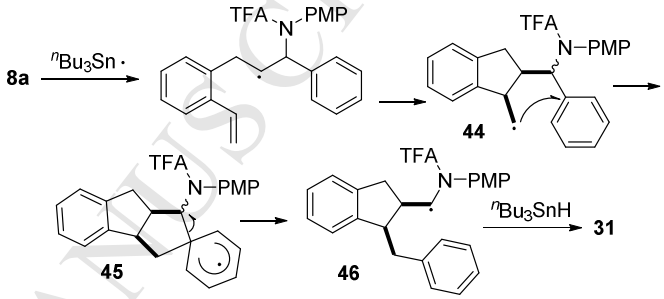
Table. Radical denitration cyclisation of β-nitroacetamides[a]

β-nitroacetamide	Total isolated yield (%)[b]	Product(s), isolated yields and diastereomeric ratio[b,d]
 **8a**	58[c]	 **30a** 38% *dr* 40:40:20  **31**
 **8b**	24	 **30b** 24% *dr* 60:20:20
 **11a**	59	 **32a**[e,f] 31%  **32a'**[e] 11%
 **11b**	47	 **32b** 47% *dr* 40:40:20
 **11c**	-	Complex mixture of inseperable products
 **12a**	21[g]	 **34a**[f] 15%  **35a**
 **12b**	10	 **34b** 10%
 **15**	55	 **36** 46% *dr* 40:30:30  **37**
 **18**	27	 **38** 24% *dr* 40:35:25  **39** 3%

 **19a**	46	 **40a** 46% *dr* 55:45
 **19b**	34	 **40b** 34% *dr* 60:40 *trans, trans*: *trans, cis*
 **19d**	12	 **40d** 12% *dr* 70:30 *trans, trans*: *trans, cis*
 **25**	-	Complex mixture of inseperable products
 **27**	12	 **41** 12% *dr* 50:30:15:5
 **28**	13	 **42** 13% *dr* 95:5
 **29**	36	 **43** 36% *dr* 50:50

[a]AIBN (0.1 equiv.), [n]Bu_3SnH (10 equiv.), benzene, reflux. [b]Isolated by flash column chromatography. [c]12% recovered **8a**. [d]Structure elucidated by NMR see text and ESI. [e]Recrystallised from CH2Cl2/hexanes. [f]Single crystal X-ray obtained. [g]50% recovered **12a**.

The β-nitroacetamides **8a** gave two isolable products **30a** in 38% yield as an inseperable mixture of diastereoisomers (40:40:20) and an additional stereochemically pure product **31** in 20% yield, with 12% recovered starting material. The mixture of diastereoisomers of **30a** were evident from doublet peaks for the methyl group on the indane ring. Signals at δ 1.00 ppm (3H, d, *J* = 7.0, CH_3, ~40 %) and δ 1.44 ppm (3H, d, *J* = 7.0, CH_3, ~ 40 %) confirmed the presence of at least two major diastereoisomers, and a third doublet at δ 1.28 ppm (3H, d, *J* = 7.3, CH_3, ~20 %) appeared to be a minor diastereoisomer, its presence was more obvious in the crude reaction mixture. The byproduct **31** was identified as a phenyl translocation product primarily as it had NMR signals consistent with an indane ring, but the attachment of one of the phenyl groups with respect to **30a**, was different. The tentative assignment of the *cis* stereochemistry of the two ring substituents is based on a NOESY correlation between the two methine substituents and would fit the rearrangement mechanism (*vide infra*) A detailed NMR analysis can be found in the supplementary information. Full NMR assignment of **31** corroborated the assignment of **30a** as a mixture of indane diastereoisomers. Many examples of radical aryl migrations are known.[31] with similar carbon-carbon bond cleavage adjacent to an amide.[32] In this particular case aryl migration from methyl radical **44** would be most likely if the substituents were *cis* as drawn (Scheme 16). Attack of the methyl radical at the *ipso*-position of the aromatic ring would lead to spiro-cyclohexadienyl radical **45** which then clollapses to give a more stable α-amidoradical **46**, which provides the driving force for the rearrangement from the primary sp^3 radical **44**.228



Scheme 16.

Submission of β-nitroacetamide **8b** to the optimised denitration-cyclisation conditions resulted in successful cyclisation to give a complex mixture. A ratio of indane diastereomers 60:20:20 of **30b** was observed from the methyl peak ratios at δ 1.02 ppm (3H, d, *J* = 7.0, 60 %), 1.13 ppm (3H, d, *J* = 7.0, 20 %) and 1.15 ppm (3H, d, *J* = 7.0, 20 %), with the presence of small underlying peaks. These peaks may correspond to a fourth isomer, or a fragmentation isomer. Analysis by MS found the molecular ion 436 ($M + H^+$) and its ammonia adduct at 453 ($M + NH_4^+$) as the only peaks, suggesting that the mixture contained indanes **30b** and possibly trace amounts of fragmentation isomers. The NMR data was similar to **30a**. Although the 1,4-acetyl-translocation of C=O type fragments is known[33] *via* radical processes, NMR analysis ruled this out.

Methyl acrylate derivative **11a** underwent radical denitration-cyclisation to give a chromatographically inseperable mixture of 3 diastereoisomers (40:40:20) in a yield of 59%. The mixture of isomers were recrystallized from CH_2Cl_2/Hexanes, affording pure samples of the two main isomers in 31 % and 11 % yield. Diastereoisomer **32a** provided a single crystal X-ray structure (Figure 2).

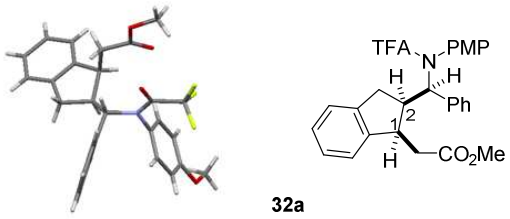


Figure 2. Single crystal X-ray structure of **32a**.

The structure or 32a' was assigned by MS and NMR. The 1H coupling constant $^3J_{1,2}$ for **32a** was 6.8 and for **32a'** 6.7. The coupling constant for the *cis*-relationship of the ring substituents was in agreement with literature values[34] for similar alkyl-substituted indanes. Diastereoisomer **32a'** was therefore assigned as the *cis,trans*-isomer. The crystal structure of **32a** allowed for the corresponding tentative assignment of values in the range $^3J_{1,2}$ ~ 7 Hz as *cis*-relative stereochemistry when obtained for similarly 1,2-dialkyl-substituted indane molecules. This supported the assignment of the phenyl translocation product **31** as the *cis*-isomer. In addition to strong nOe interactions (see ESI), **31** displayed a $^3J_{1,2}$ value of ~ 7 Hz, a value in the range of a *cis*-substituted indane. The full assignment of **32a** and **32a'** also corroborated the assignment of **30a** and **30b** as complex mixtures of indanes.

Reaction of stilbene-derived β-nitroacetamide **11b** under the same conditions resulted in the successful denitration-cyclisation reaction to afford indanes **32b** with an identical crude ratio of diastereoisomers (40:40:20) as that observed for the methyl acrylate derivative **11a** in 47 % yield. The relative stereochemistry of the ring substituents of the two major diastereoisomers were assigned as *cis*- based upon the $^3J_{1,2}$ values of 6.6 and 7.2 Hz. A higher yield of inseperable indane diastereoisomers for **32a** (59%) compared to **32b** (47%) can be attributed an electronically more favourable cyclisation with the electron withdrawn acrylate cyclisation radical acceptor in **11a** versus the stilbene acceptor in **11b**. Unfortunately radical denitration-cyclisation of the nitrostyryl β-nitroacetamide **11c** under the same conditions led to an unidentifiable complex mixture with no indication of indane products, most probably due to competing denitration of the nitro-alkene.

Cyclisation of **12a** was successful, affording two main products **34a** and **35a**, but in low yield. A single crystal X-ray of **35a** confirmed the assigned structure (Figure 3). MS analysis confirmed that **34a** and **35a** were isomeric and detailed NMR experiments comfirmed the assignment of **34a** (See ESI).

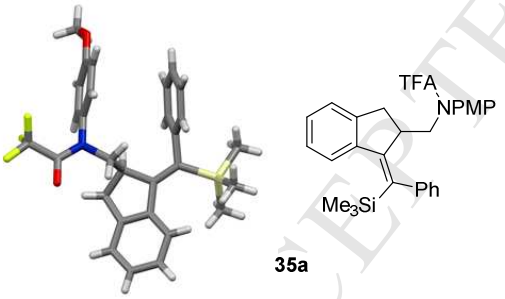


Figure 3. Single crystal X-ray structure of **35a** showing 1,4-phenyl translocation.

Cyclisation of **12b** gave a low 10% yield of **34b** and the geometry of the alkene could not be defined.

Radical cyclisation of the *gem*-dimethyl substituted hexenyl β-nitroacetamide **15** proceeded in a good 55% combined yield of products **36** and **37**. The major product **36** (46% yield) was the expected 5-*exo*-trig product and was isolated as a mixture of three diastereoisomers 40:30:30. The stereochemical assignment of these methyl cyclopentane isomers was not possible due to the complex nature of the ^{1}H NMR spectrum. The minor product **37** was the phenyl translocation isomer (see ESI for data correlation table). The relative stereochemistry of the ring substituents in either **36** or **37** could not be determined, as the $^3J_{1,2}$ values could not be deciphered. The combined yield (55%) is similar to the phenyl-tethered **8a** (58%) and shows a Thorpe Ingold effect due to the *gem*-dimethyl substituents. Radical denitration-cyclisation of **18** followed by hydrogen abstraction from ^{n}Bu$_3$SnH gave the mono-substituted hexenyl tether **38** in 24% yield as an inseperable mixture of diastereoisomers 40:35:25. The 1,4-phenyl translocated isomer **39** was also isolated in 3% yield. The relative stereochemistry of the defined ring substituents was from a strong NOESY interaction between the corresponding ring protons (see ESI for data correlation table).

Cyclisation of precursors derived from imines containing unsaturated substituents **19a,b,d** and **25** were investigated. Radical denitration-cyclisation of **19a** gave 2-amidoindane **40a** in 46% yield as a near 1:1 mixture of diastereoisomers. The *trans*-orientation of the benzyl- and acetamido- substituents was tentatively assigned based upon the coupling constant between the corresponding ring protons (J=8.7 and 8.8 Hz) being very similar to the a *trans*-coupling constant of a similar 2-aminoindane reported in the literature[35] and the detection of only a minor interaction in the NOESY spectrum. These were in contrast to the corresponding data for the *cis*-orientation of substituents in the *cis*-indane **32a**, the structure of which was confirmed by single crystal X-ray crystallography. A full data correlation is presented in the supplementary information. Cyclisation of the stilbene analogue **19b** led to indane **40b** in 34% yield as an inseperable 60:40 mixture of diastereoisomers. Full characterisation of the disatereoisomers was possible (see structural elucidation and correlation tables in ESI). Cyclisation of the (*E*)-methylstyrene derivative **19d** gave a low 12% yield of an inseperable 70:30 mixture of diastereoisomers **40d**. Further purification gave the major diastereoisomer in 95:5 *dr*, albeit at a yield of only 4 %, but which did allow full characterisation to be made. The relative stereochemistry was tentatively assigned as *trans,trans*.. The reason for the lower yield of indane **40d** is not clear, however the reaction was conducted on a small scale and separation from the ^{n}Bu$_3$SnH residues was difficult, hence it is likely that some of the product was lost during partitioning of the product between hexanes/MeCN. The analogous hexenyl tethered β-nitroacetamide **25** unfortunately led to a complex mixture of products including recovered starting material. Only trace amounts of cyclisation and protodenitration was observed, hence purification was not undertaken. It would appear that radical denitration did not readily occur in this molecule, and that cyclisation was not significantly aided by the presence of the CHN stereocentre on the hexenyl tether.

Subjection of the amino tethered alkene β-nitroacetamide **27** to radical denitration-cyclisation resulted in the formation of TFA-protected pyrrolidine **41** in low 12% yield, as a complex inseparable mixture of all four possible diastereoisomers (50:30:15:5). Characterisation of the pyrrolidine ring was limited due to the complex nature of the ^{1}H NMR spectrum, however characterisation by mass spectrometry confirmed the desired molecular ion at 438 ($M + H^+$).

Radical denitration-cyclisation of the activated secondary stilbene tethered β-nitroacetamide **28** gave the expected indane product **42** in a low 13% yield. Analysis of the NOESY interactions between protons H_1-H_2 (w), H_2-H_3 (w) and H_1-H_3 (m) and the $^3J_{1,2}$ and $^3J_{2,3}$ values (9.4 and ~ 9.0 Hz respectively) of **42** led to the tentative assignment of the major diastereoisomer as the *trans,trans*-configuration. Cyclisation of the more flexible hexenyl tethered activated secondary β-nitroacetamide **28** gave the expected cyclopentane **43** isolated in an improved 36% yield, as an inseparable 50:50 mixture of diastereoisomers.

3. Conclusion

A diverse range of β-nitroacetamides were synthesized to probe the limitations of the radical denitration-cyclisation of products derived from the nitro-Mannich reaction. It was found that cyclisation could be performed on a variety of secondary nitro groups onto tethered alkenes and alkynes. The formation of indanes or cyclopentanes was achieved in 12-59% yield in variable dr. Phenyl translocation as seen in products **31**, **35a** and **39**, normally occurs at high dilution (10-4 M),[32] but it would appear can occur at much higher concentrations (0.34 M). The stability of the resultant amidomethyl radicals providing the driving force for the translocations. Phenyl translocation in products **40a** was not observed as there is no driving force for the 1,4-translocation, which would hypothetically only give another primary radical. Cyclisation of **11b** was much more successful than cyclisation of either alkyne **12a,b** which can be attributed to the slower rate of intramolecular addition of radicals to alkynes vs alkenes.[36] The combined yields of **36** and **37** (55%) form *gem*-dimethyl substituted hexenyl β-nitroacetamide **15** are comparable to the yields of **30a** and **31** (58%) from styryl tether **8a**. Interestingly the proportion of 1,4-phenyl translocation is lower for **15**, possibly reflecting the greater degrees of freedom in the hexenyl tether. The low reactivity of **25** could also be attributed to the flexible hexenyl tether. Radical cyclisation of a comparatively sterically bulky radical derived from **28** resulted in a lower yield (13%) than the equivalent unactivated secondary β-nitroacetamide **19b**, which underwent cyclisation in 34 % yield. However the extra steric bulk at the radical centre led to an increase in diastereoselectivity (*cf* **40b** *dr* 60:40 to **42** *dr* 95:5). Activation of the secondary nitro group by an adjacent benzene ring resulted in successful cyclisation of the activated secondary radical **29** to **43** in 36% yield. This is in contrast to the unactivated secondary radical **5** (Scheme 3) which afforded a poor yield of cyclized product **7** (20%). Successful cyclisation required a 10 equivalent excess of $^{n}Bu_3SnH$ and higher yields were attained by increasing the substitution or reducing the degrees of freedom of the tether between the nitro group and the alkene.

4. Experimental section

4.1. General

See supplementary information.

Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication nos. **32a** 1843325 and **35a** 1843326. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK, (fax: +44-(0)1223-336033 or e-mail: deposit@ccdc.cam.ac.Uk)

*4.2. N-(1,3-diphenylpropyl)-2,2,2-trifluoro-N-(4-methoxyphenyl)acetamide (**2**)*

To a solution of β-nitroacetamide **1**[8a] (20.0 mg, 44.0 μmol, 1 eq), in PhMe (1 mL) under N_2 at rt were added AIBN (5.0 mg, 30 μmol, 0.7 eq) and Bu_3SnH (0.12 mL, 0.45 mmol, 10 eq), the reaction mixture degassed and heated to reflux for 15 min under N_2. The reaction mixture was then cooled to rt, concentrated. *in vacuo* and the residue taken up in MeCN/Hexane (50:50, 10 mL). The MeCN/Hexane layers were partitioned, with extraction of the Hexane layer with MeCN (5 mL x 2). The combined MeCN extracts were washed with Hexane (10 mL x 3) and the MeCN layer was concentrated *in vacuo*. Purification by flash column chromatography (0 – 10% Et_2O/Pet. ether) afforded **2** as a colourless oil (12.7 mg, 79 %); IR υ_{max} ($CDCl_3$ cast) cm^{-1} 2931, 2854 (C-H) 1687 (C=O, amide) 1606, 1585, 1510, 1455 (C=C, Ar) 1182, 1148 (C-F, CF_3) ^{1}H NMR ($CDCl_3$, 600 MHz) δ 2.19 (2H, m, CH_2CHN) 2.68 (2H, m, CH_2Ph) 3.79 (3H, s, OCH_3) 6.03 (1H, t, *J* = 7.7, C*H*N) 6.08 (1H, dd, *J* = 8.8, 2.5, Ar*H*) 6.57 (1H, dd, *J* = 8.8, 3.0, Ar*H*) 6.87 (1H, dd, *J* = 8.6, 3.1, Ar*H*) 7.10 (2H, apt d, *J* = 6.8, Ar*H*) 7.17 – 7.18 (3H, m, Ar*H*) 7.21 (1H, apt t, *J* = 7.4, Ar*H*) 7.26 – 7.31 (5H, m, Ar*H*); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 32.6 (*C*H_2) 32.8 (*C*H_2) 55.5 (O*C*H_3) 59.9 (*C*HN) 113.5 (PMP-*C*) 113.5 (PMP-*C*) 116.7 (q, *J* = 289.1, *C*F_3) 126.3 (Ar*C*) 126.8 (q, Ar*C*) 128.5 (Ar*C*) 128.5 (2C, Ar*C*) 128.6 (2C, Ar*C*) 128.7 (2C, Ar*C*) 129.2 (2C, Ar*C*) 131.4 (*C*H) 132.5 (*C*H) 137.6 (q, Ar*C*) 141.2 (q, Ar*C*) 157.5 (q, *J* = 35.0, *C*O*C*F_3) 160.0 (q, Ar*C*O); ^{19}F ($CDCl_3$, 282 MHz) δ – 67.4 ppm (3F, s, CF_3); m/z (CI^+) 414 (91 %, M + H^+) 220 (100 %, $C_9H_7F_3NO_2^+$) 195 (42 %, $C_{15}H_{15}^+$) HRMS ($C_{24}H_{22}F_3NO_2$) calcd 414.16809 found 414.167626.

4.3 Synthesis of cyclisation precursors.

*(E)-1-nitro-hexa-1,5-diene (**3**)*

A solution of nitromethane (3.40 mL, 61 mmol), triethylamine (4.20 mmol) and 4-penten-1-al (1.00 g, 12.2 mmol) was stirred overnight under N_2 at rt. The excess nitromethane and base were removed in vacuo; purification by silica plug gave nitroalcohol which was used directly in the next step. Purified nitroalcohol (12.2 mmol) was dissolved in dry CH_2Cl_2 (120 mL) under N_2 and cooled to 0 ^{o}C. MsCl (14.4 mmol) was added dropwise and the reaction stirred for 5 min before dropwise addition of a solution of DIPEA (30.0 mmol) in dry DCM (25 mL). The reaction was stirred at 0 ^{o}C until complete before warming to rt. The reaction was washed with H_2O (60 mL x 2), 2M HCl (60 mL x 2), dried ($MgSO_4$) filtered and conc *in vacuo*. Purification via flash column chromatography (5 % Et_2O/hexanes) afforded **64c** as a colourless oil (1.02 g, 8.02 mmol, 66 %); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 2.27 – 2.41 (4H, m, CH_2) 5.04 – 5.12 (2H, m, CH_2) 5.78 (1H, ddt, *J* = 17.0, 10.4, 6.5, $CH_2CHCH_2CH_2$) 6.99 (1H, d, *J* = 13.4, 1.6, C*H*NO_2) 7.26 (1H, dt, *J* = 13.4, 7.2, C*H*CHNO_2); NMR data was consistent with published data.[38]

2,2,2-trifluoro-N-(4-methoxyphenyl)-N-((1R,2S*)-2-nitro-1-phenylhept-6-en-1-yl)acetamide (**5**)*

To a solution of nitroalkene **3** (1.02 g, 8.02 mmol) in CH_2Cl_2 (40 mL) at rt under N_2 was added dropwise $LiHBEt_3$ (8.4 mL of a 1.0 M solution in THF, 8.4 mmol, 1.05 eq) and the reaction was stirred for 20 min and a white precipitate was formed. The reaction mixture was cooled to –78 ^{o}C and to this was added a solution of (*E*)-*N*-(4-methoxyphenyl)-1-phenylmethanimine (1.91 g, 9.06 mmol) in CH_2Cl_2 (25 mL). The reaction was stirred for 10 min before dropwise addition of trifluoroacetic acid (9.22 mmol, 1.15 equiv) and the reaction was stirred at –78 ^{o}C for 1.5 h or until complete by TLC. The reaction was warmed for 5 min then quenched with sat. aq. $NaHCO_3$ solution (15 mL), extracted with Et_2O (20 mL x 3) washed with brine (30 mL), dried ($MgSO_4$) filtered and concentrated *in vacuo*. Crude β-nitroamine was re-dissolved in CH_2Cl_2 (10 ml) and cooled to –78^{o}C under N_2. To this solution was added dropwise DIPEA (20.1 mmol, 2.5 equiv.) followed by dropwise addition of trifluoroacetic anhydride (20.1 mmol, 2.5 mmol) and the reaction stirred for 18 h to rt. The reaction was quenched with 2 M HCl (20 mL), extracted with CH_2Cl_2 (20 mL x 3), dried ($MgSO_4$), filtered and concentrated *in vacuo*. to give the crude β-nitroacetamide. Purification by flash column chromatography (10 % Et_2O/hexanes) afforded **5** as a mixture of diastereoisomers (>90:10) as a yellow oil (1.97 g, 4.52 mmol, 56 %); IR υ_{max} ($CDCl_3$ cast) 2936 (C-H) 1697 (C=O) 1608 (Ar, C=C) 1585 (Ar, C=C) 1554 (N-O) 1510 (Ar, C=C) 1254 (C-O) 1180 (CF_3, C-F) 1033 (C-N) cm^{-1} ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.54 – 1.63 (2H, m, $CH_2CH_2CH_2$) 2.16 – 2.34 (4H, m,

CH_2CH$_2$CH_2) 3.86 (3H, s, OCH_3) 5.08 (1H, br.d, J = 10.1, CH$_2$CH$_2$CHC$H_{2\text{-cis}}$) 5.12 (1H, dm, J = 17.1, CH$_2$CH$_2$CHC$H_{2\text{-trans}}$) 5.33 (1H, apt br t, J = 10.0, CHNO$_2$) 5.78 – 5.88 (1H, ddt, J = 17.1, 10.2, 6.7, CH$_2$CHCH$_2$) 6.04 (1H, br m, CHN) 6.29 (1H, br d, J = 7.2, ArH) 6.68 (1H, dd, J = 8.9, 6.6, PMP-H) 6.90 (1H, dd, J = 8.7, 2.8, PMP-H) 6.96 (1H, br d, J = 1.9, PMP-H) 7.09 (2H, d, J = 7.4, ArH) 7.25 -7.36 (3H, dm, ArH); ^{13}C NMR (CDCl$_3$, 125 MHz) δ 24.9 (CH$_2$$CH_2CH_2$) 31.0 ($CH_2CH_2$$CH_2$) 32.6 ($CH_2CH_2$$CH_2$) 55.6 (OC$H_3$) 59.3 ($C$HN) 87.8 ($CNO_2$) 114.0 (Ar$C$) 114.3 (Ar$C$) 116.1 ($CH_2$CHCH$_2$R) 116.3 (q, J = 286.9, CF$_3$) 128.8 (2C, ArC) 129.1 (q) 129.2 (2C, ArC) 129.7 (ArC) 130.1 (ArC) 132.2 (ArC) 133.4 (q) 137.2 (CH$_2$$CHCH_2CH_2$) 158.0 (q, J = 35.3, COCF$_3$) 160.5 (q, ArCO); ^{19}F NMR (CDCl$_3$, 282 MHz) δ -67.7 (3F, s, CF$_3$); m/z (CI$^+$) 437 (44 %, M + H$^+$) 390 (100 %, C$_{22}$H$_{23}$F$_3$NO$_2^+$) 308 (17 %, C$_{16}$H$_{13}$F$_3$NO$_2$) 220 (16 %, C$_9$H$_7$F$_3$NO$_2$); HRMS (C$_{22}$H$_{23}$F$_3$N$_2$O$_4$) calcd. 437.1688, found 437.1682.

*(E)-2-vinyl-β-nitrostyrene (**9**)*

To a solution of aldehyde 2-vinylbenzaldehyde (**9**) (2.00 g, 15.1 mmol) and nitromethane (2.05 mL, 36.0 mmol) in methanol (8 mL) at 0 °C was added aq. 1M NaOH (35 mL) dropwise while maintaining an internal reaction temperature of 10-15 °C. Ice water (25 mL) was added and the reaction stirred at 0 °C for 15 min. The reaction mixture was then added to 8 M HCl (25 mL) at 0 °C to give a blue colour. The reaction was left to stir overnight giving a yellow colour. The product was extracted with CH$_2$Cl$_2$ (80 mL x 3), washed with brine (80 mL) dried (MgSO$_4$), filtered and conc *in vacuo* to give the crude nitroalkene, which was purified by recrystallisation (Et$_2$O/Pet. Ether) to give **10** as a yellow oil (2.22 g, 12.7 mmol, 85 % yield); ^{1}H NMR (CDCl$_3$, 600 MHz) δ 5.53 (1H, dd, J = 11.0, 0.7, ArCHC$H_{2\text{-cis}}$) 5.66 (1H, dd, J = 17.3, 0.8, ArCHC$H_{2\text{-trans}}$) 7.02 (1H, dd, J = 17.2, 11.0, ArCHCH$_2$) 7.34 (1H, t, J = 7.5, ArH) 7.47 (1H, t, J = 7.4, ArH) 7.50 (1H, d, J = 13.6, CHNO$_2$) 7.51 (1H, d, J = 7.9, ArH) 7.54 (1H, d, J = 7.9, ArH) 8.36 (1H, d, J = 13.5, CHCHNO$_2$); ^{13}C NMR (CDCl$_3$, 150 MHz) δ 120.0 (ArCHCH$_2$) 127.9 (q, ArC) 127.9 (2C, ArC) 128.4 (ArC) 132.0 (ArC) 133.7 (ArCHCH$_2$) 137.1 (CHCHNO$_2$) 138.3 (CHNO$_2$) 139.7 (q, ArC); m/z (CI$^+$) 176 (22 %, M + H$^+$) 131 (100 %, C$_{10}$H$_9$D$^+$); HRMS C$_{10}$H$_{10}$NO$_2$ calcd. 176.0706 found 176.0707. NMR Data was consistent with published data.[22]

2,2,2-trifluoro-N-(4-methoxyphenyl)-N-((1R,2S*)-2-nitro-1-phenyl-3-(2-vinylphenyl)propyl)acetamide (**8a**)*

By an identical procedure to the preparation of **5** using nitrostyrene **9** (1.22 g, 6.98 mmol) and (*E*)-*N*-(4-methoxyphenyl)-1-phenylmethanimine (1.63 g, 7.72 mmol). Purification via flash column chromatography (40 % CH$_2$Cl$_2$/Hexanes followed by 20 % Et$_2$O/Hexanes) afforded **8a** as a white solid (1.27 g, 2.62 mmol, 38 %); mp 90 – 92 °C; IR ν$_{max}$ (thin film) 1696 (C=O stretch, amide) 1556 (N-O, asymm) 1510 (C=C, Ar) 1300 (N-O symm) 1153 (C-F, CF$_3$) cm^{-1}; ^{1}H NMR (CDCl$_3$, 600 MHz) δ 3.56 (1H, dd, J = 14.5, 11.2, ArCH_2) 3.67 (1H, dd, J = 11.2, 3.3, ArCH_2) 3.81 (3H, s, OCH_3) 5.50 (1H, dd, J = 10.9, 1.1, ArCHC$H_{2\text{-trans}}$) 5.74 (1H, dd, J = 17.4, 1.1, ArCHC$H_{2\text{-cis}}$) 5.74 (1H, br s, CHNO$_2$) 5.95 (1H, br s, CH) 6.52 (1H, br s, CH) 6.74 (1H, br d, J = 8.8, PMP-H) 6.89 (1H, dd, J = 8.8, 2.8, PMP-H) 7.03 (1H, br d, J = 8.1, PMP-H) 7.07 (1H, dd, J = 17.4, 10.9, ArCHCH$_2$) 7.15 (3H, br d, J = 7.4, ArH) 7.23 – 7.27 (3H, m, ArH) 7.29 (1H, dd, J = 7.7, 1.1, ArH) 7.32 (1H, d, J = 7.5, ArH) 7.52 (1H, d, J = 7.5, ArH); ^{13}C NMR (CDCl$_3$, 150 MHz) δ 35.6 (ArCH$_2$) 55.6 (OCH_3) 66.9 (CHN) 88.9 (CHNO$_2$) 114.0 (PMP-C) 114.7 (PMP-C) 116.3 (q, J = 291.2, CF$_3$) 118.0 (ArCHCH$_2$) 127.0 (ArC) 128.4 (ArC) 128.5 (ArC) 128.8 (q, ArC) 129.0 (2C, ArC) 129.5 (ArC) 129.8 (ArC) 129.9 (ArC) 130.4 (PMP-C) 131.7 (PMP-C) 131.8 (q, ArCCHCH$_2$) 133.3 (q, ArC) 134.2 (ArCCHCH$_2$) 137.6 (q, ArC) 158.2 (q, J = 36.0, COCF$_3$) 160.5 (q, ArCO); ^{19}F NMR (CDCl$_3$, 282 MHz) δ – 67.3 ppm (3F, s, CF$_3$); m/z (CI$^+$) 485 (100 %, M + H$^+$) 438 (63 %, C$_{26}$H$_{23}$F$_3$NO$_2$) 308 (55 %, C$_{16}$H$_{13}$F$_3$NO$_2$) 219 (94 %, C$_9$H$_8$F$_3$NO$_2$); HRMS (C$_{26}$H$_{24}$F$_3$N$_2$O$_4$) calcd. 485.1683, found 485.1682.

ethyl (2S,3S*)-3-nitro-2-(2,2,2-trifluoro-N-(4-methoxyphenyl)acetamido)-4-(2-vinylphenyl)butanoate (**8b**)*

By an identical procedure to the preparation of **5** using 2-vinyl-*trans*-β-nitrostyrene **9** (0.78g, 4.42 mmol) and Ethyl *N*-(4-methoxyphenyl)-formimidate (1.04 g, 5.02 mmol). Purification via flash column chromatography afforded the product **8b** as a white solid (1.34 g, 2.79 mmol, 63 %) mp 105 - 106 °C; IR ν$_{max}$ (thin film) 2983 (C-H) 1747 (C=O, ester) 1701 (C=O, amide) 1561 (N-O, asymm) 1510 (C=C, Ar) 1300 (N-O, symm) 1157 (C-F, CF$_3$) cm^{-1}; ^{1}H NMR (CDCl$_3$, 600 MHz) δ 1.30 (3H, t, J = 7.1, CH$_2$CH_3) 3.15 (1H, dd, J = 14.1, 11.7, ArCH_2) 3.51 (1H, dd, J = 14.1, 3.6, ArCH_2) 3.87 (3H, s, ArOCH_3) 4.30 (2H, q, J = 7.1, CH_2CH$_3$) 4.94 (1H, d, J = 8.5, CHN) 5.43 (1H, d, J = 10.9, ArCHC$H_{2\text{-cis}}$) 5.61 (1H, ddd, J = 11.7, 8.8, 3.6, CHNO$_2$) 5.72 (1H, d, J = 17.1, ArCHC$H_{2\text{-trans}}$) 6.84 (1H, dd, J = 17.1, 11.0, ArCHCH$_2$) 6.97 (2H, *br* s, PMP-H) 7.01 (1H, d, J = 7.6, ArH) 7.22 (1H, t, J = 7.5, ArH) 7.30 (1H, t, J = 7.6, ArH) 7.30 (1H, *br* s, PMP-H) 7.53 (2H, m, ArH, PMP-H); ^{13}C NMR (CDCl$_3$, 150 MHz) δ 13.9 (CH$_2$$CH_3$) 35.5 (Ar$CH_2$) 55.7 (ArO$CH_3$) 63.3 (O$CH_2CH_3$) 67.5 ($C$HN) 86.9 ($CNO_2$) 114.7 (PMP-$C$) 115.3 (PMP-$C$) 116.0 (q, CF$_3$) 118.2 (ArCHCH$_2$) 126.8 (ArC) 128.4 (ArC) 128.6 (ArC) 129.2 (PMP-C) 129.6 (PMP-C) 130.1 (ArC) 131.1 (q, ArCCH$_2$CHNO$_2$) 132.3 (q, ArCN) 133.3 (CHCH$_2$) 137.4 (q, ArCCHCH$_2$) 158.6 (q, J = 37.1, COCF$_3$) 160.6 (q, ArCOCH$_3$) 166.5 (q, COCH$_2$CH$_3$) ; ^{19}F NMR (CDCl$_3$, 282 MHz) δ - 67.9 ppm (3F, s, CF$_3$); m/z (ESI$^+$) 544 (58 %, M + MeCN + Na$^+$) 481 (100 %, M + H$^+$) 434 (9 %, C$_{23}$H$_{23}$F$_3$NO$_4$); HRMS (C$_{23}$H$_{24}$F$_3$N$_2$O$_6$) calcd. 481.1616, found 481.1586.

methyl (E)-3-(2-((2S,3R*)-2-nitro-3-phenyl-3-(2,2,2-trifluoro-N-(4-methoxyphenyl)acetamido)propyl)phenyl)acrylate (**11a**)*

To a solution of alkene **8a** (209 mg, 0.43 mmol) in degassed methyl acrylate (4.40 mL, 48.6 mmol) was added Hoveyda-Grubbs 2nd generation catalyst (29.4 mg, 0.046 mmol) and the reaction was stirred at 75 °C o/n. Purification by flash column chromatography using EtOAc/Hexanes (10-20 %) followed by a second column using EtOAc/Hexanes (40 %) afforded **11a** as a colourless oil (170 mg, 0.34 mmol, 82 %); mp 67 - 70 °C; IR ν$_{max}$ (thin film) 2949, 2838 (C-H) 1695 (C=O, amide & ester) 1633 (C=C) 1555 (N-O, asymm) 1508 (C=C, Ar) 1317 (N-O, symm) 1153 (C-F, CF$_3$) cm^{-1}; ^{1}H NMR (CDCl$_3$, 600 MHz) δ 3.63 (1H, dd, J = 14.7, 11.6, ArCH_2) 3.73 (1H, dd, J = 14.6, 3.6, ArCH_2) 3.81 (3H, s, ArOCH_3) 3.86 (3H, s, COOCH_3) 5.57 (1H, *br* s, CHNO$_2$) 6.15 (1H, *br* s, CHN) 6.36 (1H, *br* s, ArH) 6.48 (1H, d, J = 15.7, ArCHCHCO$_2$CH$_3$) 6.66 (1H, apt d, J = 7.3, ArH) 6.99 (1H, dd, J = 8.7, 2.5, ArH) 7.07 (2H, d, J = 7.2, ArH) 7.16 – 7.37 (7H, m, ArH) 7.60 (1H, dd, J = 7.6, 2.2, ArH) 8.08 (1H, d, J = 15.7, ArCHCHCO$_2$CH$_3$); ^{13}C NMR (CDCl$_3$, 150 MHz) δ 35.5 (ArCH$_2$) 52.0 (COOCH$_3$) 55.6 (ArOCH$_3$) 65.9 (CHN) 89.2 (CNO$_2$) 114.4 (PMP-C) 114.5 (PMP-C) 116.3 (q, J = 287.3, CF$_3$) 121.4 (CHCOOCH$_3$) 127.4 (ArC) 128.1 (ArC) 128.7 (ArC) 128.9 (ArC) 129.5 (ArC) 129.8 (ArC) 130.6 (ArC) 130.8 (2C, PMP-C) 132.1 (q, ArCCHCHCO) 133.0 (q, ArCCH$_2$) 133.7 (q, ArCN) 133.7 (ArCCN) 140.9 (CHCHCOOCH$_3$) 158.4 (q, J = 35.4, COCF$_3$) 160.5 (ArCOCH$_3$) 167.0 (q, COOCH$_3$); ^{19}F NMR (CDCl$_3$, 282 MHz) δ – 67.1 ppm (3F, s, CF$_3$); m/z (CI$^+$) 543 (22 %, M + H$^+$) 511 (100 %, C$_{27}$H$_{22}$F$_3$N$_2$O$_5^+$) 220 (60 %,

$C_9H_7F_3NO_2D^+$); HRMS ($C_{28}H_{26}F_3N_2O_6$) calcd. 543.1743, found 543.1740.

2,2,2-trifluoro-N-(4-methoxyphenyl)-N-((1R,2S*)-2-nitro-1-phenyl-3-(2-((E)-styryl)phenyl)propyl)acetamide (**11b**)*

To a degassed mixture of alkene **8a** (876 mg, 1.81 mmol) in CH_2Cl_2 (15 mL) was added Hoveyda-Grubbs 2nd generation catalyst (56.7 mg, 0.091 mmol) followed by degassed styrene (2.10 mL, 18.9 mmol) and the reaction was heated to 40 °C for 7 h before the addition of a second portion of catalyst (28.6 mg, 0.05 mmol) and degassed styrene (1.00 mL, 9.00 mmol), the reaction was heated o/n until complete by TLC. The reaction was concentrated *in vacuo*. Purification by flash column chromatography using EtOAc/Hexanes (0-10 %) afforded **11b** as a white solid (0.79 g, 1.41 mmol, 78 %); mp 68 - 70 °C; IR ν_{max} (thin film) 1697 (C=O, amide) 1557 (N-O, asymm) 1510 (C=C, Ar) 1301 (N-O, symm) 1182 (C-F, CF_3) cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.56 (1H, dd, *J* = 14.4, 11.5, CH_2) 3.70 (3H, s, OCH_3) 3.77 (1H, dd, *J* = 14.4, 3.3, CH_2) 5.65 (1H, br s, C*H*NO_2) 6.02 (1H, br s, C*H*N) 6.22 (1H, br s, PMP-*H*) 6.39 (1H, br s, PMP-*H*) 6.62 (1H, br d, *J* = 7.3, PMP-*H*) 6.89 (1H, dd, *J* = 8.5, 1.8, PMP-*H*) 7.05 (2H, br d, *J* = 6.5, Ar*H*) 7.12 (1H, d, *J* = 7.5, 1.2, Ar*H*) 7.13 (1H, d, *J* = 16.0, PhC*H*CHAr) 7.19 (2H, t, *J* = 7.8, Ar*H*) 7.24 (1H, td, *J* = 7.5, 1.2, Ar*H*) 7.28 (1H, m, Ar*H*) 7.33 (2H, m, Ar*H*) 7.42 (2H, m, Ar*H*) 7.48 (1H, d, *J* = 16.0, ArC*H*CHPh) 7.64 (1H, d, *J* = 7.6, Ar*H*) 7.67 (2H, d, *J* = 7.4, Ar*H*); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 36.1 (*C*H_2) 55.6 (O*C*H_3) 66.3 (*C*HN) 89.3 (*C*HNO_2) 113.5 (PMP-*C*) 114.9 (PMP-*C*) 116.3 (q, *C*F_3, *J* = 290.3) 125.3 (ArCH*C*HPh) 127.1 (Ar*C*) 127.2 (2C, Ar*C*) 128.3 (Ar*C*) 128.5 (Ar*C*) 128.6 (2C, Ar*C*) 128.9 (2C, Ar*C*) 129.0 (2C, Ar*C*) 129.4 (2C, Ar*C*) 129.7 (Ar*C*) 130.4 (2C, PMP-*C*) 131.7 (q, Ar*C*CHCHPh) 132.2 (q, Ar*C*N) 132.8 (Ar*C*HCHPh) 133.2 (q, Ar*C*CHN) 136.8 (q, Ar*C*CH_2) 137.1 (q, Ar*C*CHCHArCH_2) 158.3 (q, *J* = 35.6, *C*OCF_3) 160.3 (Ar*C*OCH_3) ; ^{19}F NMR ($CDCl_3$, 282 MHz) δ – 67.2 ppm (3F, s, CF_3); m/z (CI^+) 578 (20 %, M + H_2O + H^+) 560 (7 %, M + H^+) 514 (14 %, $C_{32}H_{27}F_3NO_2$); HRMS ($C_{32}H_{27}N_2O_4F_3$) calcd. 560.1923, found 560.1919.

2,2,2-trifluoro-N-(4-methoxyphenyl)-N-((1R,2S*)-2-nitro-3-(2-((E)-2-nitrovinyl)phenyl)-1-phenylpropyl)acetamide (**11c**)*

A mixture of alkene **8a** (0.30 g, 0.62 mmol), $AgNO_2$ (0.29 g, 1.86 mmol) 4 Å molecular sieves (0.19 g) and TEMPO (0.02 mg, 0.12 mmol) in DCE (6 mL) was stirred at 70 °C for 1.5 h under air. On completion, the reaction mixture was filtered through celite, washed with DCM and concentrated *in vacuo*. Purification via flash column chromatography (10-20 % EtOAc/Hexanes) afforded **11c** as a white solid (271 mg, 0.51 mmol, 83 %) as a mixture of isomers (90:10); mp 72 – 74 °C; IR ν_{max} (thin film) 2968, 2841 (C-H) 1695 (C=O, amide) 1556 (N-O, asymm) 1509 (C=C, Ar) 1341 (N-O, symm) 1180, 1154 (C-F, CF_3) cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ_{anti} 3.68 (1H, dd, *J* = 14.7, 10.9, CH_2) 3.72 (1H, dd, *J* = 14.7, 4.6, CH_2) 3.83 (3H, s, OCH_3) 5.70 (1H, *br* s, C*H*NO_2) 5.99 (1H, *br* s, C*H*N) 6.50 (1H, *br* s, PMP-*H*) 6.74 (1H, dd, *J* = 8.7, 2.4, PMP-*H*) 6.98 (1H, dd, *J* = 8.7, 2.7, PMP-*H*) 7.09 (1H, d, *J* = 7.6, PMP-*H*) 7.13 (2H, m, Ar*H*) 7.25 (2H, d, *J* = 7.5, Ar*H*) 7.30 – 7.42 (4H, m, Ar*H*) 7.55 (1H, d, *J* = 13.4, C*H*NO_2) 7.56 (1H, dd, *J* = 7.7, 1.1, Ar*H*) 8.37 (1H, d, *J* = 13.4, C*H*CHNO_2) δ_{syn} 3.02 (1H, dd, *J* = 15.2, 2.9, CH_2) 3.18 (1H, dd, *J* = 15.2, 11.6, CH_2) 7.93 (1H, d, *J* = 13.4, C*H*CHNO_2); ^{13}C NMR ($CDCl_3$, 150 MHz) δ_{anti} 35.3 (*C*H_2) 55.6 (O*C*H_3) 66.8 (*C*HN) 89.6 (*C*HNO_2) 114.2 (PMP-*C*) 115.0 (PMP-*C*) 116.3 (q, *J* = 289.1, *C*F_3) 128.0 (Ar*C*) 128.5 (q, Ar*C*) 129.0 (3C, Ar*C*) 129.3 (q, Ar*C*) 129.4 (2C, Ar*C*) 130.0 (*C*H) 130.2 (*C*H) 131.4 (PMP-*C*) 131.7 (br *C*H) 132.5 (Ar*C*) 133.0 (q, Ar*C*) 135.2 (*C*HCHNO_2) 135.3 (q, Ar*C*) 139.4 (CH*C*HNO_2) 158.5 (q, *J* = 36.0, *C*OCF_3) 160.6 (q, Ar*C*O); ^{19}F NMR ($CDCl_3$, 282 MHz)) δ_{anti} – 67.4 ppm (3F, s, CF_3) δ_{syn} – 67.2 ppm (3F, s, CF_3); m/z (ESI^+) 552 (23 %, M + Na^+) 547 (45 %, M + NH_4^+) 530 (100%, M + H^+); HRMS ($C_{26}H_{23}F_3N_3O_6$) calcd. 530.1539, found 530.1535.

2,2,2-trifluoro-N-(4-methoxyphenyl)-N-((1R,2S*)-2-nitro-1-phenyl-3-(2-((trimethylsilyl)ethynyl)phenyl)propyl)acetamide (**12a**)*

By an identical procedure to the preparation of **5** using nitroalkene **14a**[23] (2.28 g, 9.30 mmol) and (*E*)-*N*-(4-methoxyphenyl)-1-phenylmethanimine (2.28 g, 10.0 mmol). Purification by flash column chromatography (50 % CH_2Cl_2/Hexanes followed by 5 % EtOAc/Petrol) afforded **12a** as a white solid (3.06 g, 5.52 mmol, 58 %); mp 49 – 51 °C; IR ν_{max} (thin film) 2962 (C-H) 2155 (C-C, alkyne) 1698 (C=O, amide) 1556 (N-O, asymm) 1300 (N-O, symm) 1179, 1153 (C-F, CF_3) cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 0.32 (9 H, s, OSi(CH_3)$_3$) 3.72 (1H, dd, *J* = 14.5, 4.0, ArCH_2) 3.81 (1H, dd, *J* = 14.8, 10.5, ArCH_2) 3.81 (3H, s, OCH_3) 5.79 (1H, apt t, *J* = 8.6, C*H*NO_2) 6.13 (1H, d, *J* = 7.3) 6.38 (1H, d, *J* = 6.2, PMP-*H*) 6.67 (1H, dd, *J* = 8.9, 2.7, PMP-*H*) 6.89 (1H, dd, *J* = 8.7, 2.8, PMP-*H*) 7.10 (2H, d, *J* = 7.5, Ar*H*) 7.13 (1H, d, *J* = 8.6, Ar*H*) 7.23 (2H, apt d, *J* = 7.8, Ar*H*) 7.26 (2H, apt d, *J* = 8.8, Ar*H*) 7.29 – 7.33 (2H, m, Ar*H*) 7.54 (1H, d, *J* = 7.7, Ar*H*); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 0.05 (Si(*C*H_3)$_3$) 36.5 (*C*H_2Ar) 55.6 (ArCO*C*H_3) 65.8 (*C*HN) 88.0 (*C*NO_2) 100.1 (q, *C*Si(CH$_3$)$_3$) 102.9 (*CC*Si) 114.1 (PMP-*C*) 114.3 (PMP-*C*) 116.3 (q, *J* = 288.3, *C*F_3) 123.3 (q) 127.8 (Ar*C*) 128.3 (q, PMP-*C*N) 128.8 (Ar*C*) 128.9 (Ar*C*) 129.3 (Ar*C*) 129.5 (Ar*C*) 129.7 (Ar*C*) 130.6 (Ar*C*) 132.1 (PMP-*C*) 133.3 (q) 133.8 (Ar*C*) 136.3 (q) 158.1 (q, *J* = 36.0, CF_3*C*O) 160.4 (Ar*C*OCH_3); ^{19}F NMR ($CDCl_3$, 282 MHz) δ - 67.1 ppm (3F, s, CF_3); m/z (EI) 554 (10 %, M^+) 508 (7 %, $C_{29}H_{29}F_3NO_2Si$) 217 (10 %, $C_9H_7F_3NO_2$); HRMS ($C_{29}H_{29}F_3N_2O_4Si$) calcd. 554.1849, found 554.1827.

2,2,2-trifluoro-N-(4-methoxyphenyl)-N-((1R,2S*)-2-nitro-1-phenyl-3-(2-(phenylethynyl)phenyl)propyl)acetamide (**12b**)*

By an identical procedure to the preparation of **5** using nitroalkene **14b**[24] (4.23 g, 17.0 mmol) and (*E*)-*N*-(4-methoxyphenyl)-1-phenylmethanimine (4.06 g, 19.2 mmol). Purification by trituration in MeOH afforded **102wa** as a mixture of isomers (90:10 *anti:syn*, 6.17 g, 11.1 mmol, 65 %). Further recrystallisation (Et_2O/Hexanes followed CH_2Cl_2/Hexanes x 2) afforded *anti*-**12b** as a white solid (3.60 g, 6.44 mmol, 38 %); mp 160 – 162 °C; IR ν_{max} (thin film) 1696 (C=O, amide) 1556 (N-O, asymm) 1509, 1495 (C=C, Ar) 1300 (N-O, symm) 1180, 1153 (C-F, CF_3) cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.62 (3H, s, OCH_3) 3.73 (1H, dd, *J* = 14.1, 11.3, CH_2) 3.91 (1H, dd, *J* = 14.1, 3.8, CH_2) 5.71 (1H, dt, *J* = 11.0, 3.8, C*H*NO_2) 6.07 – 6.17 (2H, m, PMP-*H*) 6.44 (1H, d, *J* = 9.1, C*H*N) 6.49 (1H, dd, *J* = 8.8, 2.8, PMP-*H*) 7.00 (2H, d, *J* = 7.6, Ar*H*) 7.17 – 7.23 (3H, m, Ar*H*) 7.25 – 7.29 (2H, m, PMP-*H* & Ar*H*) 7.30 – 7.33 (2H, m, Ar*H*) 7.40 – 7.44 (Ar*H*) 7.61 – 7.67 (Ar*H*); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 37.0 (*C*H_2) 55.5 (O*C*H_3) 64.4 (*C*HN) 87.7 (q, *CC*) 88.2 (*C*HNO_2) 94.1 (*CC*) 113.2 (PMP-*C*) 114.5 (PMP-*C*) 116.3 (q, *J* = 288.4, *C*F_3) 122.9 (q, Ar*C*CC) 122.9 (Ar*C*CC) 127.3 (q, Ar*C*N) 128.1 (Ar*C*) 128.7 (2C, Ar*C*) 128.8 (2C, Ar*C*) 128.9 (Ar*C*) 129.4 (Ar*C*) 129.5 (2C, Ar*C*) 129.7 (Ar*C*) 129.9 (Ar*C*) 130.6 (Ar*C*) 132.1 (2C, PMP-*C*) 132.4 (Ar*C*) 132.9 (Ar*C*CHN) 133.6 (Ar*C*) 135.8 (q, Ar*C*CH_2) 158.3 (q, *J* = 35.6, *C*OCF_3) 160.2 (q, Ar*C*O); ^{19}F NMR ($CDCl_3$, 282 MHz) δ – 67.0 (3F, s, CF_3); m/z (EI) 558 (100 %, M^+) 190 (84 %, $C_{15}H_{11}$); HRMS ($C_{32}H_{25}F_3N_2O_4$) calcd. 558.1766, found 558.1734.

*(E)-1-nitro-2,2-dimethyl-hexa-1,5-diene (**17**)*

A solution of 2,2-dimethylpent-4-enal (2.00 mL, 14.7 mmol), triethylamine (1.03 mmol, 0.35 equiv.) and nitromethane (4.00

mL, 74.1 mmol, 5.0 equiv.) was stirred overnight under N_2 at rt. The nitromethane and trimethylamine were removed in vacuo; purification by silica plug gave nitroalcohol which was used directly in the next step. To a solution of the purified nitroalcohol (14.7 mmol) in dry DCM (45 mL) under N_2 at -78 °C was added TFAA (17.6 mmol, 1.2 equiv.) dropwise and the reaction stirred for 5 min before the dropwise addition of DIPEA (36.8 mmol, 2.50 equiv.). The reaction was stirred at - 78 °C until complete reaction (tlc) before warming to rt. The reaction was quenched with 2M HCl (50 mL) extracted with CH_2Cl_2 (50 mL x 3), washed with sat. NaCl solution (50 mL), dried ($MgSO_4$) filtered and conc *in vacuo*. Purification by flash column chromatography (2 % EtOAc/Hexanes) afforded **17** as a colourless oil (1.19 g, 7.67 mmol, 52 %); IR ν_{max} (thin film) 2966 (C-H) 1642 (C=C) 1524 (N-O, asymm) 1348 (N-O, symm) cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 1.13 (6H, s, $C(CH_3)_2$) 2.18 (2H, apt dt, *J* = 7.4, 1.0, CCH_2) 5.07 (1H, dm, *J* = 17.0, $CH_2CHCH_{2\text{-trans}}$) 5.12 (1H, dm, *J* = 10.2, $CH_2CHCH_{2\text{-cis}}$) 5.70 (1H, ddt, *J* = 17.0, 10.3, 7.4, CH_2CH) 6.88 (1H, d, *J* = 13.6, $CHCHNO_2$) 7.25 (1H, d, *J* = 13.7, $CHCHNO_2$); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 26.1 (2C, CH_3) 35.9 (q, $C(CH_3)_2$) 46.3 ($C(CH_3)_2CH_2$) 119.0 (CCH_2CHCH_2) 133.1 ($CHCH_2$) 138.0 ($CHNO_2$) 150.9 ($CHCHNO_2$); m/z (ESI+) 194.1 (6 %, M + K^+) 178.1 (72 %, M + Na^+) 156.1 (100 %, M + H^+); HRMS $C_8H_{14}NO_2$ calcd. 156.1024 found 156.1030.

N-((1R*,2S*)-4,4-dimethyl-2-nitro-1-phenylhept-6-en-1-yl)-2,2,2-trifluoro-N-(4-methoxyphenyl)acetamide (**15**)

By an identical procedure to the preparation of **5** using nitroalkene **17** (0.70 g, 4.51 mmol) and (*E*)-*N*-(4-methoxyphenyl)-1-phenylmethanimine (1.08 g, 5.11 mmol). Purification by flash column chromatography (50 % CH_2Cl_2/Hexanes) afforded **15** as a yellow oil (1.41g, 3.04 mmol, 67 %); IR ν_{max} (thin film) 2964 (C-H) 1701 (C=O, amide) 1556 (N-O asymm) 1510 (C=C, Ar) 1350 (N-O, symm) 1181, 1157 (C-F, CF_3) cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 0.95 (3H, s, CH_3) 1.07 (3H, s, CH_3) 2.05 – 2.11 (3H, m, CH_2) 2.33 (1H, dd, *J* = 15.3, 11.2, CH_2CHNO_2) 3.81 (3H, s, OCH_3) 5.11 (1H, dm, *J* = 17.0, $CH_2CHCH_{2\text{-trans}}$) 5.16 (1H, dm, *J* = 10.3, $CH_2CHCH_{2\text{-cis}}$) 5.53 – 5.78 (2H, m, $CHNO_2$ & CHN) 5.84 (1H, ddt, *J* = 17.1, 10.1, 7.4, CH_2CHCH_2) 6.40 (1H, m, PMP-*H*) 6.71 (1H, dd, *J* = 8.8, 2.2, PMP-*H*) 6.86 (1H, dd, *J* = 8.8, 2.9, PMP-*H*) 6.93 (1H, apt d, *J* = 8.1, PMP-*H*) 7.12 (2H, d, *J* = 7.4, Ar*H*) 7.25 (2H, apt t, *J* = 7.7, Ar*H*) 7.32 (1H, tm, *J* = 7.4, Ar*H*); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 25.5 (CH_3) 26.6 (CH_3) 33.4 ($C(CH_3)_2$) 42.1 (CH_2CHNO_2) 47.9 ($CH_2C(CH_3)_2$) 55.6 (OCH_3) 66.8 (CHN) 85.0 ($CHNO_2$) 113.9 (PMP-*C*) 114.5 (PMP-*C*) 116.3 (q, *J* = 289.4, CF_3) 118.8 ($CH_2CHCH_2C(CH_3)_2$) 128.5 (q, Ar*C*N) 128.8 (2C, Ar*C*) 129.7 (2C, Ar*C*) 129.8 (Ar*C*) 130.3 (PMP-*C*) 131.9 (PMP-*C*) 132.9 (q, Ar*C*CHN) 134.2 (CH_2CHCH_2) 157.9 (q, *J* = 34.8, $COCF_3$) 160.4 (q, Ar*C*O); ^{19}F NMR ($CDCl_3$, 282 MHz) δ - 67.4 ppm (3F, s, CF_3); m/z (ESI^+) m/z 503 (21 %, M + K^+) 497 (40 %, M + CH_3OH + H^+) 465 (100 %, M + H^+); HRMS ($C_{24}H_{28}F_3N_2O_4$) calcd. 465.2001, found 465.2018.

2,2,2-trifluoro-N-(4-methoxyphenyl)-N-((1R,3R*)-2-nitro-1,3-diphenylhept-6-en-1-yl)acetamide (**18**)*

A flask charged with Mg (39.2 mg, 1.60 mmol) was flame dried and stirred overnight under N_2 to activate the magnesium. Dry THF (2 mL) and a crystal of I_2 were added and the mixture heated to 70 °C. A portion of 4-bromobutene (0.03 mL, 0.30 mmol) was added to the reaction. After 50 min stirring at reflux, the rest of the bromide (0.12 mL, 1.20 mmol) in THF (1 mL) was added over 1 h at 0 °C, then the reaction was stirred at rt for 90 min to complete the generation of the Grignard reagent. The but-3-enyl magnesium bromide was added to a solution of *trans*-β-nitrostyrene (0.15 g, 1.00 mmol) and CuI (17.7 mg, 0.093 mmol) in DCM (5 mL) under N_2 at – 78 °C over 7 min. The reaction was stirred at – 78 °C for 0.5 h before addition of a solution of (*E*)-*N*-(4-methoxyphenyl)-1-phenylmethanimine (340 mg, 1.60 mmol) in DCM (2.5 mL) to the reaction mixture at – 78 °C. The reaction was stirred for 10 min before the addition of TFA (0.13 mL, 1.80 mmol) the reaction was then stirred for a further 1.5 h at – 78 °C. The reaction was warmed for 5 min before the addition of sat. aq. $NaHCO_3$ solution (15 mL) giving a yellow colour. The product was extracted with Et_2O (20 mL x 2), washed with brine (20 mL), dried ($MgSO_4$) filtered and concentrated *in vacuo.* to give the crude nitroamine. The crude β-nitroamine was redissolved in dry DCM (10 mL) under N_2 and cooled to – 78 °C. To the solution was added DIPEA (0.44 mL, 2.5 mmol) followed quickly by dropwise addition of TFAA (0.35 mL, 2.5 mmol). The reaction mixture was left to stir overnight and warm to rt and quenched on addition of 2M HCl (15 mL). The phases were separated and the aq. layer extracted with DCM (20 mL x 2), dried ($MgSO_4$), filtered and conc *in vacuo*. Purification by flash column chromatography (5 % EtOAc/PE followed by 10 % EtOAc/Petrol) afforded **18** as a mixture of diastereoisomers *anti*:*syn* 75:25 as a yellow oil (0.19 g, 0.37 mmol, 37 %); IR υ_{max} ($CDCl_3$ cast) 2947 (C-H) 1697 (C=O) 1607, 1585 (Ar, C=C) 1552 (N-O) 1510 (Ar, C=C) 1254 (C-O) 1179, 1154 (CF_3, C-F) 1033 (C-N) cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) ^1H NMR major *anti* δ 1.81 – 2.10 (3H, m, CH_2) 2.30 (1H, m, CH_2) 3.49 (1H, dt, *J* = 12.5, 3.4, $PhCHC_4H_7$) 3.78 (3H, s, OCH_3) 4.97 (1H, dd, *J* = 16.9, 1.3, $CH_2CH_2CHCH_{2\text{-trans}}$) 5.04 (1H, dd, *J* = 9.7, 0.7, $CH_2CH_2CHCH_{2\text{-cis}}$) 5.61 (1H, dd, *J* = 10.8, 4.2, $CHNO_2$) 5.80 – 5.82 (1H, m, CH_2CH) 6.20 (1H, apt d, *J* = 8.3, PMP-*H*) 6.35 (1H, d, *J* = 10.8, CHN) 6.60 (1H, dd, *J* = 8.8, 2.9, PMP-*H*) 6.87 (1H, dd, *J* = 8.7, 3.0, PMP-*H*) 7.03 (3H, m, PMP-*H* & Ar*H*) 7.45 – 7.19 (8H, m, Ar*H*); ^1H NMR minor *syn* δ 3.56 (1H, dt, *J* = 11.6, 3.1, $PhCHC_4H_7$) 3.81 (3H, s, OCH_3) 5.09 (1H, dd, *J* = 10.2, 1.2, $CH_2CH_2CHCH_{2\text{-trans}}$) 6.65 (1H, dd, *J* = 8.9, 2.9, PMP-*H*) further signals indistinguishable; ^{13}C NMR ($CDCl_3$, 125 MHz) major *anti* δ 23.9 (CH_2) 28.3 (CH_2) 44.9 (CHC_4H_7) 55.5 (OCH_3) 62.4 (CHN) 91.7 (CNO_2) 113.8 (PMP-*C*) 114.1 (PMP-*C*) 116.5 (CH_2CH) 116.5 (q, CF_3, *J* = 288.7) 127.5 (Ar*C*) 128.1 (Ar*C*) 128.2 (Ar*C*) 128.4 (Ar*C*) 128.7 (Ar*C*) 128.8 (Ar*C*) 128.9 (Ar*C*) 129.3 (Ar*C*) 129.5 (Ar*C*) 130.5 (Ar*C*) 132.4 (Ar*C*) 133.4 (q, Ar*C*) 134.8 (q, Ar*C*) 137.0 (Ar*C*) 137.3 (CH_2CH) 138.8 (q, Ar*C*) 158.5 (q, *J* = 35.5, $COCF_3$) 160.4 (q, Ar*C*O); ^{19}F ($CDCl_3$, 282 MHz) major *anti* δ -67.5 (3F, s, CF_3); m/z (CI^+) 513 (42 %, M + H^+) 466 (100 %, $C_{28}H_{27}F_3NO_2^+$) 308 (52 %, $C_{16}H_{13}F_3NO_2^+$) 294 (22 %, $C_{19}H_{20}NO_2^+$) 220 (32 %, $C_9H_7F_3NO_2^+$) 145 (22 %$C_{11}H_{13}^+$) HRMS $C_{28}H_{28}F_3N_2O_4$ calcd. 513.2001 found 513.2006.

2,2,2-trifluoro-N-(4-methoxyphenyl)-N-((1R,2S*)-2-nitro-3-phenyl-1-(2-vinylphenyl)propyl)acetamide (**19a**)*

By an identical procedure to the preparation of **5** using *trans*-β-nitrostyrene (1.00 g, 6.70 mmol) and imine **20a**[25] (1.80 g, 7.60 mmol). Purification by recrystallisation (MeOH/Hexanes) afforded nitroacetamide **19a** as a white solid (1.08 g, 2.22 mmol, 33 %); mp 128 – 130 °C; IR ν_{max} (thin film) 1697 (C=O, amide) 1556 (N-O, asymm) 1511 (C=C, Ar) 1325 (N-O, symm) 1182 (C-F, CF_3) cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 3.55 (2H, m, CH_2CHNO_2) 3.80 (3H, s, OCH_3) 5.45 (1H, d, *J* = 10.9, $ArCHCH_{2\text{-cis}}$) 5.45 (1H, br s, $CHNO_2$) 5.64 (1H, d, *J* = 17.2, $ArCHCH_{2\text{-trans}}$) 6.07 (1H, br d, *J* = 6.1, PMP-*H*) 6.55 (1H, dd, *J* = 6.3, 2.8, PMP-*H*) 6.71 (2H, m, PMP-*H*, CHN) 6.91 (1H, dd, *J* = 8.7, 3.0, PMP-*H*) 6.96 (1H, t, *J* = 7.6, Ar*H*) 7.03 (1H, dd, *J* = 17.0, 11.0, $ArCHCH_2$) 7.06 (1H, m, Ar*H*) 7.23 – 7.28 (3H, m, Ar*H*) 7.32 (1H, apt t, *J* = 7.2, Ar*H*) 7.37 (2H, apt t, *J* = 7.5, Ar*H*) 7.49 (1H, d, *J* = 7.8, Ar*H*); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 38.4 ($PhCH_2$) 55.6 (OCH_3) 58.5 ($CHNPMP$) 89.4 (CNO_2) 113.9

(PMP-*C*) 114.4 (PMP-*C*) 116.4 (q, *J* = 289.5) 119.2 (Ar*C*HCH$_2$) (*C*HNO$_2$) 101.2 (*C*HO$_2$) 113.6 (PMP-*C*) 114.1 (PMP-*C*) 116.5 126.9 (q, Ar*C*N) 127.4 (Ar*C*) 127.6 (PMP-*C*) 127.8 (Ar*C*) 128.0 (Ar*C*) 128.7 (2C, Ar*C*) 129.3 (2C, Ar*C*) 129.8 (Ar*C*) 129.9 (q, Ar*C*CHN) 130.0 (Ar*C*) 132.6 (PMP-*C*) 133.7 (Ar*C*HCH$_2$) 134.7 (q, Ar*C*CH$_2$) 139.3 (q, Ar*C*CHCH$_2$) 158.0 (q, *J* = 35.6, CF$_3$*C*O) 160.5 (Ar*C*OCH$_3$); ^{19}F NMR (CDCl$_3$, 282 MHz) δ - 67.0 ppm (3F, s, CF$_3$); m/z (ES$^+$) 507 (100%, M + Na$^+$) 485 (80 %, M + H$^+$) 438 (75 %, $C_{26}H_{23}F_3NO_2$); HRMS ($C_{26}H_{24}F_3N_2O_4$) calcd. 485.1668, found 485.1688; Anal. Calcd. For $C_{26}H_{23}F_3N_2O_4$: C, 64.46; H, 4.79; N, 5.78; found: C, 64.46; H, 4.80; N, 5.76%.

2,2,2-trifluoro-N-(4-methoxyphenyl)-N-((1R,2S*)-2-nitro-3-phenyl-1-(2-((E)-styryl)phenyl)propyl)acetamide (**19b**)*

A solution of Al_2O_3 (1 g per mmol) and *p*-anisidine (6.22 mmol) in dry DCM (30 mL) was stirred at rt under N_2 for 5 min before the addition of (*E*)-2-styrylbenzaldehyde[38] (6.22 mmol) and the reaction was stirred until complete (tlc). The reaction mixture was filtered through celite and concentrated *in vacuo* to give the crude imine **20b** as an oil which was used directly without further purification (97 % conversion).

By an identical procedure to the preparation of **5** using *trans*-β-nitrostyrene (0.83 g, 5.55 mmol) and imine **20b** (1.95 g, 6.22 mmol). Purification by flash column chromatography (40 % CH_2Cl_2/Hexanes) afforded **19b** as a mixture of diastereomers (95:5) as a white solid (1.11 mg, 2.00 mmol, 36 %); mp 65 - 67 ^{o}C; IR ν_{max} (thin film) 1695 (C=O, amide) 1556 (N-O, asymm) 1510 (C=C, Ar) 1301 (N-O, symm) 1181 (C-F, CF$_3$) cm^{-1}; ^{1}H NMR (CDCl$_3$, 600 MHz) δ 3.58 (1H, dd, *J* = 14.6, 10.6, C*H*$_2$) 3.61 (1H, dd, 14.6, 4.0, C*H*$_2$) 3.77 (3H, s, OC*H*$_3$) 5.53 (1H, br s, C*H*NO$_2$) 6.18 (1H, br s, PMP-*H*) 6.58 (1H, dd, *J* = 8.8, 2.6, PMP-*H*) 6.81 (2H, br s, C*H*) 6.92 (1H, dd, *J* = 8.7, 2.8, PMP-*H*) 6.95 – 7.02 (2H, m, C*H*) 7.09 (1H, br d, *J* = 8.0, C*H*) 7.27 (2H, d, *J* = 7.2, C*H*) 7.30 – 7.35 (3H, m, C*H*) 7.36 – 7.44 (5H, m, C*H*) 7.57 (2H, d, *J* = 7.2, Ar*H*) 7.65 (1H, d, *J* = 7.6, Ar*H*); ^{13}C NMR (CDCl$_3$, 150 MHz) δ 38.4 (*C*H$_2$) 55.5 (OCH$_3$) 58.9 (*C*HN) 89.3 (*C*HNO$_2$) 113.9 (PMP-*C*) 114.4 (PMP-*C*) 116.3 (q, *J* = 288.1, *C*F$_3$) 124.4 (*C*H) 127.0 (*C*H) 127.0 (*C*H) 127.4 (*C*H) 128.0 (*C*H) 128.1 (*C*H) 128.3 (*C*H) 128.7 (4C, *C*H) 128.7 (*C*H) 128.9 (*C*H) 129.0 (*C*H) 129.3 (*C*H) 129.8 (*C*H) 130.0 (*C*H) 130.1 (q, *C*) 132.4 (q, *C*) 133.5 (*C*H) 134.7 (q, *C*) 136.9 (q, *C*) 138.6 (q, *C*) 158.0 (q, *J* = 35.9, *C*OCF$_3$) 160.5 (q, Ar*C*O); ^{19}F NMR (CDCl$_3$, 282 MHz) δ – 67.1 ppm (3F, s, CF$_3$); m/z (ESI$^+$) 583 (100 %, M + Na$^+$); HRMS ($C_{32}H_{27}F_3N_2O_4Na$) calcd. 583.1821, found 583.1823.

N-((1R,2S*)-1-(2-(1,3-dioxolan-2-yl)phenyl)-2-nitro-3-phenylpropyl)-2,2,2-trifluoro-N-(4-methoxyphenyl)acetamide (**23**)*

Imine **22** was formed in an identical method to **20b** above using 2-(1,3-dioxolan-2-yl)benzaldehyde.[26]

By an identical procedure to the preparation of **5** using *trans*-β-nitrostyrene (0.30 g, 2.00 mmol) and imine **22** (2.26 mmol). Purification by flash column chromatography (40 - 60 % CH_2Cl_2/Hexanes) afforded **23** as a white solid (0.51 g, 0.96 mmol, 48 %); mp 109 - 110 ^{o}C; IR ν_{max} (thin film) 2890 (C-H) 1696 (C=O, amide) 1554 (N-O asymm) 1509 (C=C, Ar) 1299 (N-O, symm) 1180 (C-F, CF$_3$) cm^{-1}; ^{1}H NMR (CDCl$_3$, 600 MHz) δ 3.55 – 3.60 (2H, m, C*H*$_2$) 3.78 (3H, s, OC*H*$_3$) 4.01 – 4.23 (4H, m, OC*H*$_2$C*H*$_2$O) 5.37 (1H, ddd, *J* = 10.9, 9.5, 5.0, C*H*NO$_2$) 5.99 (1H, s, C*H*O$_2$) 6.16 (1H, dd, *J* = 8.8, 2.1, PMP-*H*) 6.47 (1H, dd, *J* = 8.8, 2.9, PMP-*H*) 6.61 (1H, d, *J* = 7.9, Ar*H*) 6.93 (1H, dd, *J* = 8.7, 3.0, PMP-*H*) 6.99 – 7.03 (2H, m, C*H*N & Ar*H*) 7.14 (1H, dd, *J* = 8.7, 2.6, PMP-*H*) 7.23 – 7.40 (6H, m, Ar*H*) 7.69 (1H, dd, *J* = 7.8, 1.2, Ar*H*); ^{13}C NMR (CDCl$_3$, 150 MHz) δ 38.4 (Ar*C*H$_2$) 55.5 (OCH$_3$) 56.7 (*C*HN) 65.3 (OCH$_2$*C*H$_2$O) 65.4 (OCH$_2$*C*H$_2$O) 89.5 (*C*HNO$_2$) 101.2 (*C*HO$_2$) 113.6 (PMP-*C*) 114.1 (PMP-*C*) 116.5 (q, *J* = 288.5, *C*F$_3$) 126.8 (q, Ar*C*N) 127.6 (Ar*C*) 128.0 (Ar*C*) 128.4 (Ar*C*) 128.7 (2C, Ar*C*) 128.8 (Ar*C*) 129.2 (2C, Ar*C*) 129.6 (Ar*C*) 130.0 (PMP-*C*) 131.1 (q, Ar*C*CHN) 133.2 (PMP-*C*) 135.0 (q, Ar*C*CH$_2$) 136.7 (q, Ar*C*CHO$_2$) 158.1 (q, *J* = 35.5, *C*OCF$_3$) 160.3 (Ar*C*OCH$_3$); ^{19}F NMR (CDCl$_3$, 282 MHz) δ – 67.4 ppm (3F, s, CF$_3$); m/z (CI$^+$) 531 (100 %, M + H$^+$) 484 (43 %, $C_{27}H_{25}F_3NO_4$) 440 (6 %, $C_{20}H_{19}F_3N_2O_6$); HRMS ($C_{27}H_{26}F_3N_2O_6$) calcd. 531.1738, found 531.1737.

2,2,2-trifluoro-N-((1R,2S*)-1-(2-formylphenyl)-2-nitro-3-phenylpropyl)-N-(4-methoxyphenyl)acetamide (**21**)*

A solution of nitroacetamide **23** (1.42 g, 2.69 mmol) and $FeCl_3/SiO_2$ (0.29 g, 5 % by weight) in acetone (64 mL) and the reaction was stirred for 30 h. Additional portions of $FeCl_3/SiO_2$ (2 x 0.14 g) were added after 6 h and 24 h until there was no further conversion. The reaction mixture was filtered through celite and concentrated in *vacuo*. Purification by flash column chromatography (15 – 25 % EtOAc/Hexanes) followed by recrystallisation ($CHCl_3$/Hexanes) afforded **21** as a white solid (1.08 g, 2.22 g, 82 %); mp 90 - 92 ^{o}C; IR ν_{max} (thin film) 2836 (C-H) 1692 (C=O, amide, aldehyde overlapped) 1604, 1508, 1454 (C=C, Ar) 1553 (N-O, asymm) 1300 (N-O, symm) 1150 (C-F, CF$_3$) cm^{-1}; ^{1}H NMR (CDCl$_3$, 600 MHz) δ 3.55 (1H, dd, *J* = 14.6, 10.4, C*H*$_2$) 3.59 (1H, dd, *J* = 14.5, 4.0, C*H*$_2$) 3.81 (3H, s, OC*H*$_3$) 5.81 (1H, td, *J* = 10.4, 3.5, C*H*NO$_2$) 6.48 (1H, br d, *J* = 7.8, PMP-*H*) 6.71 (1H, dd, *J* = 8.9, 2.8, PMP-*H*) 6.86 (1H, dd, *J* = 8.7, 2.8, PMP-*H*) 6.90 (1H, apt d, *J* = 8.5, PMP-*H*) 7.17 (1H, d, *J* = 10.8, C*H*N) 7.26 (2H, d, *J* = 7.5, Ar*H*) 7.29 – 7.39 (4H, m, Ar*H*) 7.42 (1H, td, *J* = 7.7, 1.2, Ar*H*) 7.52 (1H, td, *J* = 7.5, 1.0, Ar*H*) 7.84 (1H, dd, *J* = 7.7, 1.3, Ar*H*) 10.12 (1H, s, C*H*O); ^{13}C NMR (CDCl$_3$, 150 MHz) δ 38.5 (*C*H$_2$) 55.6 (OCH$_3$) 58.7 (*C*HN) 90.2 (*C*HNO$_2$) 114.0 (PMP-*C*) 114.9 (PMP-*C*) 116.2 (q, *J* = 289.0, *C*F$_3$) 128.1 (2C, Ar*C*) 128.1 (q, Ar*C*N) 128.8 (2C, Ar*C*) 129.2 (Ar*C*) 129.7 (Ar*C*) 130.1 (PMP-*C*) 130.2 (Ar*C*) 131.8 (PMP-*C*) 133.1 (Ar*C*) 133.9 (Ar*C*) 134.1 (q, Ar*C*) 134.6 (q, Ar*C*) 134.7 (q, Ar*C*) 158.1 (q, *J* = 36.0, *C*OCF$_3$) 160.6 (Ar*C*OCH$_3$) 191.3 (*C*HO); ^{19}F NMR (CDCl$_3$, 282 MHz) δ – 67.2 ppm (3F, s, CF$_3$); m/z (ESI$^+$) 504.2 (15 %, M + NH$_4^+$) 487.2 (100 %, M + H$^+$) 440.2 (7 %, $C_{25}H_{21}F_3NO_3$); HRMS ($C_{25}H_{22}F_3N_2O_5$) calcd. 487.1481, found 487.1472.

2,2,2-trifluoro-N-(4-methoxyphenyl)-N-((1R,2S*)-2-nitro-3-phenyl-1-(2-((E)-prop-1-en-1-yl)phenyl)propyl)acetamide (**19d**)*

To a solution of aldehyde **21** (111 mg, 0.23 mmol) and 3-pentanone (22 μL, 0.21 mmol) in hexane (1 mL) was added $BF_3.OEt_2$ (0.015 mL, 0.15 mmol) and the solution was refluxed for 90 mins and quenched with water (2 mL), extracted with Et_2O (5 mL x 3), dried and concentrated *in vacuo*. Purification by flash column chromatography (15 % EtOAc/hexanes) afforded **19d** as a colourless yellow oil (63.5 mg, 0.13 mmol, 61 % yield); IR ν_{max} (thin film) 2914, 2847 (C-H) 1694 (C=O, amide) 1554 (N-O, asymm) 1509 (C=C, Ar) 1298 (N-O, symm) 1178 (C-F, CF$_3$) cm^{-1}; ^{1}H NMR (CDCl$_3$, 600 MHz) δ 1.92 (3H, dd, *J* = 6.6, 1.5, CHCHC*H*$_3$) 3.54 – 3.58 (2H, m, C*H*$_2$) 3.79 (3H, s, OC*H*$_3$) 5.45 (1H, m, C*H*NO$_2$) 6.07 (2H, m, CHC*H*CH$_3$ & PMP-*H*) 6.55 (1H, dd, *J* = 8.9, 2.8, PMP-*H*) 6.67 – 6.77 (3H, m, C*H*N, C*H*CHCH$_3$ & Ar*H*) 6.91 (1H, dd, *J* = 8.7, 2.6, PMP-*H*) 6.92 (1H, m, Ar*H*) 7.06 (1H, apt d, *J* = 8.4, PMP-*H*) 7.23 (1H, td, *J* = 7.6, 0.5, Ar*H*) 7.25 – 7.27 (2H, m, Ar*H*) 7.30 – 7.39 (3H, m, Ar*H*) 7.40 (1H, d, *J* = 7.5, Ar*H*); ^{13}C NMR (CDCl$_3$, 150 MHz) δ 18.8 (CH*C*H$_3$) 38.4 (*C*H$_2$) 55.6 (OCH$_3$) 58.8 (*C*HN) 89.4 (*C*HNO$_2$) 113.8 (PMP-*C*) 114.3 (PMP-*C*) 116.4 (q, *J* = 287.9, *C*F$_3$) 126.7 (Ar*C*) 127.0 (q, Ar*C*N) 127.5 (Ar*C*) 127.6 (*C*H) 127.8 (Ar*C*) 128.0 (Ar*C*) 128.7 (2C, Ar*C*) 129.2 (2C, Ar*C*) 129.6 (q, Ar*C*CHN) 129.6 (*C*H) 130.0 (PMP-*C*) 131.1 (CH*C*HCH$_3$) 132.4 (PMP-*C*) 134.8 (q,

Ar*C*CH_2) 139.6 (q, Ar*C*CHCHCH$_3$) 157.9 (q, *J* = 35.6, *C*OCF$_3$) 160.4 (q, Ar*C*O); ^{19}F NMR ($CDCl_3$, 282 MHz) δ - 67.2 ppm (3F, s, CF_3); m/z (CI^+) 516 (76 %, M + NH_4^+) 499 (100 %, M + H^+) 452 (100 %, $C_{27}H_{25}F_3NO_2^+$) 348 (20 %, $C_{19}H_{17}F_3NO_2^+$) 280 (18 %, $C_{18}H_{18}NO_2^+$); HRMS ($C_{27}H_{26}F_3N_2O_4$) calcd. 499.1839, found 499.1839.

2,2,2-trifluoro-N-(4-methoxyphenyl)-N-((2S,3R*)-2-nitro-1-phenylhept-6-en-3-yl)acetamide (**25**)*

Imine **24** was formed in an identical method to **20b** (in preparation of **19b**) using pent-4-enal.

By an identical procedure to the preparation of **5** using trans-β-nitrostyrene (0.53 g, 3.60 mmol) and imine **24** (0.77 g, 4.07 mmol). Purification by flash column chromatography (40 % CH_2Cl_2/Hexanes) and recrystallisation (Et_2O/Hexanes) afforded **102ac** as colourless crystals (0.72 g, 1.65 mmol, 46 %); mp 86 - 88 °C; IR ν_{max} (thin film) 2935 (C-H) 1697 (C=O, amide) 1554 (N-O asymm) 1509 (C=C, Ar) 1298 (N-O symm) 1151 (C-F, CF_3) cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 1.56 (1H, m, CHNC*H*$_2$) 1.80 (1H, apt br d, *J* = 8.3, CHNC*H*$_2$) 2.16 (1H, m, CH_2C*H*$_2$CH) 2.26 (1H, m, CH_2C*H*$_2$CH) 3.34 (1H, dd, *J* = 14.8, 3.8, PhC*H*$_2$) 3.38 (1H, dd, *J* = 14.8, 10.6, PhC*H*$_2$) 3.88 (3H,s, OC*H*$_3$) 4.91 (1H, m, C*H*NO$_2$) 5.00 (1H, m, C*H*N) 5.03 – 5.06 (2H, m, $CH_2CH_2CHCH_2$) 5.74 (1H, ddt, *J* = 16.0, 11.4, 6.3, CH_2CHCH_2) 7.00 (2H, m, PMP-*H*) 7.15 (2H, m, Ar*H*) 7.20 (2H, d, *J* = 8.5, PMP-*H*) 7.27 – 7.30 (1H, m, Ar*H*) 7.30 – 7.34 (2H, m, Ar*H*); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 27.5 (CHN*C*H$_2$) 30.3 ($CH_2CH_2CHCH_2$) 37.8 (Ph*C*H$_2$) 55.7 (O*C*H$_3$) 60.3 (*C*HN) 91.4 (*C*NO$_2$) 114.7 (PMP-*C*) 114.9 (PMP-*C*) 116.3 (q, *J* = 288.6, *C*F$_3$) 116.7 ($CH_2CH_2CHCH_2$) 127.4 (q, Ar*C*N) 127.9 (Ar*C*) 128.6 (2C, Ar*C*) 129.2 (2C, Ar*C*) 130.4 (PMP-*C*) 131.0 (PMP-*C*) 134.6 (q, Ar*C*CH$_2$) 135.9 (*C*HCH$_2$) 158.8 (q, *J* = 35.7, *C*OCF$_3$) 160.7 (q, Ar*C*O); ^{19}F NMR ($CDCl_3$, 282 MHz) δ – 67.0 ppm (3F, s, CF_3); m/z (ESI^+) 453 (96 %, M + NH_4^+) 437 (100 %, M + H^+); HRMS ($C_{22}H_{24}F_3N_2O_4$) calcd. 437.1688, found 437.1678.

N-allyl-2,2,2-trifluoro-N-((1R,2S*)-2-nitro-1,3-diphenylpropyl)acetamide (**27**)*

By an identical procedure to the preparation of **5** using trans-β-nitrostyrene (1.50 g, 10.0 mmol) and imine **26**[30] (2.91 g, 20.0 mmol). Purification via flash column chromatography (40 % CH_2Cl_2/Hexanes followed by 20 % Et_2O/Hexanes) afforded **27** as a mixture of diastereomers (75:25) as a yellow oil (1.53 g, 3.90 mmol, 39 %); mp$_{anti}$ 90 - 91 °C; IR major *anti* ν_{max} (thin film) 3029 (C-H) 1691 (C=O, amide) 1555 (N-O, asymm) 1454 (C=C, Ar) 1146 (C-F, CF_3) cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) major *anti* δ 3.16 (2H, m, C*H*$_2$Ph) 3.86 (1H, dd, *J* = 16.3, 7.2, C*H*$_2$N) 4.14 (1H, dd, *J* = 16.3, 5.8, C*H*$_2$N) 5.22 (1H, d, *J* = 10.6, C*H*N) 5.51 (2H, m, C*H*$_2$CHCH$_2$N) 5.88 (1H, ddt, *J* = 17.0, 10.2, 6.7, C*H*CH$_2$N) 6.07 (1H, ddd, *J* = 10.7, 9.6, 5.0, C*H*NO$_2$) 7.17 (2H, m, Ar*H*) 7.26 – 7.38 (6H, m, Ar*H*) 7.46 (2H, m, Ar*H*); ^{1}H NMR ($CDCl_3$, 600 MHz) minor *syn* δ 2.85 (1H, dd, *J* = 14.7, 3.0, C*H*$_2$Ph) 3.01 (1H, dd, *J* = 14.8, 11.1, C*H*$_2$Ph) 3.93 – 4.04 (2H, m, C*H*$_2$N) 4.96 (1H, d, *J* = 11.0, C*H*N) 5.33 (2H, m, C*H*$_2$CHCH$_2$N) 5.65 (1H, ddt, *J* = 17.0, 10.0, 6.4, C*H*CH$_2$N) 6.26 (1H, td, *J* = 11.0, 3.0, C*H*NO$_2$) 7.03 (2H, m, Ar*H*) further signals indistinguishable;^{13}C NMR ($CDCl_3$, 150 MHz) major *anti* δ 38.0 (Ar*C*H$_2$) 50.9 (*C*H$_2$N) 64.8 (*C*HN) 91.0 (*C*HNO$_2$) 116.4 (q, *J* = 288.1, *C*F$_3$) 122.2 (*C*H$_2$CHCH$_2$N) 127.9 (Ar*C*) 128.8 (2C, Ar*C*) 129.1 (2C, Ar*C*) 129.1 (2C, Ar*C*) 129.4 (Ar*C*) 129.9 (Ar*C*) 132.0 (Ar*C*) 134.0 (q, Ar*C*) 134.6 (q, Ar*C*) 157.8 (q, *J* = 36.4, *C*OCF$_3$); ^{19}F NMR ($CDCl_3$, 282 MHz) major *anti* δ - 68.9 ppm (3F, s, CF_3); m/z (CI^+) 410 (100 %, M + NH_4^+); HRMS ($C_{20}H_{19}F_3O_3N_2$ + NH_4^+) calcd. 410.1686, found 410.1685.

2,2,2-trifluoro-N-(4-methoxyphenyl)-N-((1R,2R*)-2-nitro-2-phenyl-1-(2-((E)-styryl)phenyl)ethyl)acetamide (**28**)*

To a solution of α-nitrotoluene (0.54 mL g, 4.50 mmol) in THF (20 mL) at – 78 °C under N_2 was added dropwise ^{n}BuLi (4.95 mL of a 1.0 M solution in hexanes, 4.95 mmol, 1.10 eq,). The reaction mixture was stirred for 15 min before addition of a solution of imine **20b** (1.60 g, 5.10 mmol) in THF (12 mL). The reaction was stirred for 10 min before dropwise addition of trifluoroacetic acid (5.13 mmol, 1.14 equiv) and the reaction was stirred at – 78 °C for 1.5 h or until complete by TLC. The reaction was warmed for 5 min then quenched with sat. aq. $NaHCO_3$ solution (50 mL), extracted with Et_2O (50 mL x 3) washed with brine (50 mL), dried ($MgSO_4$) filtered and concentrated *in vacuo*. Crude β-nitroamine was re-dissolved in CH_2Cl_2 (50 ml) and cooled to – 78°C under N_2. To this solution was added dropwise DIPEA (11.3 mmol, 2.5 equiv.) followed by dropwise addition of trifluoroacetic anhydride (11.3 mmol, 2.5 equiv.) and the reaction stirred for 18 h to rt. The reaction was quenched with 2 M HCl (80 mL), extracted with CH_2Cl_2 (50 mL x 3), dried ($MgSO_4$), filtered and concentrated *in vacuo*. to give the crude β-nitroacetamide. Purification by flash column chromatography (40 % CH_2Cl_2/Hexanes followed by 10 – 20 % Et_2O/Hexanes) gave **28** as white crystals (276 mg, 0.51 mmol, 11 %); mp 153 - 155 °C; IR ν_{max} (thin film) 1698 (C=O, amide) 1558 (N-O, asymm) 1511 (C=C, Ar) 1357 (N-O, symm) 1181 (C-F, CF_3) cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz) δ 3.80 (3H, s, OC*H*$_3$) 6.44 (2H, br s, C*H*NO$_2$ & PMP-*H*) 6.59 (1H, br s, C*H*) 6.68 (1H, dd, *J* = 8.8, 2.8, PMP-*H*) 6.79 (1H, d, *J* = 15.3, ArC*H*CH) 6.89 (1H, apt t, *J* = 6.4, C*H*) 6.95 (1H, dd, *J* = 8.8, 2.7, PMP-*H*) 7.15 – 7.24 (5H, m, C*H*) 7.28 – 7.34 (2H, m, C*H*) 7.37 (2H, d, *J* = 7.3, C*H*) 7.42 (2H, t, *J* = 7.7, C*H*) 7.47 – 7.58 (4H, m, C*H*); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 55.6 (O*C*H$_3$) 59.5 (*C*HN) 91.3 (*C*HNO$_2$) 113.9 (PMP-*C*) 114.4 (PMP-*C*) 116.2 (q, *J* = 288.3, *C*F$_3$) 124.9 (*C*H) 126.9 (2C, *C*H) 127.1 (2C, PMP-*C*) 128.3 (2C, *C*H) 128.8 (2C, *C*H) 128.9 (2C, *C*H) 129.0 (*C*H) 129.3 (*C*H) 129.7 (*C*H) 130.1 (q, *C*H) 130.3 (*C*H) 131.1 (q, *C*H) 131.3 (*C*H) 132.7 (q, *C*H) 133.6 (*C*H) 136.9 (q, *C*H) 138.6 (q, *C*H) 157.6 (q, *J* = 35.6, *C*OCF$_3$) 160.5 (q, Ar*C*O) ; ^{19}F NMR ($CDCl_3$, 282 MHz) δ - 67.2 ppm (3F, s, CF_3); m/z (ESI^+) 579 (22 %, M + CH_3OH + H^+) 569 (21 %, M + Na^+) 564 (100 %, M + NH_4^+) 547 (38 %, M + H^+); HRMS ($C_{31}H_{26}F_3N_2O_4$) calcd. 547.1845, found 547.1870.

2,2,2-trifluoro-N-(4-methoxyphenyl)-N-((1S,2R*)-1-nitro-1-phenylhex-5-en-2-yl)acetamide (**29**)*

By an identical procedure to the preparation of **28** using α-nitrotoluene (0.92 g, 6.73 mmol) and imine **24** (1.44 g, 7.62 mmol). Purification by flash column chromatography (40 % CH_2Cl_2/Hexanes) and recrystallisation from Et_2O/Hexanes afforded **29** as white crystals (1.56 g, 3.69 mmol, 55 %); mp 93 - 94 °C; IR ν_{max} (thin film) 2936, 2838 (C-H) 1693 (C=O, amide) 1606, 1508, 1456 (C=C, Ar) 1552 (N-O, asymm) 1357 (N-O, symm) 1150 (C-F, CF_3) cm^{-1}; ^{1}H NMR ($CDCl_3$, 600 MHz, 60 °C) δ 1.70 – 1.80 (1H, m, CHNC*H*$_2$) 2.09 – 2.40 (3H, m, CHNC*H*$_2$ & CHNCH$_2$C*H*$_2$) 3.79 (3H, s, OC*H*$_3$) 5.08 (1H, dm, *J* = 10.2, CHC*H*$_{2\text{-cis}}$) 5.11 (1H, dm, *J* = 17.2, CHC*H*$_{2\text{-trans}}$) 5.31 (1H, br s, C*H*N) 5.72 (1H, br s, C*H*NO$_2$) 5.84 (1H, ddt, *J* = 17.0, 10.3, 6.4, CH_2CHCH_2) 6.36 (1H, br s, PMP-*H*) 6.61 (1H, br s, PMP-*H*) 6.75 (2H, br m, PMP-*H*) 7.39 – 7.55 (5H, m, Ar*H*); ^{13}C NMR ($CDCl_3$, 150 MHz, 60 °C) δ 28.8 (CHN*C*H$_2$) 30.3 (CHNCH$_2$*C*H$_2$) 55.4 (O*C*H$_3$) 92.5 (*C*HNO$_2$) 114.2 (2C, PMP-*C*) 115.7 (q, *J* = 288.5, *C*F$_3$) 116.2 ($CH_2CH_2CHCH_2$) 128.7 (2C, Ar*C*) 129.1 (2C, Ar*C*) 130.1 (q, Ar*C*) 130.7 (Ar*C*) 131.8 (q, Ar*C*) 136.0 (CH_2CHCH_2) 158.1 (q, *J* = 36.2, *C*OCF$_3$) 160.3 (Ar*C*O) further signals indistinguishable; ^{19}F NMR ($CDCl_3$, 282 MHz) δ - 67.4 ppm (3F, s, CF_3); m/z (ESI^+) 867 (6 %, 2M + Na^+) 445 (23 %, M

+ Na^+) 423 (M + H^+) 376 (100 %, $C_{21}H_{21}F_3NO_2$); HRMS ($C_{21}H_{22}F_3N_2O_4$) calcd. 423.1532, found 423.1522.

4.4 Radical denitration cyclisation.

General procedure.

To a solution of β-nitroacetamide (1 mmol) in benzene (48 mL) under N_2 at rt were added AIBN (0.3 mmol) and Bu_3SnH (10 mmol) and the reaction mixture was degassed. The reaction mixture was heated to reflux for 6 hours or until no change was observed by TLC. The reaction mixture was cooled to rt, concentrated *in vacuo* and taken up in MeCN/Hexane (50:50, 20 mL). The layers were seperated, the Hexane layer extracted with MeCN (10 mL x 2). The combined MeCN extracts were washed with Hexane (20 mL x 3) and the MeCN layer was concentrated *in vacuo*. The crude product was purified by flash column chromatography (0 – 10 % Et_2O). In some cases recrystallization afforded single separation of diastereoisomers.

*2,2,2-trifluoro-N-(4-methoxyphenyl)-N-((1-methyl-2,3-dihydro-1H-inden-2-yl)(phenyl)methyl)acetamide (**30a**) and N-(((1R*,2R*)-1-benzyl-2,3-dihydro-1H-inden-2-yl)methyl)-2,2,2-trifluoro-N-(4-methoxyphenyl)acetamide (**31**).*

Prepared by the g*eneral procedure* using β-nitroacetamide **8a** (51.5 mg, 0.11 mmol). Purification using flash column chromatography (0 – 10 % Et_2O/Hexanes) gave **30a** as a mixture of diastereoisomers (40:40:20) as a colourless oil (16.7 mg, 0.038 mmol, 38 %) and **31** as a colourless oil (8.6 mg, 0.020 mmol, 20 %); Data for **30a** IR ν_{max} (thin film) 3019, 2931, 2836 (C-H) 1685 (C=O, amide) 1604, 1582, 1509 (C=C, Ar) 1180, 1146 (C-F, CF_3) cm^{-1}; ^1H and ^{13}C NMR data display a complex mixture; m/z (ESI^+) 462 (100 %, M + H^+); HRMS ($C_{26}H_{24}F_3NO_2Na$) calcd. 462.1639, found 462.1657. Data for **31** IR ν_{max} (thin film) 2923 (C-H) 1694 (C=O, amide) 1511 (C=C, Ar) 1152 (C-F, CF_3) cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 2.62 (1H, dd, *J* = 13.3, 10.3, CH_2Ph) 2.72 (1H, m, C*H*CH$_2$N) 2.90 (1H, dd, 13.4, 6.0, CH_2Ph) 2.93 (2H, d, *J* = 8.1, CH_2CHCH$_2$N) 3.36 (1H, dt, *J* = 10.2, 6.5, C*H*CHCH$_2$N) 3.74 (1H, dd, *J* = 13.3, 5.3, CH_2N) 3.84 (3H, s, OCH_3) 4.31 (1H, dd, *J* = 13.3, 9.8, CH_2N) 6.42 (1H, d, *J* = 7.5, Ar*H*) 6.87 – 6.92 (2H, m, PMP-*H*) 6.94 (1H, td, *J* = 7.5, 1.0, Ar*H*) 6.96 – 7.00 (2H, m, Ar*H*) 7.13 (1H, td, *J* = 7.5, 0.9, Ar*H*) 7.14 – 7.25 (6H, m PMP-*H* & Ar*H*); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 35.2 (*C*H$_2$CHCH$_2$N) 35.4 (*C*H$_2$Ph) 41.5 (*C*HCH$_2$N) 48.0 (*C*HCH$_2$Ph) 52.0 (*C*H$_2$N) 55.6 (OCH$_3$) 115.0 (2C, br, PMP-*C*) 116.6 (q, *J* = 284.9, *C*F$_3$) 124.7 (Ar*C*) 125.0 (Ar*C*) 125.8 (Ar*C*) 126.2 (Ar*C*) 126.9 (Ar*C*) 128.3 (2C, Ar*C*) 129.4 (2C, Ar*C*) 130.0 (2C, br, PMP-*C*) 131.2 (q, Ar*C*N) 139.8 (q, Ar*C*CH$_2$) 141.8 (q, Ar*C*CH$_2$) 145.6 (q, Ar*C*CHCH$_2$Ph) 157.5 (q, *J* = 34.9, *C*OCF$_3$) 159.9 (q, Ar*C*O); ^{19}F NMR ($CDCl_3$, 282 MHz) δ – 66.9 ppm (3F, s, CF_3); m/z (ESI^+) 440 (100 %, M + H^+); HRMS ($C_{26}H_{25}F_3NO_2$) calcd. 440.1837, found 440.1821. See supplementary information for details of structural elucidation and data correlation table.

*ethyl 2-(1-methyl-2,3-dihydro-1H-inden-2-yl)-2-(2,2,2-trifluoro-N-(4-methoxyphenyl)acetamido)acetate (**30b**)*

Prepared by the g*eneral procedure* using β-nitroacetamide **8b** (0.30 g, 0.63 mmol). Purification via flash column chromatography (0 – 10 % Et_2O/Hexanes) afforded **30b** as a mixture of diastereoisomers (60:20:20) as a colourless oil (66.9 mg, 0.15 mmol, 24 %); IR ν_{max} (thin film) 2957, 2933, 2839 (C-H) 1739 (C=O, ester) 1694 (C=O, amide) 1509 (C=C, Ar) 1149 (C-F, CF_3) cm^{-1}; ^1H and ^{13}C NMR data display a complex mixture; m/z (CI^+) 453 (100 %, M + NH_4^+) 436 (6 %, M + H^+); HRMS ($C_{23}H_{25}F_3NO_4$) calcd. 436.1730, found 436.17298.

methyl 2-((1R,2R*)-2-((R*)-phenyl(2,2,2-trifluoro-N-(4-methoxyphenyl)acetamido)methyl)-2,3-dihydro-1H-inden-1-yl)acetate (**32a**) and methyl 2-((1R*,2R*)-2-((S*)-phenyl(2,2,2-trifluoro-N-(4-methoxyphenyl)acetamido)methyl)-2,3-dihydro-1H-inden-1-yl)acetate (**32a'**)*

Prepared by the general procedure using β-nitroacetamide **11a** (0.50 g, 0.92 mmol). Purification by flash column chromatography (10 % Et_2O/Hexanes) afforded **32** as a mixture of diastereoisomers (40:40:20) as a colourless oil (267 mg, 0.54 mmol, 59 %). Recrystallisation (CH_2Cl_2/hexanes) afforded **32a** as a white solid (140 mg, 0.28 mmol, 31 %) and **32a'** as a white solid (49.8 mg, 0.10 mmol, 11 %). Data for **32a**; mp 152 – 153 ^oC; IR νmax (thin film) 2954 (C-H) 1735 (C=O, ester) 1688 (C=O, amide) 1511 (C=C, Ar) 1184, 1154 (C-F, CF_3) cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 2.41 (1H, dd, J = 15.2, 10.9,CH_2CO$_2$CH$_3$) 2.54 (2H, d, J = 9.5, ArCH_2CHCHN) 2.96 (1H, dd, J = 15.2, 4.0, CH_2CO$_2$CH$_3$) 3.07 (1H, m, C*H*CHN) 3.70 (3H, s, COOCH_3) 3.80 (3H, s, ArOCH_3) 3.94 (1H, ddd, J = 10.9, 6.8, 4.0, ArC*H*CH$_2$COOCH$_3$) 6.07 (1H, dd, J = 9.0, 1.9, PMP-*H*) 6.15 (1H, d, J = 12.1, C*H*N) 6.61 (1H, dd, J = 8.8, 3.0, PMP-*H*) 6.92 (1H, dd, J = 8.8, 3.0, PMP-*H*) 7.04 (1H, m, Ar*H*) 7.12 – 7.16 (4H, m, Ar*H*) 7.25 (1H, d, J = 5.5, Ar*H*) 7.29 – 7.37 (3H, m, Ar*H*) 7.49 (1H, dd, J = 8.8., 2.1, PMP-*H*); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 35.2 (*C*H$_2$CO) 35.7 (Ar*C*H$_2$) 42.4 (Ar*C*HCH$_2$CO) 43.6 (*C*HCHN) 51.8 (COOCH_3) 55.5 (ArOCH_3) 60.3 (*C*HN) 113.4 (PMP-*C*) 113.7 (PMP-*C*) 116.6 (q, J = 288.4, *C*F$_3$) 124.6 (Ar*C*) 124.7 (Ar*C*) 126.2 (q, Ar*C*N) 126.8 (Ar*C*) 127.4 (Ar*C*) 128.5 (2C, Ar*C*) 128.8 (Ar*C*) 129.8 (2C, Ar*C*) 131.2 (PMP-*C*) 133.2 (PMP-*C*) 137.3 (q, Ar*C*CHN) 141.2 (q, Ar*C*CH$_2$) 146.1 (q, Ar*C*CHCH$_2$CO) 158.0 (q, J = 35.2, *C*OCF$_3$) 160.2 (q, Ar*C*OCH$_3$) 173.1 (*C*O$_2$CH$_3$); ^{19}F NMR ($CDCl_3$, 282 MHz) δ – 66.9 (3F, s, CF_3); m/z (CI+) 466 (12 %, $C_{27}H_{23}F_3NO_3^+$) 279 (100 %, $C_{19}H_{19}O_2^+$); HRMS ($C_{29}H_{26}F_3NO_4$) calcd. 498.18922, found 498.189495; Anal. Calcd. For $C_{28}H_{26}F_3NO_4$: C, 67.60; H, 5.27; N, 2.82; found: C, 67.68; H, 5.29; N, 2.79%. X-ray Crystallography data in supplementary information. Data for **32a'**; mp 157 – 158 ^oC; IR ν_{max} (thin film) 2951 (C-H) 1735 (C=O, ester) 1687 (C=O, amide) 1510 (C=C, Ar) 1183, 1168 (C-F, CF_3) cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 2.31 (1H, dd, *J* = 14.7, 3.9, CH_2CO$_2$Me) 2.38 (1H, dd, *J* = 14.5, 11.5, CH_2CO$_2$Me) 3.18 – 3.23 (2H, m, C*H*CHN & CH_2Ar) 3.30 (1H, apt dd, *J* = 15.1, 12.6, CH_2Ar) 3.40 (1H, ddd, *J* = 11.2, 6.7, 4.5, C*H*CH$_2$CO$_2$CH$_3$) 3.48 (3H, s, OCH_3) 3.76 (3H, s, OCH_3) 5.84 (1H, br s, PMP-*H*) 6.30 (1H, br d, *J* = 6.9, C*H*N) 6.48 (1H, br d, *J* = 5.0, PMP-*H*) 6.83 (1H, dd, *J* = 8.8, 2.9, PMP-*H*) 6.99 – 7.15 (4H, m, Ar*H*) 7.21 – 7.34 (6H, m, Ar*H*); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 34.5 (*C*H$_2$CO$_2$CH$_3$) 35.1 (Ar*C*H$_2$) 42.5 (*C*HCH$_2$CO$_2$CH$_3$) 43.5 (*C*HCHN) 51.5 (CO$_2$*C*H$_3$) 55.5 (ArOCH_3) 61.3 (*C*HN) 113.5 (2C, PMP-*C*) 116.8 (q, *J* = 289.0, *C*F$_3$) 124.9 (Ar*C*) 124.9 (2C, Ar*C*)126.5 (Ar*C*) 126.7 (Ar*C*) 127.5 (PMP-*C*) 128.8 (Ar*C*) 129.1 (2C, Ar*C*) 129.6 (q) 130.6 (Ar*C*) 133.1 (PMP-*C*) 135.9 (q) 141.5 (q) 145.9 (q) 157.5 (q, *J* = 35.4, *C*OCF$_3$) 160.0 (q, Ar*C*OCH$_3$) 172.4 (q, *C*O$_2$CH$_3$); ^{19}F NMR ($CDCl_3$, 282 MHz) δ – 66.9 (3F, s, CF_3); m/z (EI) 497 (100 %, M^+) 466 (25 %, $C_{27}H_{23}F_3NO_3^+$) 428 (8 %, $C_{27}H_{26}NO_4^+$) 400 (7 %, $C_{26}H_{26}NO_3^+$) 279 (10 %, $C_{19}H_{19}O_2^+$); HRMS ($C_{28}H_{26}F_3NO_4$) calcd. 497.18139, found 497.181034.

N-(((1R,2R*)-1-benzyl-2,3-dihydro-1H-inden-2-yl)(phenyl)methyl)-2,2,2-trifluoro-N-(4-methoxyphenyl)acetamide (**33b**)*

Prepared by the g*eneral procedure* using β-nitroacetamide **11b** (450 mg, 0.80 mmol). Purification by flash column chromatography (0 - 8 % Et_2O/Hexanes) a mixture of diastereoisomers (40:40:20) as a colourless oil (172 mg, 0.33 mmol, 47 %). Recrystallisation (CH_2Cl_2/Hexanes) afforded **32b** as a single diastereomer as a white solid (11.0 mg, 0.021 mmol, 3

%); mp 162 – 164 °C; IR ν_{max} (thin film) 2934 (C-H) 1684 (C=O, amide) 1584, 1510, 1454 (C=C, Ar) 1181, 1148 (C-F, CF_3) cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 2.39 (1H, apt t, *J* = 12.3, PhC*H*$_2$CH) 2.77 (1H, dd, *J* = 12.6, 3.4, PhC*H*$_2$CH) 3.03 (1H, ddd, *J* = 11.2, 6.6, 3.4, BnC*H*Ar) 3.17 – 3.25 (2H, m, C*H*CHN & ArC*H*$_2$CHCHN) 3.38 (1H, m, ArC*H*$_2$CHCHN) 3.77 (3H, s, OC*H*$_3$) 5.95 (1H, br s, PMP-*H*) 6.10 (1H, d, *J* = 7.5, Ar*H*) 6.46 – 6.59 (4H, m, C*H*N, Ar*H*, 2 x PMP-*H*) 6.84 (1H, dd, *J* = 8.8, 3.0, PMP-*H*) 6.87 (1H, t, *J* = 7.5, Ar*H*) 7.06 – 7.12 (4H, m, Ar*H*) 7.16 (2H, dt, *J* = 7.5, 0.7, Ar*H*) 7.25 – 7.28 (1H, m, Ar*H*) 7.30 – 7.36 (3H, m, Ar*H*) 7.39 (1H, tm, *J* = 7.3, Ar*H*); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 35.2 (ArC*H*$_2$) 35.2 (ArC*H*$_2$) 44.2 (*C*HCHN) 48.7 (*C*HCHCHN) 55.5 (OC*H*$_3$) 61.6 (*C*HN) 113.4 (2C, PMP-*C*) 116.8 (q, *J* = 288.8, *C*F$_3$) 124.6 (Ar*C*) 125.5 (2C, Ar*C*) 125.5 (Ar*C*) 126.0 (Ar*C*) 126.9 (PMP-*C*) 128.0 (2C, Ar*C*) 128.7 (2C, Ar*C*) 128.9 (Ar*C*) 129.6 (3C, Ar*C*) 129.8 (q, Ar*C*N) 130.8 (Ar*C*) 133.2 (PMP-*C*) 136.5 (q, Ar*C*CHN) 139.9 (q, Ar*C*CH$_2$) 141.6 (q, Ar*C*CH$_2$CHCHN) 146.0 (q, Ar*C*CH) 157.5 (q, *J* = 35.4, *C*OCF$_3$) 160.0 (Ar*C*OCH$_3$); ^{19}F NMR ($CDCl_3$, 282 MHz) δ – 66.8 (3F, s, CF_3); m/z (ESI^+) 538 (100 %, M + Na^+) 516 (100 %, M + H^+); HRMS ($C_{32}H_{29}F_3NO_2$) calcd. 516.2150, found 516.2166.

*(Z)-2,2,2-trifluoro-N-(4-methoxyphenyl)-N-(phenyl(1-((trimethylsilyl)methylene)-2,3-dihydro-1H-inden-2-yl)methyl)acetamide (**34a**) and (Z)-2,2,2-trifluoro-N-(4-methoxyphenyl)-N-((1-(phenyl(trimethylsilyl)methylene)-2,3-dihydro-1H-inden-2-yl)methyl)acetamide (**35a**)*

Prepared by the g*eneral procedure* using β-nitroacetamide **12a** (556 mg, 1.00 mmol). Purification by flash column chromatography (0 - 10 % Et_2O/Hexanes afforded **34a** as a yellow oil (74.0 mg, 0.15 mmol, 15 % yield) and **35a** as a white solid (30.0 mg, 0.59 mmol, 6 % yield). Data for **34a**; IR ν_{max} (thin film) 2952 (C-H) 1690 (C=O, amide) 1606, 1583, 1509 (C=C, Ar) 1179, 1148 (C-F, CF_3) cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 0.29 (9H, s, Si(C*H*$_3$)$_3$) 2.27 (1H, apt d, *J* = 16.7, C*H*$_2$) 3.04 (1H, dd, *J* = 16.6, 7.5, C*H*$_2$) 3.78 (3H, s, OC*H*$_3$) 4.21 (1H, br dd, *J* = 10.8, 7.6, C*H*CHN) 4.55 (1H, br d, *J* = 10.8, C*H*N) 5.99 (1H, s, C*H*Si) 6.67 (1H, dd, *J* = 8.9, 3.0, PMP-*H*) 6.71 – 6.74 (1H, m, PMP-*H*) 6.80 (1H, dd, *J* = 8.7, 2.7, PMP-*H*) 7.07 (1H, m, PMP-*H*) 7.11 (1H, d, *J* = 7.7, Ar*H*) 7.18 – 7.31 (7H, m, Ar*H*) 7.67 (1H, d, *J* = 7.5, Ar*H*); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 0.05 (Si(*C*H$_3$)$_3$) 35.5 (*C*H$_2$) 48.0 (*C*HCHN) 55.5 (O*C*H$_3$) 71.1 (*C*HN) 113.5 (PMP-*C*) 114.3 (PMP-*C*) 124.6 (Ar*C*) 124.8 (Ar*C*) 125.7 (Ar*C*) 126.6 (Ar*C*) 128.3 (2C, Ar*C*) 128.5 (2C, Ar*C*) 128.7 (Ar*C*) 130.1 (PMP-*C*) 130.4 (q, Ar*C*N) 131.2 (PMP-*C*) 137.3 (q, Ar*C*) 140.4 (q, Ar*C*) 145.7 (q, Ar*C*CH$_2$) 156.9 (q, *J* = 35.5, *C*OCF$_3$) 159.3 (q, *C*CHSi) 159.6 (Ar*C*O) further signals indistinguishable; ^{19}F NMR ($CDCl_3$, 282 MHz) δ – 67.5 ppm (3F, s, CF_3); m/z (EI) 509 (< 5 %, M^+) 308 (100 %, $C_{16}H_{13}F_3NO_2^+$) 202 (37 %, $C_{13}H_{17}Si^+$). See supplementary information for data correlation table. Data for **35a**; mp 144 – 146 °C; IR ν_{max} (thin film) 3056, 2956, 2092, 2840 (C-H) 1696 (C=O, amide) 1511 (C=C, Ar) 1201, 1153 (C-F, CF_3) cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 0.07 (9H, s, Si(C*H*$_3$)$_3$) 2.72 (1H, apt d, *J* = 15.4, ArC*H*$_2$) 2.90 (1H, dd, *J* = 13.3, 3.3, C*H*$_2$N) 2.93 – 3.03 (2H, m, C*H*CH$_2$N & ArC*H*$_2$) 3.85 (3H, s, OC*H*$_3$) 4.01 (1H, dd, *J* = 13.1, 11.5, C*H*$_2$N) 6.60 – 7.17 (9H, br m, Ar*H* & PMP-*H*) 7.24 (1H, apt t, *J* = 7.4, Ar*H*) 7.28 (1H, dd, *J* = 7.2, 1.0, Ar*H*) 7.32 (1H, d, *J* = 7.3, Ar*H*) 7.66 (1H, d, *J* = 7.5, Ar*H*); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 0.5 (Si(*C*H$_3$)$_3$) 33.5 (ArC*H*$_2$) 42.1 (*C*HCH$_2$N) 52.3 (*C*H$_2$N) 55.6 (O*C*H$_3$) 116.5 (q, *J* = 288.9, *C*F$_3$) 125.2 (Ar*C*) 125.5 (1C, Ar*C*) 126.0 (1C, Ar*C*) 126.3 (1C, Ar*C*) 127.4 (br, Ar*C*) 128.8 (Ar*C*) 130.0 (q, Ar*C*N) 139.4 (q, *C*SiMe$_3$) 139.8 (q, Ar*C*CH$_2$) 145.2 (Ar*C*CSiMe$_3$) 146.6 (Ar*C*CCSiMe$_3$) 153.5 (*C*CSiMe$_3$) 157.6 (q, *J* = 35.4, *C*OCF$_3$) 159.3 (q, Ar*C*O); ^{19}F NMR ($CDCl_3$, 282 MHz) δ – 67.0 ppm (3F, s, CF_3); m/z (CI^+) 527 (46 %, M + NH_4^+) 510 (100 %, M + H^+) 291 (6 %, $C_{20}H_{23}Si^+$); HRMS ($C_{29}H_{31}F_3NO_2Si$) calcd. 510.2071, found 510.2070. Anal. Calcd. For $C_{29}H_{30}F_3NO_2Si$: C, 68.35; H, 5.93; N, 2.75; found: C, 68.39; H, 5.91; N, 2.69 %. See supplementary information for data correlation table and X-ray crystallography data.

N-((1-benzylidene-2,3-dihydro-1H-inden-2-yl)(phenyl)methyl)-2,2,2-trifluoro-N-(4-methoxyphenyl)acetamide (**34b**)

Prepared by the g*eneral procedure* using β-nitroacetamide **12b** (422 mg, 0.75 mmol). Purification by flash column chromatography (0 - 10 % Et_2O/Hexanes gave **34b** followed by recrystallisation (Et_2O/hexanes) as a white solid (40.3 mg, 0.078 mmol, 10 % yield); mp 100 – 102 °C; IR ν_{max} (thin film) 2956 (C-H) 1692 (C=O, amide) 1509 (C=C, Ar) 1185, 1150 (C-F, CF_3) cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 2.85 (1H, m, C*H*CHN) 2.91 (1H, dd, *J* = 16.0, 7.5, C*H*$_2$) 3.16 (1H, dd, *J* = 15.8, 8.0, C*H*$_2$) 3.80 (3H, s, OC*H*$_3$) 6.23 – 6.27 (2H, m, C*H*N & C*H*) 6.79 (1H, dd, *J* = 9.0, 2.7, PMP-*H*) 6.85 – 6.88 (2H, m, C*H*) 6.94 (1H, dd, *J* = 8.9, 2.7, PMP-*H*) 7.10 – 7.14 (2H, m, Ar*H*) 7.21 (1H, m, Ar*H*) 7.25 (1H, d, *J* = 7.4, Ar*H*) 7.28 – 7.58 (10H, m, Ar*H*); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 36.8 (*C*H$_2$) 39.9 (*C*HCHN) 55.6 (O*C*H$_3$) 64.4 (*C*HN) 113.6 (PMP-*C*) 114.5 (PMP-*C*) 124.4 (C*C*H) 130.7 (q) 131.8 (q) 138.1 (q) 138.4 (q) 139.0 (q) 139.8 (q) 146.0 (q) 158.9 (q, *J* = 35.2, *C*OCF$_3$) 160.1 (q, Ar*C*O) further signals indistinguishable; m/z (ESI) 514 (100 %, M + H^+) 295 (33 %, $C_{23}H_{19}^+$); HRMS ($C_{32}H_{27}F_3NO_2$) calcd. 514.1994, found 514.1999.

*2,2,2-trifluoro-N-(4-methoxyphenyl)-N-(phenyl(2,4,4-trimethylcyclopentyl)methyl)acetamide (**36**) and N-((1-benzyl-2,3-dihydro-1H-inden-2-yl)methyl)-2,2,2-trifluoro-N-(4-methoxyphenyl)acetamide (**37**)*

Prepared by the g*eneral procedure* using β-nitroacetamide **15** (257 mg, 0.55 mmol). Purification by flash column chromatography (10 % Et_2O/Hexanes) afforded **36** as a mixture of diastereoisomers (40:30:30) as a white solid (52.6 mg, 0.13 mmol, 46 %) and **37** as a white solid (19.6 mg, 0.047 mmol, 9 %). Data for **36**; IR ν_{max} (thin film) 3031, 2450, 2862 (C-H) 1685 (C=O, amide) 1606, 1582, 1509 (C=C, Ar) 1179, 1146 (C-F, CF_3) cm^{-1}; ^1H and ^{13}C NMR data display a complex mixture; m/z (ESI^+) 839 (23 %, 2M + H^+) 461 (9 %, M + MeCN + H^+) 420 (100 %, M + H^+); HRMS ($C_{24}H_{29}F_3NO_2$) calcd. 420.2150, found 420.2153. Data for **37**; mp 109 – 111 °C; IR ν_{max} (thin film) 2951 2933 2865 (C-H) 1697 (C=O, amide) 1512 (C=C, Ar) 1202, 1151 (C-F, CF_3) cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 0.92 (3H, s, C*H*$_3$) 1.11 (3H, s, C*H*$_3$) 1.34 (1H, dd, *J* = 13.0, 8.5, C*H*$_2$C(CH$_3$)$_2$) 1.40 (1H, dd, *J* = 13.0, 6.6, C*H*$_2$C(CH$_3$)$_2$) 1.50 (1H, dd, *J* = 13.0, 7.8, C*H*$_2$CHCH$_2$N) 1.58 (1H, dd, *J* = 13.0, 7.3, C*H*$_2$CHCH$_2$N) 2.27 (1H, m, C*H*CH$_2$N) 2.38 (1H, m, C*H*CH$_2$Ph) 2.43 (1H, dd, *J* = 12.8, 10.7, C*H*$_2$Ph) 2.70 (1H, dd, *J* = 12.8, 4.7, C*H*$_2$Ph) 3.49 (1H, dd, *J* = 13.1, 4.9, C*H*$_2$N) 3.85 (3H, s, OC*H*$_3$) 4.25 (1H, dd, *J* = 13.0, 11.0, C*H*$_2$N) 6.91 (2H, apt d, *J* = 8.7, PMP-*H*) 7.08 (2H, apt d, *J* = 7.8, Ar*H*) 7.11 (2H, d, *J* = 8.6, PMP-*H*) 7.16 (1H, tm, *J* = 7.4, Ar*H*) 7.22 – 7.25 (2H, m, Ar*H*); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 30.6 (C(*C*H$_3$)$_2$) 31.4 (C(*C*H$_3$)$_2$) 36.5 (*C*H$_2$Ph) 37.4 (q, *C*(CH$_3$)$_2$) 38.8 (*C*HCH$_2$N) 42.4 (CHCH$_2$Ph) 44.7 (*C*H$_2$CHCH$_2$N) 46.3 (CH$_2$CHCH$_2$Ph) 52.4 (*C*H$_2$N) 55.6 (O*C*H$_3$) 114.0 (PMP-*C*) 114.7 (PMP-*C*) 116.7 (q, *J* = 288.8, *C*F$_3$) 125.9 (Ar*C*) 128.4 (2C, Ar*C*) 128.8 (2C, Ar*C*) 129.4 (br, PMP-*C*) 130.0 (br, PMP-*C*) 131.2 (Ar*C*N) 141.4 (q, Ar*C*CH$_2$) 157.5 (q, *J* = 34.8, *C*OCF$_3$) 159.8 (q, Ar*C*OCH$_3$); ^{19}F NMR ($CDCl_3$, 282 MHz) δ – 66.9 ppm (3F, s, CF_3); m/z (ESI^+) 839 (27 %, 2M + H^+) 420 (100 %, M + H^+) ; HRMS ($C_{24}H_{29}F_3NO_2$) calcd. 420.2150, found 420.2152. See supplementary information for data correlation table.

*2,2,2-trifluoro-N-(4-methoxyphenyl)-N-((2-methyl-5-phenylcyclopentyl)(phenyl)methyl)acetamide (**38**) and N-(((1S*,5R*)-2-benzyl-5-phenylcyclopentyl)methyl)-2,2,2-trifluoro-N-(4-methoxyphenyl)acetamide (**39**)*

Prepared by the g*eneral procedure* using β-nitroacetamide **18** (87.0 mg, 0.17 mmol). Purification by flash column chromatography (10 % Et_2O/Hexanes) afforded **38** as a mixture of diastereoisomers (40:35:25) as white solid (19.0 mg, 0.041 mmol, 24 %) and **39** as a white solid (2.5 mg, 0.003 mmol, 3 %). Data for **38**; IR ν_{max} (thin film) 2960, 2932 (C-H) 1689 (C=O, amide) 1511, 1445 (C=C, Ar) 1204, 1184 (C-F, CF_3) cm^{-1}; ^1H and ^{13}C NMR data display a complex mixture; m/z (EI) 935 (8 %, $2M^+$) 468 (100 %, M^+); HRMS ($C_{28}H_{28}F_3NO_2$) calcd. 468.2152, found 468.2150. Data for **39**; IR ν_{max} (thin film) 3027, 2954, 2935 (C-H) 1692 (C=O, amide) 1602, 1511, 1445 (C=C, Ar) 1202, 1152 (C-F, CF_3) cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) δ 1.54 (1H, m, CH_2CH$_2$CHPh) 1.61 (1H, m, CH_2CHPh) 1.74 (1H, m, CH_2CH$_2$CHPh) 2.25 -2.33 (2H, m, 1H, m, CH_2CHPh & C*H*CH$_2$N) 2.40 – 2.47 (2H, m, CH_2Ph & C*H*CH$_2$Ph) 2.77 (1H, m, CH_2Ph) 3.13 (1H, dt, *J* = 9.0, 8.2, C*H*Ph) 3.62 (1H, dd, *J* = 13.5, 6.0, CH_2N) 3.79 (3H, s, OCH_3) 4.28 (1H, dd, *J* = 13.4, 9.1, CH_2N) 6.84 – 7.55 (14 H, m, Ar*H* & PMP-*H*); ^{13}C NMR ($CDCl_3$, 150 MHz) δ 30.8 (*C*H$_2$) 34.7 (*C*H$_2$CHPh) 35.6 (*C*H$_2$Ph) 43.9 (*C*HCH$_2$Ph) 47.6 (*C*HCH$_2$N) 49.0 (*C*HPh) 52.6 (*C*H$_2$N) 55.5 (O*C*H$_3$) 126.0 (Ar*C*) 126.4 (Ar*C*) 127.5 (Ar*C*) 128.5 (Ar*C*) 128.7 (Ar*C*) 128.9 (Ar*C*) 131.0 (q, Ar*C*N) 141.2 (q, Ar*C*) 146.5 (q, Ar*C*) 157.6 (q, *J* = 34.4, *C*F$_3$) 159.5 (Ar*C*O) further signals indistinguishable; ^{19}F NMR ($CDCl_3$, 282 MHz) δ – 67.0 ppm (3F, s, CF_3); m/z (ES^+) 935 (16 %, 2M + H^+) 468 (100 %, M + H^+); HRMS ($C_{28}H_{29}F_3NO_2$) calcd. 468.2150, found 468.2154. See supplementary information for data correlation table.

N-(2-benzyl-3-methyl-2,3-dihydro-1H-inden-1-yl)-2,2,2-trifluoro-N-(4-methoxyphenyl)acetamide (**40a**)

Prepared by the g*eneral procedure* using β-nitroacetamide **19a** (0.48 g, 0.99 mmol). Purification by flash column chromatography (10 % Et_2O/Hexanes) afforded **437** as an inseparable mixture of diastereomers (55:45) as a colourless oil (200 mg, 0.46 mmol, 46 %); IR ν_{max} (thin film) 1686 (C=O, amide) 1510 (C=C, Ar) 1186, 1153 (C-F, CF_3) cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) major *trans*, *trans* δ 0.97 (3H, d, *J* = 7.0, CHCH_3) 1.99 (1H, tdd, *J* = 8.7, 7.6, 6.1, C*H*CHN) 2.85 (1H, m, C*H*CH$_3$) 2.95 (1H, dd, *J* = 13.7, 6.0, CH_2Ph) 3.03 (1H, dd, *J* = 13.7, 7.5, CH_2Ph) 3.76 (3H, s, OCH_3) 6.28 (1H, d, *J* = 8.8, C*H*N) 6.37 (1H, apt d, *J* = 8.6, PMP-*H*) 6.59 (1H, dd, *J* = 8.9, 2.9, PMP-*H*) 6.61 – 6.65 (1H, m, PMP-*H*) 6.76 (1H, dd, *J* = 8.8, 2.9, PMP-*H*) 7.09 – 7.13 (2H, m, Ar*H*) 7.23 -7.39 (7H, m, Ar*H*); minor *trans*, *cis* δ 1.12 (3H, d, *J* = 7.3, CH_3) 2.60 (1H, tdd, *J* = 9.2, 7.9, 6.7, C*H*CHN) 2.90 (1H, dd, *J* = 14.5, 9.2, CH_2Ph) 2.96 – 3.04 (2H, m, CH_2Ph & C*H*CHCHN) 3.77 (3H, s, OCH_3) 6.24 (1H, d, *J* = 9.2, C*H*N) 6.61 – 6.65 (1H, m, PMP-*H*) 6.70 (1H, dm, *J* = 8.7, PMP-*H*) 6.83 (2H, m, PMP-*H*) 7.18 (2H, apt d, *J* = 7.5, Ar*H*) 7.23 – 7.39 (7H, m, Ar*H*); ^{13}C NMR ($CDCl_3$, 150 MHz) major *trans*, *trans* δ 18.8 (*C*H$_3$CH) 39.2 (*C*H$_2$) 42.6 (CH$_3$*C*H) 51.4 (*C*HCHN) 55.4 (O*C*H$_3$) 67.0 (*C*HN) 113.6 – 132.1 (Ar*C* & PMP-*C*) 116.6 (q, *J* = 288.3, *C*F$_3$) 127.9 (q, Ar*C*N) 139.6 (q, Ar*C*CHN) 139.6 (q, Ar*C*CH$_2$) 146.7 (q, Ar*C*CHCH$_3$) 158.2 (q, *J* = 35.1, CF$_3$*C*O) 159.8 (q, Ar*C*O); minor *trans*, *cis* δ 17.3 (*C*H$_3$CH) 34.4 (*C*H$_2$) 39.3 (CH$_3$*C*H) 45.3 (*C*HCHN) 55.5 (O*C*H$_3$) 66.3 (*C*HN) 113.6 – 132.1 (Ar*C* & PMP-*C*) 116.6 (q, *J* = 289.2, *C*F$_3$) 127.8 (q, Ar*C*N) 139.1 (q, Ar*C*) 140.0 (q, Ar*C*) 148.7 (q, Ar*C*CHCH$_3$) 158.5 (q, *J* = 34.6, CF$_3$*C*O) 160.0 (q, Ar*C*O) ; ^{19}F NMR ($CDCl_3$, 282 MHz) major *trans*, *trans* δ – 66.9 ppm (3F, s, CF_3); minor *trans*, *cis* δ – 66.8 ppm (3F, s, CF_3); m/z (EI) 439 (6 %, M^+) 221 (100 %, $C_{17}H_{17}^+$) 91 (98 %, $C_7H_7^+$); HRMS ($C_{26}H_{24}F_3NO_2$) calcd. 439.17591, found 439.176345. See supplementary information for data correlation table.

*N-(2,3-dibenzyl-2,3-dihydro-1H-inden-1-yl)-2,2,2-trifluoro-N-(4-methoxyphenyl)acetamide (**40b**)*

Prepared by the g*eneral procedure* using β-nitroacetamide **19b** (558 mg, 1.00 mmol). Purification by flash column chromatography (10 % Et_2O/Hexanes) afforded **40b** as two diastereomers (60:40) as a colourless oil (174 mg, 0.34 mmol, 34 %); IR ν_{max} (thin film) 3063, 3026, 2934 (C-H) 1689 (C=O, amide) 1584, 1511 (C=C, Ar) 1186, 1170 (C-F, CF_3) cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) major *trans*, *trans* δ 2.21 (1H, dtd, *J* = 9.6, 7.1, 4.8 CHNC*H*) 2.24 (1H, dd, *J* = 13.4, 8.2, CHNCHCHCH_2) 2.51 (1H, dd, *J* = 13.3, 4.6, CHNCHCH_2) 2.70 (1H, dd, *J* = 13.4, 9.6, CHNCHCH_2) 2.79 (1H, dd, *J* = 13.6, 6.3, CHNCHCHCH_2) 3.13 – 3.18 (1H, m, CHNCHC*H*) 3.78 (3H, s, OCH_3) 6.17 (1H, d, *J* = 7.8, PMP-*H*) 6.31 (1H, d, *J* = 7.1, C*H*N) 6.42 (1H, dd, *J* = 8.7, 2.6, PMP-*H*) 6.54 (1H, dd, *J* = 8.9, 3.0, PMP-*H*) 6.75 (1H, dd, *J* = 8.8, 3.0, PMP-*H*) 6.91 (2H, m, Ar*H*) 7.05 (3H, apt d, *J* = 7.0, Ar*H*) 7.15 – 7.35 (8H, m, Ar*H*) 7.37 (1H, d, *J* = 7.4, Ar*H*) minor *trans*, *cis* δ 2.44 (1H, dd, *J* = 13.4, 8.2, CHNCHCHCH_2) 2.69 (1H, m, CHNC*H*) 3.05 (2H, m, CHNCHCH_2) 3.10 (1H, ddd, *J* = 10.8, 7.5, 5.0, CHNCHC*H*) 3.13 – 3.18 (1H, m, CHNCHCHCH_2) 3.78 (3H, s, OCH_3) 6.24 (1H, d, *J* = 7.3, Ar*H*) 6.28 (1H, d, *J* = 9.2, C*H*N) 6.63 (1H, dd, *J* = 8.9, 2.9, PMP-*H*) 6.69 (1H, dd, *J* = 8.9, 2.5, PMP-*H*) 6.78 (2H, m, Ar*H*) 6.86 (1H, dd, *J* = 8.8, 2.9, PMP-*H*) 6.95 (1H, m, PMP-*H*) 7.00 (1H, apt t, *J* = 7.4, Ar*H*) 7.15 – 7.35 (9H, m, Ar*H*) 7.40 (1H, d, *J* = 7.6, Ar*H*); ^{13}C NMR ($CDCl_3$, 150 MHz) major *trans*, *trans* δ 41.0 (*C*H$_2$CHCHN) 41.2 (*C*H$_2$CHCHCHN) 47.5 (*C*HCHN) 49.8 (*C*HCHCHN) 55.5 (O*C*H$_3$) 67.3 (*C*HN) 113.5 (PMP-*C*) 113.7 (PMP-*C*) 116.6 (q, *J* = 288.7, *C*F$_3$) 124.5 – 129.4 (14C, Ar*C*, indistinguishable) 128.0 (q, Ar*C*N) 130.3 (PMP-*C*) 132.3 (PMP-*C*) 139.3 (q, Ar*C*CH$_2$CHCHCHN) 139.6 (q, Ar*C*CH$_2$CHCHN) 140.2 (Ar*C*CHN) 145.6 (q, Ar*C*CHCHCHN) 157.6 (q, *J* = 34.8, *C*OCF$_3$) 159.8 (q, Ar*C*O) minor *trans*, *cis* δ 34.1 (*C*H$_2$CHCHN) 36.5 (*C*H$_2$CHCHCHN) 46.0 (*C*HCHN) 46.2 (*C*HCHCHN) 55.5 (O*C*H$_3$) 66.0 (*C*HN) 113.9 (PMP-*C*) 114.0 (PMP-*C*) 116.7 (q, *J* = 289.4, *C*F$_3$) 124.5 – 129.4 (14C, Ar*C*, indistinguishable) 127.8 (q, Ar*C*N) 130.8 (PMP-*C*) 131.6 (PMP-*C*) 139.5 (q, Ar*C*CH$_2$CHCHN) 139.6 (q, Ar*C*CHN) 139.8 (q, Ar*C*CH$_2$CHCHCHN) 145.7 (q, Ar*C*CHCHCHN) 158.6 (q, *J* = 34.7, *C*OCF$_3$) 160.1 (q, Ar*C*O); ^{19}F NMR ($CDCl_3$, 282 MHz) major *trans*, *trans* δ – 67.0 ppm (3F, s, CF_3) minor *trans*, *cis* δ – 66.8 ppm (3F, s, CF_3); m/z (ESI^+) 533 (37 %, M + NH_4^+) 516 (48 %, M + H^+); HRMS ($C_{32}H_{29}F_3NO_2$) calcd. 516.2150, found 516.2152. See supplementary information for data correlation table.

N-((1S,2R*,3R*)-2-benzyl-3-ethyl-2,3-dihydro-1H-inden-1-yl)-2,2,2-trifluoro-N-(4-methoxyphenyl)acetamide (**40d**)*

Prepared by g*eneral procedure I* using β-nitroacetamide **19d** (134 mg, 0.27 mmol). Purification via flash column chromatography (0 – 10 % Et_2O/hexanes) afforded **40d** as a mixture of diastereoisomers (70:30) as a colourless oil (14.7 mg, 0.032 mmol, 12 %); IR ν_{max} (thin film) 2958, 2928, 2857 (C-H) 1688 (C=O, amide) 1510, 1454 (C=C, Ar) 1187, 1150 (C-F, CF_3) cm^{-1}; ^1H NMR ($CDCl_3$, 600 MHz) $\delta_{trans,trans}$ 0.44 (3H, s, CH$_2$CH_3) 1.29 (1H, m, CH_2CH$_3$) 1.41 (1H, m, CH_2CH$_3$) 2.22 (1H, apt quint, *J* = 7.3, C*H*CHN) 2.86 (1H, m, C*H*Et) 2.93 (2H, d, *J* = 7.1, CH_2Ph) 3.73 (3H, s, OCH_3) 6.25 (1H, dd, *J* = 8.7, 1.1, PMP-*H*) 6.30 (1H, d, *J* = 7.6, C*H*N) 6.48 (1H, dd, *J* = 8.8, 2.6, PMP-*H*) 6.53 (1H, dd, *J* = 8.8, 2.9, PMP-*H*) 6.72 (1H, dd, *J* = 8.8, 2.9, PMP-*H*) 7.09 (1H, m, Ar*H*) 7.24 – 7.30 (5H, m, Ar*H*) 7.32 – 7.37 (3H, m, Ar*H*); ^{13}C NMR ($CDCl_3$, 150 MHz) $\delta_{trans,trans}$ 9.76 (CH$_2$*C*H$_3$) 25.1 (*C*H$_2$CH$_3$) 40.8 (PhCH$_2$) 46.4 (*C*HCHN) 49.0

(*C*HEt) 55.5 (O*C*H$_3$) 67.3 (*C*HN) 113.5 (PMP-*C*) 113.7 (PMP-*C*) 116.6 (q, *J* = 288.2, *C*F$_3$) 124.2 (Ar*C*) 124.5 (Ar*C*) 126.7 (Ar*C*) 127.2 (Ar*C*) 127.9 (q, Ar*C*N) 128.5 (Ar*C*) 128.6 (2C, Ar*C*) 129.4 (2C, Ar*C*) 130.5 (PMP-*C*) 132.2 (PMP-*C*) 139.9 (q, Ar*C*CH$_2$) 140.3 (q, Ar*C*CHN) 145.5 (q, Ar*C*CHEt) 157.8 (q, *J* = 34.9, *C*OCF$_3$) 159.8 (Ar*C*OCH$_3$); ^{19}F NMR (CDCl$_3$, 282 MHz) δ - 67.0 ppm (3F, s, CF$_3$); m/z (ESI$^+$) 929 (47 %, 2M + H + Na$^+$) 476 (100 %, M + H$^+$) 235 (30 %, $C_{18}H_{19}^+$); HRMS ($C_{27}H_{26}NO_2F_3Na$) calcd. 476.1808, found 476.1808.

*1-(3-benzyl-4-methyl-2-phenylpyrrolidin-1-yl)-2,2,2-trifluoroethan-1-one (**41**)*

Prepared by the g*eneral procedure* using nitro compound **27** (150 mg, 0.38 mmol). Purification by flash column chromatography (10 % Et$_2$O/Hexanes) afforded **41** as a mixture of diastereoisomers (50:30:15:5) as a colourless oil (16.3 mg, 0.05 mmol, 12 %); IR ν_{max} (thin film) 3059, 3026, 2918, 2847 (C-H) 1686 (C=O, amide) 1601, 1493, 1451 (C=C, Ar) 1196, 1135 (C-F, CF$_3$); ^{1}H and ^{13}C NMR data display a complex mixture; m/z (ESI) 717 (100 %, 2M + Na$^+$) 370 (63 %, M + Na$^+$) 348 (100 %, M + H$^+$); HRMS ($C_{20}H_{21}F_3NO$) calcd. 348.1570, found 348.1575.

N-((1R,2R*,3S*)-3-benzyl-2-phenyl-2,3-dihydro-1H-inden-1-yl)-2,2,2-trifluoro-N-(4-methoxyphenyl)acetamide (**42**)*

Prepared by the g*eneral procedure* using nitro compound **28** (253 mg, 0.46 mmol). Purification by flash column chromatography (10 % Et$_2$O/Hexanes) afforded **42** as a mixture of diastereoisomers (95:5) as a colourless oil (30.0 mg, 0.06 mmol, 13 %); IR ν_{max} (thin film) 2920, 2836 (C-H) 1689 (C=O, amide) 1603, 1509, 1453 (C=C, Ar) 1147, 1109 (C-F, CF$_3$) cm^{-1}; ^{1}H NMR (CDCl$_3$, 600 MHz) δ 2.67 (1H, dd, *J* = 14.5, 7.9, C*H*$_2$Ar) 2.85 (1H, dd, *J* = 14.5, 5.0, C*H*$_2$Ar) 3.02 (1H, t, *J* = 9.2, C*H*CH$_2$Ar) 3.53 (1H, m, C*H*CHN) 3.81 (3H, s, OC*H*$_3$) 6.48 (1H, d, *J* = 9.4, C*H*N) 6.61 (1H, dd, *J* = 8.8, 2.6, PMP-*H*) 6.65 (1H, apt d, *J* = 8.9, PMP-*H*) 6.84 (1H, dd, *J* = 8.7, 2.6, PMP-*H*) 6.90 – 6.94 (3H, m, Ar*H*) 7.01 (1H, d, *J* = 7.6, Ar*H*) 7.09 – 7.18 (5H, m, PMP-*H* & Ar*H*) 7.24 – 7.28 (2H, m, Ar*H*) 7.30 – 7.35 (3H, m, Ar*H*) 7.38 (1H, d, *J* = 7.6, Ar*H*); ^{13}C NMR (CDCl$_3$, 150 MHz) δ 38.5 (*C*H$_2$Ar) 51.9 (*C*HCHN) 53.7 (*C*HCH$_2$Ar) 55.5 (O*C*H$_3$) 68.8 (*C*HN) 113.7 (PMP-*C*) 114.1 (PMP-*C*) 116.6 (q, *J* = 288.5, *C*F$_3$) 124.0 (Ar*C*) 124.6 (Ar*C*) 126.1 (Ar*C*) 127.2 (Ar*C*) 127.6 (2C, Ar*C*) 128.0 (q, Ar*C*N) 128.3 (2C, Ar*C*) 128.5 (2C, Ar*C*) 128.5 (Ar*C*) 128.9 (Ar*C*) 129.3 (2C, Ar*C*) 130.6 (PMP-*C*) 132.2 (PMP-*C*) 139.3 (q, Ar*C*CH$_2$) 139.7 (q, Ar*C*CHN) 140.8 (q, Ar*C*CHCHN) 144.5 (q, Ar*C*CHCHCHN) 158.2 (q, *J* = 35.2, *C*OCF$_3$) 160.0 (Ar*C*O) ; ^{19}F NMR (CDCl$_3$, 282 MHz) δ – 67.0 ppm (3F, s, CF$_3$); m/z (EI) 501.2 (2 %, M$^+$) 283.2 (59 %, $C_{22}H_{19}^+$); HRMS ($C_{31}H_{26}F_3NO_2$) calcd. 501.19102, found 501.190981.

*2,2,2-trifluoro-N-(4-methoxyphenyl)-N-(3-methyl-2-phenylcyclopentyl)acetamide (**43**)*

Prepared by the g*eneral procedure* using β-nitroacetamide **29** (0.42 g, 1.00 mmol). Purification by flash column chromatography (10 % Et$_2$O/Hexanes) afforded **43** as a mixture of inseparable diastereomers (50:50) as a colourless oil (134 mg, 0.36 mmol, 36 %); IR ν_{max} (thin film) 2954, 2914 (C-H) 1684 (C=O, amide) 1509, 1453 (C=C, Ar) 1187, 1149 (C-F, CF$_3$) cm^{-1}; ^{1}H and ^{13}C NMR data display a complex mixture; m/z (CI$^+$) 772 (100 %, 2M + CH_5^+) 755 (99 %, 2M + H$^+$) 395 (100 %, M + CH_5^+) 378 (90 %, M + H$^+$); HRMS ($C_{21}H_{22}F_3NO_2$) calcd. 378.16754, found 378.167530

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