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PAPER

Transannular dipolar cycloaddition as an approach towards the synthesis of the core ring system of the sarain alkaloids†

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Intramolecular transannular dipolar cycloaddition was investigated as a key step in a synthetic approach to the core of the sarain alkaloids; although the use of an azomethine ylide was unsuccessful with the chosen aldehyde substrate, cycloaddition with a nitrone did give the alternative regioisomeric bridged cycloadduct.

Introduction

The sarain alkaloids, sarain A, B and C, consist of a unique polycyclic ring system containing a tricyclic core and two macrocyclic tethers with a zwitterionic structure due to the promixity of a tertiary amine and an aldehyde group (Fig. 1). These natural products were isolated in 1989 from the marine sponge *Reniera sarai*, and were shown to possess moderate anticancer, antibacterial and insecticidal activity.[1] The sarains are thought to derive biosynthetically from the reductive condensation of a bispyridinium macrocycle.[2] Their fascinating structures together with their biological activity has led to several synthetic endeavors in this area. So far, there is one reported synthesis of sarain A, by Overman and co-workers, that uses a cyclization of a silyl enol ether onto an iminium ion to set up the core tricyclic ring system.[3] The groups of Heathcock and Weinreb independently reported the use of aziridines as azomethine ylide precursors that undergo cycloaddition to access a bicyclic ring system.[4,5] Subsequent cyclization of an allyl silane onto an iminium ion has provided the desired bridged tricyclic core. Cha and co-workers have reported an approach that relies on an intermolecular [4+3] cycloaddition of cyclopentadiene and an oxyallyl cation.[6] Two different strategies using conjugate addition chemistry to give a bicyclic system that was elaborated to the tricyclic core have been reported by Mons and Marazano and co-workers[7] and by Yang and Huang.[8] Porter has investigated an approach using aminals.[9]

Our interest in the synthesis of the marine alkaloid manzamine A using an intramolecular cycloaddition of an azomethine ylide as a key step[10] prompted us to investigate a new and efficient approach to the sarain alkaloids. Our retrosynthetic analysis is shown in Scheme 1. Disconnection of the macrocyclic rings suggested that the tricyclic core **1** would be a suitable target [a variety of heteroatom substituents R, R′, Boc (= $CO_2{}^tBu$) could be chosen]. Our plan was to access this core directly from the azomethine ylide **2**. Transannular dipolar cycloaddition reactions of azomethine ylides are rare, although one example across a seven-membered ring has been reported.[11] The ylide **2** could be constructed *in situ* from the condensation of an aldehyde such as **3** (or **4**) and an amine.[12] In this paper we report the results of our efforts using this strategy.

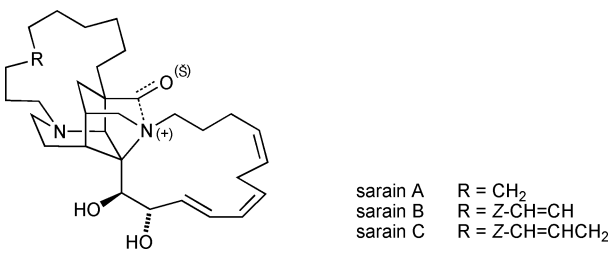
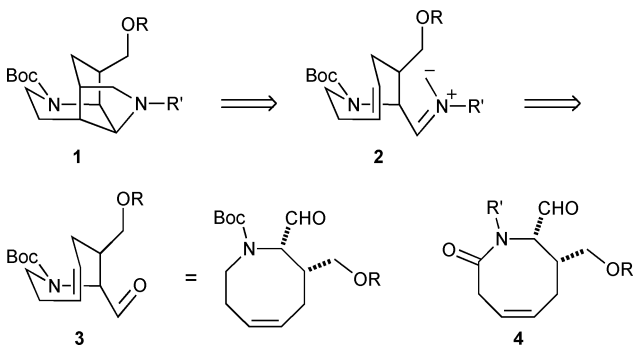


Fig. 1 Sarain alkaloids.



Scheme 1 Disconnection approach to the core ring system.

Results and Discussion

The synthesis of the aldehyde **4** is shown in Schemes 2 and 3 and started with the enantiomerically pure lactone **5** (available

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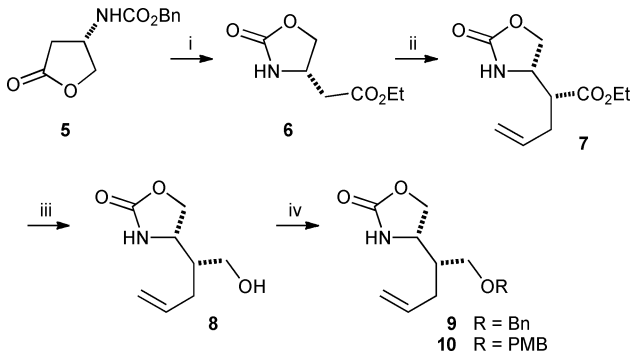
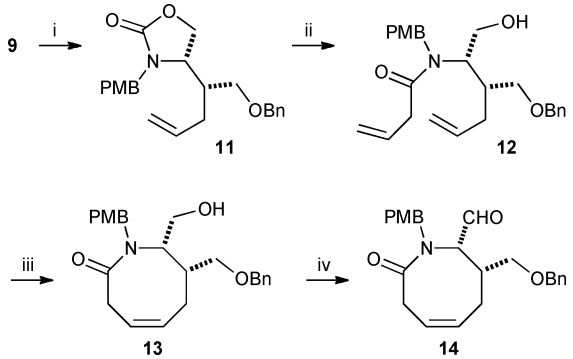
† Electronic supplementary information (ESI) available: Procedures and data for compounds **9** to **21**; crystallographic information and ORTEP diagrams for the alcohol **8** and the amide **23**. (CCDC reference numbers 791948 and 791949 respectively). For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c0ob01019g



Scheme 2 Preparation of oxazolidinones **9** and **10**. *Reagents and conditions*: i, NaOEt, EtOH, r.t., 72%; ii, 2 equiv. NaHMDS, THF, –78 °C, allyl bromide, 70%; iii, $Ca(BH_4)_2$ (or $LiBH_4$), EtOH, r.t., 85% (or 77%); iv, $Cl_3CC(=NH)OR$, CH_2Cl_2, 20 mol% TMSOTf or 10 mol% camphor sulfonic acid, r.t., 18 h, R = Bn 79%, or R = PMB 81%.



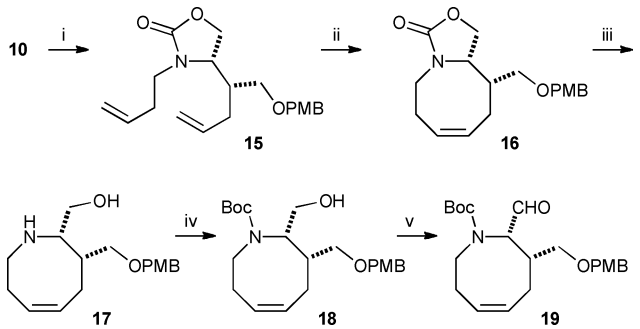
Scheme 3 Preparation of aldehyde **14**. *Reagents and conditions*: i, KH, PMBCl, 10 mol% Bu_4NI, THF, r.t., 22 h, 79%; ii, allyl magnesium bromide (2 equiv.), THF, –78 °C, 2.5 h, 63%; iii, 2 × 5 mol% $Cl_2(PCy_3)[(CH_2NMes)_2C]Ru{=}CHPh$, $ClCH_2CH_2Cl$, 80 °C, 9 h, 58%; iv, Dess–Martin periodinane, CH_2Cl_2, 0 °C, 2 h, 60%.

commercially but alternatively prepared from *N*-carboxybenzyl aspartic acid).[13] Treatment of the lactone **5** with sodium ethoxide gave the oxazolidinone **6**, which was deprotonated and alkylated with allyl bromide to give a single diastereomer of the product **7**.[14] The high selectivity is thought to be a result of conformational effects arising from chelation of the ester sodium enolate with the (deprotonated) oxazolidinone nitrogen atom.[14] Reduction of the ester (in the presence of the oxazolidinone using calcium or lithium borohydride) and protection of the alcohol **8** gave the products **9** and **10**. The relative stereochemistry of the alcohol **8** was verified by single crystal X-ray diffraction (see ESI†).

The oxazolidinone **9** was protected to give the oxazolidinone **11**, which was subjected to ring-opening with allyl magnesium bromide to give the amide **12** (Scheme 3).[15] Ring-closing metathesis[16] then gave the 8-membered ring product **13** and oxidation of the alcohol gave the aldehyde **14** (akin to **4**).

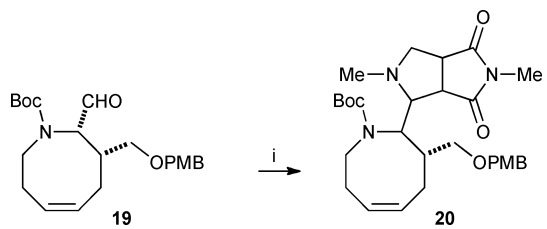
With one of the desired aldehydes in hand, we attempted some cycloaddition reactions. There are various methods reported for the formation of azomethine ylides.[12] To generate a 'non-stabilized' ylide, one method involves decarboxylation of an intermediate oxazolidinone formed from an aldehyde and an amino-acid.[17] On heating the aldehyde **14** with the amino-acid sarcosine (*N*-methyl glycine) in toluene, an inseparable mixture of many products was obtained. To generate the stabilized ylide, we heated the aldehyde **14** with sarcosine ethyl ester but this also gave a mixture of products.

As an alternative substrate, we alkylated the oxazolidinone **10** to give the oxazolidinone **15** (Scheme 4). This compound was subjected to ring-closing metathesis to give the 8-membered ring product **16**. Hydrolysis of the oxazolidinone **16** gave the amino-alcohol **17** which was protected as the N-Boc derivative **18**. Finally, oxidation of the alcohol gave the aldehyde **19** (akin to **3**).



Scheme 4 Preparation of aldehyde **19**. *Reagents and conditions*: i, $NaOH_{(s)}$, PhMe, K_2CO_3, Bu_4NHSO_4, heat, 1 h, 99%; ii, 2 × 3.3 mol% $Cl_2(PCy_3)[(CH_2NMes)_2C]Ru{=}CHPh$, PhMe, 40 °C, 2.5 h, 73%; iii, NaOH, EtOH, H_2O, 80 °C, 18 h, 95%; iv, Boc_2O, dioxane, H_2O, $NaHCO_3$, 98%; v, Dess–Martin periodinane, CH_2Cl_2, 0 °C, 2 h, 86%.

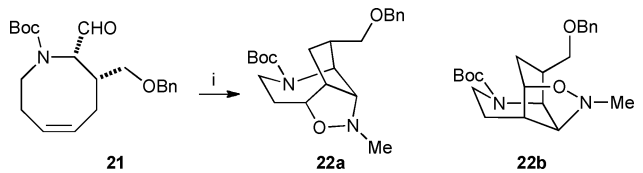
Unfortunately, we found that no discernable reaction took place on heating the aldehyde **19** with the amino-acid sarcosine or sarcosine ethyl ester or glycine ethyl ester in various solvents (PhMe, dioxane, DMF). At higher temperatures (130 °C, PhMe, sealed tube or 215 °C, DMF, microwave heating) decomposition occurred. We were able to show that the azomethine ylide was being formed by heating the aldehyde **19** with sarcosine in the presence of the dipolarophile *N*-methylmaleimide (Scheme 5). This gave a mixture of four diastereomeric products **20** from intermolecular cycloaddition.



Scheme 5 Intermolecular cycloaddition using the aldehyde **19**. *Reagents and conditions*: i, $MeHNCH_2CO_2H$, *N*-methylmaleimide, DMF, heat, 18 h, 77%.

We were disappointed that no transannular dipolar cycloaddition of the azomethine ylides took place. This may be compounded by the unactivated nature of the alkene (electron-withdrawing groups are known to promote such cycloadditions).[12] We were keen to demonstrate that dipolar cycloaddition was possible and were aware that nitrones are typically more amenable to cycloaddition with a range of alkene dipolarophiles.[18] Therefore, we heated the aldehyde **19** with *N*-methyl-hydroxylamine and were pleased to find that a single product was formed (65% yield as an oil) that had the desired mass and no longer contained the alkene functional group (see ESI†). We were unable to determine the regiochemistry

of the cycloaddition from the spectroscopic data and attempts to deprotect the Boc and/or PMB groups with acid gave a very polar product that did not provide any desired amide or ester products after acylation. Therefore, to avoid problems with concommitant deprotection of both the Boc and PMB groups, we converted the oxazolidinone **9** through the same sequence as performed with oxazolidinone **10** (shown in Scheme 4). This gave the analogous aldehyde **21** with which we carried out the same cycloaddition reaction using *N*-methyl-hydroxylamine (Scheme 6).



Scheme 6 Nitrone cycloaddition using the aldehyde **21**. *Reagents and conditions*: i, MeNHOH·HCl, EtOH, $NaHCO_3$, sealed tube, 125 °C, 4 h, 73% (**22a**).

We were pleased to find that a single cycloadduct was formed (73% yield), although once again we were unclear as to the regiochemistry of the cycloaddition reaction (product **22a** or **22b**). Removal of the N-Boc group with TFA and treatment with *p*-bromobenzoyl chloride gave a crystalline product, for which X-ray crystal structure analysis indicated the structure **23** (Fig. 2).

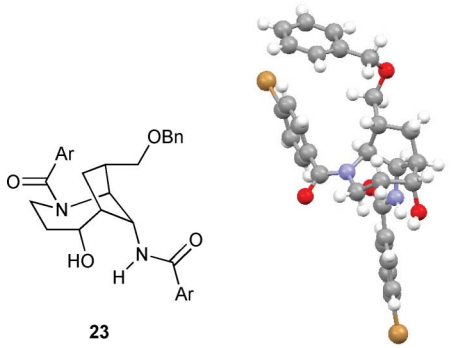


Fig. 2 X-ray structure of **23** (Ar = C_6H_4-*p*-Br), derived from **22a**.

The compound **23** must have derived from the cycloadduct **22a** (rather than **22b**), thereby showing that the cycloaddition of the nitrone (derived from aldehyde **21**) had occurred to give the undesired regiochemistry. After removal of the N-Boc group from **22a** and treatment with *p*-bromobenzoyl chloride, the amide **23** must have formed by acylation of both nitrogen atoms, together with breakage of the N–O bond and N-demethylation. It is not clear how this occurs, but one possibility is that acylation of the tertiary amine gives a quaternary ammonium salt that could fragment (N–O bond breakage) to give an iminium ion that hydrolyses to the secondary amide.

Conclusions

We have shown that a transannular dipolar cycloaddition onto an unactivated alkene in an eight-membered ring is possible using a nitrone, but not using an azomethine ylide. This led to the undesired regioisomer of the bridged tricyclic product. To form the desired pyrrolidine ring present in the sarain alkaloids using this approach, further work will be required to direct the regiochemistry and also allow cycloaddition of the azomethine ylide, possibly by activating the alkene dipolarophile with a suitable electron-withdrawing group.

Experimental

General methods

For general experimental details, including information on solvent purifications and the spectrometers used in this research, see previous descriptions.[19] For procedures and spectroscopic data for compounds not reported below, together with crystallographic data for the alcohol **8** and the amide **23**, see ESI.†

(*S*)-Ethyl 2-(2-oxo-oxazolidin-4-yl)acetate 6. Freshly prepared NaOEt (1.0 M, 85 mL, 85 mmol) was added to lactone **5**[20] (8 g, 34 mmol) in EtOH (170 mL) at room temperature. After 2 h, HCl (1.0 M, 85 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 100 mL), dried ($MgSO_4$) and evaporated. Purification by column chromatography on silica, eluting with EtOAc–Et_2O (1 : 4 to 3 : 2), gave the oxazolidinone **6** (4.2 g, 72%) as an oil; $[\alpha]_D^{20}$ −14.2 (2.3, MeOH); ν_{max}/cm^{-1} 3285, 1750, 1720; ^1H NMR (250 MHz, C_6D_6) δ = 6.16–5.99 (br, 1H), 3.80 (q, 2H, *J* 7 Hz), 3.68 (t, 1H, *J* 8 Hz), 3.36–3.25 (m, 1H), 3.22 (dd, 1H, *J* 8, 6 Hz), 1.83 (dd, 1H, *J* 17, 7.5 Hz), 1.62 (dd, 1H, *J* 17, 5.5 Hz), 0.88 (t, 3H, *J* 7 Hz); ^{13}C NMR (75 MHz, $CDCl_3$) δ = 170.4, 159.1, 69.4, 61.2, 48.9, 39.6, 14.5; HRMS (EI) found 173.0689, $C_7H_{11}NO_4$ requires (M) 173.0688; *m*/*z* (EI) 173 (5%), 129 (45), 86 (100); Found: C, 48.82; H, 6.55; N, 7.89; $C_7H_{11}NO_4$ requires C, 48.55; H, 6.40; N, 8.09%. Compound **6** has been reported, but no characterization data were given.[14]

(*R*)-Ethyl 2-[(*S*)-2-oxo-oxazolidin-4-yl]pent-4-enoate 7. Oxazolidinone **6** (0.2 g, 1.2 mmol) in THF (3 mL) was added to $NaN(TMS)_2$ (0.47 g, 2.43 mmol) in THF (6 mL) at −78 °C over 5 min. After 1 h, allyl bromide (0.2 mL, 2.4 mmol) in THF (3 mL) was added over 5 min and the mixture was warmed to −40 °C. After 4 h, saturated NH_4Cl solution (20 mL) was added, the mixture was extracted with CH_2Cl_2 (3 × 20 mL), dried ($MgSO_4$) and evaporated. Purification by column chromatography on silica, eluting with EtOAc–petrol (1 : 5 to 1 : 0), gave the oxazolidinone **7** as a single diastereoisomer (0.18 g, 70%) as an oil; $[\alpha]_D^{20}$ −24.5 (2.5, $CHCl_3$); ν_{max}/cm^{-1} 3255, 1750, 1720, 1640; ^1H NMR (400 MHz, $CDCl_3$) δ = 6.31–6.24 (br, 1H), 5.68 (ddt, 1H, *J* 17, 10, 7.5 Hz), 5.14–5.05 (m, 2H), 4.46 (t, 1H, *J* 8.5 Hz), 4.21–4.14 (m, 3H), 4.11–4.06 (m, 1H), 2.64 (td, 1H, *J* 7.5, 5.5 Hz), 2.43–2.28 (m, 2H), 1.26 (t, 3H, *J* 7 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ = 172.4, 159.2, 133.3, 118.4, 67.9, 61.3, 52.8, 49.5, 32.4, 14.1; HRMS (EI) found 213.0999, $C_{10}H_{15}NO_4$ requires (M) 213.1001; *m*/*z* (EI) 213 (20), 171 (50), 128 (100); Found: C, 56.03; H, 7.28; N, 6.32; $C_{10}H_{15}NO_4$ requires C, 56.33; H, 7.09; N, 6.57%. Compound **7** has been reported, but no characterization data were given.[14]

(*S*)-4-[(*R*)-1-Hydroxypent-4-en-2-yl]oxazolidin-2-one 8. $NaBH_4$ (0.92 g, 24 mmol) was added to oxazolidinone **7** (0.43 g, 2 mmol) and dry $CaCl_2$ (1.34 g, 12 mmol) in dry EtOH (63 mL) at 0 °C and the mixture was allowed to warm to room temperature. After 16 h, saturated $CaCO_3$ (23 mL) and sodium potassium tartrate (62 mL, 1.0 M) were added. The mixture was extracted with EtOAc (3 × 60 mL), dried ($MgSO_4$) and

evaporated. Purification by column chromatography on silica, eluting with EtOAc–petrol (7 : 3), gave the alcohol **8** (0.29 g, 85%) as needles; m.p. 57–58 °C; $[\alpha]_D^{20}$ 9.3 (2.5, MeOH); ν_{max}/cm^{-1} 3350, 2960, 2870, 1725; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 6.97–6.90 (br, 1H), 5.91–5.63 (m, 1H), 5.11–5.02 (m, 2H), 4.47 (t, 1H, *J* 8.5 Hz), 4.20–4.13 (m, 1H), 3.96–3.89 (m, 1H), 3.75 (dd, 1H, *J* 11, 4 Hz) 3.59 (dd, 1H, *J* 11, 6 Hz), 3.56–3.39 (br, 1H), 2.07–2.00 (m, 2H), 1.77–1.71 (m, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 160.5, 135.1, 117.6, 69.5, 62.2, 54.7, 44.5, 31.9; HRMS (EI) found 172.0973, $C_8H_{14}NO_3$ requires (MH) 172.0970; *m/z* (EI) 172 (10%), 140 (100); Found: C, 55.79; H, 7.58; N, 8.09; $C_8H_{13}NO_3$ requires C, 56.13; H, 7.65; N, 8.18%.

(*S*)-4-[(*R*)-1-(Benzyloxy)pent-4-en-2-yl]oxazolidin-2-one 9. TMSOTf (0.29 mL, 1.63 mmol) was added to the alcohol **8** (1.4 g, 8.2 mmol) and benzyl trichloroacetimidate (1.6 mL, 9.0 mmol) in CH_2Cl_2 (140 mL) at 0 °C and the mixture was allowed to warm to room temperature. After 18 h, the solvent was evaporated and the mixture was purified by column chromatography on silica, eluting with EtOAc–petrol (1 : 3), to give the ether **9** (1.3 g, 79%) as an oil; $[\alpha]_D^{22}$ −6.0 (0.5, CH_2Cl_2); ν_{max}/cm^{-1} 3260, 2910, 2860, 1740, 1640; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 7.35–7.20 (m, 5H), 5.92 (br, 1H), 5.77–5.60 (m, 1H), 5.10–5.00 (m, 2H), 4.56–4.39 (m, 3H), 4.17 (dd, 1H, *J* 8.5, 7 Hz), 3.90 (q, 1H, *J* 7 Hz), 3.55 (dd, 1H, *J* 9.5, 4 Hz), 3.44 (dd, 1H, *J* 9.5, 6.5 Hz), 2.05 (t, 2H, *J* 7 Hz), 2.00–1.75 (m, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 159.9, 137.9, 135.0, 128.5, 127.8, 127.7, 117.7, 73.4, 70.2, 68.8, 54.9, 42.6, 31.8; HRMS (ES) found 284.1253, $C_{15}H_{19}NO_3Na$ requires (MNa) 284.1263; *m/z* (ES) 284 (100%), 262 (22).

(*S*)-4-[(*R*)-1-(4-Methoxybenzyloxy]pent-4-en-2-yl)oxazolidin-2-one 10. To a suspension of NaH (50 mg, 2 mmol) in Et_2O (28 ml) was added *p*-methoxybenzyl alcohol (2.4 mL, 20 mmol) at room temperature. After 30 min, the mixture was cooled to 0 °C and Cl_3CCN (2.1 mL, 20 mmol) was added. The mixture was allowed to warm to room temperature. After 4 h, the solvent was evaporated, then petrol (30 mL) and MeOH (1 mL) were added. The mixture was filtered through celite and evaporated. To this oil was added alcohol **8** (1.7 g, 9.9 mmol) in CH_2Cl_2 (56 mL) and CSA (250 mg, 1 mmol) at room temperature. After 18 h, saturated aqueous $NaHCO_3$ (15 mL) was added, the mixture was extracted with Et_2O (3 × 60 mL), and the organic layers were combined, washed with water (100 mL), dried ($MgSO_4$) and evaporated. Purification by column chromatography on silica, eluting with EtOAc–petrol (1 : 4 to 4 : 5) gave the ether **10** (2.53 g, 81%) as an oil; $[\alpha]_D^{20}$ −2.0 (1.0, CH_2Cl_2); ν_{max}/cm^{-1} 3260, 2910, 2860, 1750, 1640; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 7.23 (d, 2H, *J* 8.5 Hz), 6.90 (d, 2H, *J* 8.5), 5.77–5.61 (m, 1H), 5.53 (br, 1H), 5.08–5.02 (m, 2H), 4.48–4.45 (m, 1H), 4.41 (br, 2H), 4.18–4.12 (dd, 1H, *J* 8.5, 7 Hz), 3.91–3.84 (m, 1H), 3.82 (s, 3H), 3.54 (dd, 1H, *J* 9.5, 4 Hz), 3.37 (dd, 1H, *J* 9.5, 7 Hz), 2.10–1.99 (m, 2H), 1.97–1.84 (m, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 159.6, 159.3, 134.9, 129.8, 129.4, 117.6, 113.9, 73.0, 70.1, 68.8, 55.3, 55.0, 42.6, 31.9; HRMS (ES) found 314.1356, $C_{16}H_{21}NO_4Na$ requires (MNa) 314.1368.

(*S*)-4-[(*R*)-1-Benzyloxymethyl-but-3-enyl]-3-(4-methoxybenzyl)-oxazolidin-2-one 11. The oxazolidinone **10** (1.50 g, 8.76 mmol) in THF (15 mL) was added to a suspension of KH (30% in oil, 1.40 g, 10.5 mmol, prewashed with dry pentane under N_2) in THF (30 mL) at 0 °C and the mixture was heated under reflux. After 20 min, the mixture was cooled to room temp. and *n*-Bu_4NI (330 mg, 0.88 mmol) and *p*-methoxybenzyl chloride (1.37 mL, 10.1 mmol) were added. After 22 h, brine (15 mL) was added and the mixture was extracted with EtOAc (3 × 20 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), filtered and evaporated. Purification by column chromatography on silica, eluting with EtOAc–petrol (1 : 4), gave the oxazolidinone **11** (1.73 g, 79%) as an oil; $[\alpha]_D^{22}$ +18.2 (0.55, CH_2Cl_2); ν_{max}/cm^{-1} 2905, 1740; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 7.34–7.11 (m, 5H), 7.14 (d, 2H, *J* 8.5 Hz), 6.83 (d, 2H, *J* 8.5 Hz), 5.64–5.44 (m, 1H), 5.03–4.89 (m, 2H), 4.67 (d, 1H, *J* 15 Hz), 4.35 (ABq, 2H, *J* 12 Hz), 4.20–4.13 (m, 2H), 4.02 (d, 1H, *J* 15 Hz), 3.85 (td, 1H, *J* 7.5, 2 Hz), 3.77 (s, 3H), 3.40–3.26 (m, 2H), 2.10–1.91 (m, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 159.0, 158.6, 137.6, 135.3, 129.3, 128.1, 127.7, 127.5, 127.2, 116.9, 113.9, 72.9, 68.8, 63.7, 56.2, 55.0, 45.5, 37.9, 28.2; HRMS (ES) found 404.1843, $C_{23}H_{27}NO_4Na$ requires (MNa) 404.1838; Found: C, 72.60; H, 7.00; N, 3.38; $C_{23}H_{27}NO_4$ requires C, 72.42; H, 7.13; N, 3.67%.

But-3-enoic acid [(1*S*,2*R*)-2-benzyloxymethyl-1-hydroxymethyl-pent-4-enyl]-(4-methoxybenzyl)amide 12. Allyl magnesium bromide (2.83 mL, 2.83 mmol, 1 M in Et_2O) was added over 5 min to the oxazolidinone **11** (540 mg, 1.41 mmol) in THF (10 mL) at −78 °C. After 2.5 h, saturated $NH_4Cl_{(aq)}$ (5 mL) was added, the mixture was allowed to warm to room temp., and was extracted with Et_2O (3 × 15 mL). The combined organic extracts were dried (Na_2SO_4), filtered and evaporated. Purification by column chromatography on silica, eluting with EtOAc–petrol (1 : 3), gave the diene **12** (380 mg, 63%) as an oil; $[\alpha]_D^{22}$ −8.0 (0.5, CH_2Cl_2); ν_{max}/cm^{-1} 3405, 3075, 2935, 2865, 1635, 1615; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 7.40–7.24 (m, 5H), 7.03 (d, 2H, *J* 8.5 Hz), 6.84 (d, 2H, *J* 8.5 Hz), 6.05–5.65 (m, 2H), 5.24–4.94 (m, 4H), 4.58 (d, 1H, *J* 16 Hz), 4.49 (ABq, 2H, *J* 12 Hz), 4.16 (d, 1H, *J* 16 Hz), 3.79 (s, 3H), 3.74–3.61 (m, 2H), 3.53 (dd, 1H, *J* 9.5, 3 Hz), 3.39 (dd, 1H, *J* 9.5, 2.5 Hz), 3.34–3.12 (m, 3H), 2.74–2.59 (m, 1H), 2.43–2.30 (m, 1H), 2.21–2.04 (m, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 173.5, 159.4, 138.3, 136.7, 131.3, 129.1, 128.5, 128.3, 128.1, 127.9, 118.6, 116.7, 114.4, 73.4, 68.4, 64.2, 63.9, 55.4, 54.2, 39.9, 35.5, 32.6; HRMS (ES) found 424.2486, $C_{26}H_{34}NO_4$ requires (MH) 424.2488; Found: C, 73.82; H, 7.96; N, 3.02; $C_{26}H_{33}NO_4$ requires C, 73.73; H, 7.85; N, 3.31%.

(Z)-(7*R*,8*S*)-7-Benzyloxymethyl-8-hydroxymethyl-1-(4-methoxybenzyl)-3,6,7,8-tetrahydro-1*H*-azocin-2-one 13. Grubbs catalyst 2nd generation catalyst (38 mg, 0.045 mmol) in 1,2-dichloroethane (2 mL) was added *via* canula to the diene **12** (380 mg, 0.90 mmol) in degassed 1,2-dichloroethane (400 mL) at 80 °C under N_2. After 4.5 h, an additional portion of GrubbsII catalyst (38 mg, 0.045 mmol) in 1,2-dichloroethane (2 mL) was added and heating was continued. After 4 h, the mixture was cooled to room temp. and the solvent was evaporated. Purification by column chromatography on silica gel, eluting with EtOAc–petrol (1 : 1) + 1% v/v Et_3N, gave the oxazolidinone **13** (270 mg, 58%) as an oil; $[\alpha]_D^{22}$ +28.6 (0.55, CH_2Cl_2); ν_{max}/cm^{-1} 3385, 2930, 2870, 1610; ^{1}H NMR (250 MHz, $CDCl_3$) δ = 7.45–7.22 (m, 5H), 7.14 (d, 2H, *J* 9 Hz), 6.71 (d, 2H, *J* 9 Hz), 5.70–5.55 (m, 2H), 5.14 (d, 1H, *J* 15 Hz), 4.51 (ABq, 2H, *J* 12 Hz), 4.42–4.30 (m, 1H), 4.10–3.93 (m, 1H), 3.82 (d, 1H, *J* 15 Hz), 3.77 (s, 3H), 3.75–3.65 (m, 1H), 3.58–3.15 (m, 3H), 2.27–1.95 (m, 2H), 1.78–1.58 (m, 2H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 174.3, 158.9, 137.5, 131.0,

128.7, 128.5, 128.3, 128.1, 127.9, 126.6, 114.2, 73.6, 71.5, 62.4, 61.1, 55.3, 46.4, 42.1, 40.1, 26.3; HRMS (ES) found 396.2172, $C_{24}H_{30}NO_4$ requires (MH) 396.2175; Found: C, 72.60; H, 7.00; N, 3.38; $C_{24}H_{29}NO_4$ requires C, 72.89; H, 7.39; N, 3.54%.

(*Z*)-(2*S*,3*R*)-3-Benzyloxymethyl-1-(4-methoxy-benzyl)-8-oxo-1,2,3,4,7,8-hexahydro-azocine-2-carbaldehyde 14. Dess–Martin periodinane (118 mg, 0.28 mmol) was added to the lactam **13** (100 mg, 0.25 mmol) in CH_2Cl_2 (2 mL) at 0 °C. After 2 h, Et_2O (10 mL) and petrol (10 mL) were added, the mixture was filtered on a short pad of silica (rinsing with Et_2O–petrol, 1 : 1). The solvent was evaporated to give the aldehyde **14** (60 mg, 60%) as an oil; $[\alpha]_D^{22}$ −37.5 (0.56, CH_2Cl_2); ν_{max}/cm^{-1} 2960, 2920, 2850, 1725, 1655; ^1H NMR (250 MHz, $CDCl_3$) δ = 9.47 (s, 1H), 7.35–7.16 (m, 5H), 7.15 (d, 2H, *J* 8.5 Hz), 6.65 (d, 2H, *J* 8.5 Hz), 5.85–5.63 (m, 2H), 4.72 (br d, 1H, *J* 14 Hz), 4.48–4.42 (m, 1H), 4.38 (ABq, 2H, *J* 12 Hz), 4.19 (br d, 1H, *J* 14 Hz), 3.70 (s, 3H), 3.55—3.35 (m, 2H), 3.06 (dd, 1H, *J* 14, 4.5 Hz), 2.87 (dd, 1H, *J* 14, 5.5 Hz), 2.40–2.15 (m, 2H), 1.95–1.82 (m, 1H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 198.8, 173.7, 159.0, 137.0, 129.8, 128.5, 127.9, 127.8, 114.0, 73.2, 71.9, 66.4, 55.3, 50.8, 43.2, 29.8, 24.8; HRMS (ES) found 416.1830, $C_{24}H_{27}NO_4Na$ requires (MNa) 416.1838; *m*/*z* (ES) 416 (48%), 394 (100).

(*S*)-4-[(*R*)-1-(4-Methoxybenzyloxy)pent-4-en-2-yl]-3-(but-3-enyl)oxazolidin-2-one 15. NaOH (610 mg, 15 mmol), K_2CO_3 (620 mg, 4.5 mmol) and *n*-Bu_4NHSO_4 (70 mg, 0.2 mmol) were added to the oxazolidinone **10** (640 mg, 2 mmol) in PhMe (11 mL). To this mixture was added 4-bromo-1-butene (0.64 mL, 6.1 mmol) and the mixture was heated under reflux. After 30 min, water (15 mL) was added and the mixture was extracted with Et_2O (3 × 40 mL). The organic layers were dried ($MgSO_4$) and evaporated to give the diene **15** (697 mg, 99%) as an oil; $[\alpha]_D^{20}$ 7.6 (7.5, MeOH); ν_{max}/cm^{-1} 2910, 2860, 1740, 1640, 1610; ^1H NMR (250 MHz, $CDCl_3$) δ = 7.21 (d, 2H, *J* 9 Hz), 6.90 (d, 2H, *J* 9 Hz), 5.82–5.67 (m, 2H), 5.14–5.04 (m, 4H), 4.42 (d, 1H, *J* 11.5 Hz), 4.36 (d, 1H, *J* 11.5 Hz), 4.2–4.14 (m, 2H), 4.09–4.05 (m, 1H), 3.82 (s, 3H), 3.59 (dt, 1H, *J* 14, 7.5 Hz), 3.48 (dd, 1H, *J* 9.5, 3.5 Hz) 3.37 (dd, 1H, *J* 9.5, 6 Hz), 3.06–2.95 (ddd, 1H, *J* 14, 7, 5.5 Hz), 2.37–2.23 (m, 2H), 2.13–2.01 (m, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 159.2, 158.5, 135.4, 134.6, 129.8, 129.2, 117.3, 117.2, 113.8, 72.9, 68.7, 63.8, 56.3, 55.2, 41.1, 38.4, 31.6, 28.6; HRMS (ES) found 368.1854, $C_{20}H_{27}NO_4Na$ requires (MNa) 368.1838; Found: C, 69.31; H, 7.84; N, 4.00; $C_{20}H_{27}NO_4$ requires C, 69.54; H, 7.88; N, 4.05%.

(10*R*,10a*S*,*Z*)-10-[(4-Methoxybenzyloxy)methyl]-5,6,10,10a-tetrahydro-1*H*-oxazolo[3,4-a]azocin-3(9*H*)-one 16. Diene **15** (116 mg, 0.34 mmol) was added to de-gassed dry PhMe (85 mL) at room temperature. Grubbs 2nd generation ruthenium catalyst[14] (9.5 mg, 0.007 mmol, 3.3 mol%) was added at 40 °C. After 1 h, further catalyst (9.5 mg, 0.0073 mmol, 3.3 mol%) was added. After a further 1 h, DMSO (0.5 mL) was added and the mixture was allowed to cool to room temperature. After 18 h, the solvent was evaporated, and the residue was purified by column chromatography on silica, eluting with EtOAc–petrol (1 : 9 to 2 : 3), to give the alkene **16** (78.6 mg, 73%) as an oil; $[\alpha]_D^{20}$ −21.1 (2.5, CH_2Cl_2); ν_{max}/cm^{-1} 2930, 2860, 1740, 1610; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.23 (d, 2H, *J* 9 Hz), 6.89 (d, 2H, *J* 9 Hz), 5.68–5.58 (m, 2H), 4.41 (d, 1H, *J* 11.5 Hz), 4.37 (d, 1H, *J* 11.5 Hz), 4.23–4.13 (m, 3H), 3.85–3.77 (m, 1H), 3.81 (s, 3H), 3.39 (dd, 1H, *J* 10, 6 Hz), 3.34 (dd, 1H, *J* 10, 7.5, Hz), 3.12 (ddd, 1H, *J* 15, 4, 3 Hz), 2.69–2.64 (m, 1H), 2.60–2.52 (m, 1H), 2.30 (m, 2H), 2.17–2.13 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 159.3, 129.8, 129.5, 129.3, 125.7, 113.8, 73.1, 70.3, 63.7, 57.4, 55.2, 43.0, 39.7, 27.6, 26.7; HRMS (ES) found 340.1517, $C_{18}H_{23}NO_4Na$ requires (MH) 340.1525.

(*Z*)-{3-[(4-Methoxybenzyloxy)methyl]-1,2,3,4,7,8-hexahydro-azocin-2-yl}methanol 17. NaOH (342 mg, 8.56 mmol) in ethanol (5.2 mL) and water (1.7 mL) was added to oxazolidinone **16** (435 mg, 1.52 mmol) and the mixture was heated under reflux. After 18 h, CH_2Cl_2 (10 mL) was added and the mixture was washed with brine (3 × 15 mL). The organic layer was dried ($MgSO_4$) and the solvent was evaporated. Purification by column chromatography on silica, eluting with CH_2Cl_2–MeOH–NH_3 (95 : 5 : 1), gave the amine **17** (387 mg, 95%) as an oil; $[\alpha]_D^{20}$ −8.1 (3.8, MeOH); ν_{max}/cm^{-1} 3380, 3330, 3010; ^1H NMR (250 MHz, $CDCl_3$) δ = 7.25 (d, 2H, *J* 8.5 Hz), 6.89 (d, 2H, *J* 8.5 Hz), 5.85–5.64 (m, 2H), 4.42 (s, 2H), 3.81 (s, 3H), 3.52–3.38 (m, 4H), 3.10–3.01 (m, 1H), 2.89 (dt, 1H, *J* 7, 4 Hz), 2.61–2.47 (m, 2H), 2.30–1.87 (m, 4H); ^{13}C NMR (63 MHz, $CDCl_3$) δ = 159.3, 130.4, 130.0, 129.8, 129.3, 113.8, 73.2, 71.1, 64.7, 59.6, 55.3, 49.3, 41.8, 30.3, 28.5; HRMS (ES) found 292.1912, $C_{17}H_{26}NO_3$ requires (MH) 292.1913.

(*Z*)-*tert*-Butyl 3-((4-methoxybenzyloxy)methyl)-2-(hydroxymethyl)-3,4,7,8-tetrahydroazocine-1(2*H*)-carboxylate 18. $NaHCO_3$ (72 mg, 0.86 mmol) in water (1.25 mL) was added to the amine **17** (249 mg, 0.86 mmol) in dioxane (2.5 mL) at room temperature. After 10 min, further $NaHCO_3$ was added until the pH of the solution reached 10. To the mixture was added di-*tert*-butyldicarbonate (0.2 mL, 0.86 mmol). After 18 h, water (10 mL) was added and the mixture was extracted with CH_2Cl_2 (3 × 10 mL). The organic layers were dried ($MgSO_4$), evaporated and purified by column chromatography on silica, eluting with EtOAc-petrol (1 : 1), to give the carbamate **18** (329 mg, 98%) as an oil; $[\alpha]_D^{20}$ 2.9 (0.7, MeOH); ν_{max}/cm^{-1} 3430, 3010, 2920, 2860, 1690; ^1H NMR (500 MHz, $CDCl_3$) δ = 7.27–7.19 (m, 2H), 6.88–6.82 (m, 2H), 5.79–5.67 (m, 2H), 4.52–4.38 (m, 2H), 4.13–3.87 (m, 4H), 3.81 (s, 3H), 3.52–3.34 (m, 2H), 2.72–2.62 (m, 1H), 2.41–2.35 (m, 1H), 2.31–1.98 (m, 4H), 1.45 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 159.1, 155.7, 130.7, 130.6, 129.3, 129.1, 113.8, 79.4, 72.7, 72.6, 63.4, 61.8, 55.3, 50.8, 43.5, 28.5, 27.2, 27.1; HRMS (ES) found 414.2241, $C_{22}H_{33}NO_5Na$ requires (MNa) 414.2256.

(*Z*)-*tert*-Butyl 3-[(4-methoxybenzyloxy)methyl]-2-formyl-3,4,7,8-tetrahydroazocine-1(2*H*)-carboxylate 19. Dess–Martin periodinane (330 mg, 0.76 mmol) was added to the alcohol **18** (259 mg, 0.66 mmol) in CH_2Cl_2 (3.6 mL) at 0 °C and the mixture was allowed to warm to room temperature. After 4 h, NaOH (1 M, 2.6 mL) was added and the mixture was extracted with Et_2O (3 × 10 mL). The organic layers were dried ($MgSO_4$) and evaporated to give the aldehyde **19** (221 mg, 86%) as an oil; $[\alpha]_D^{20}$ −22.4 (1.05, CH_2Cl_2); ν_{max}/cm^{-1} 2930, 2860, 1735, 1685; ^1H NMR (250 MHz, $CDCl_3$, mixture of rotamers) δ = 9.58 (s, 0.5H), 9.53 (s, 0.5H), 7.27 (d, 2H, *J* 8.5 Hz), 6.89–6.83 (m, 2H), 5.90–5.66 (m, 2H), 4.55 (d, 0.5H, *J* 11.5 Hz), 4.52 (d, 0.5H, *J* 11.5 Hz), 4.45–4.40 (m, 0.5H), 4.39 (d, 0.5H, *J* 11.5 Hz), 4.32 (d, 0.5H, *J* 11.5 Hz), 4.19–4.10 (m, 0.5H), 3.82–3.71 (m, 1H), 3.81 (s, 3H), 3.68-3.48 (m, 1H), 3.21–3.07 (m, 1H), 2.76–2.34 (m, 4H), 2.20–1.97 (m, 2H), 1.47 (s, 4.5H), 1.36 (s, 4.5H); ^{13}C NMR (63 MHz, $CDCl_3$, mixture of rotamers)

δ = 199.4, 198.5, 159.2, 159.0, 155.8, 154.7, 131.0, 130.8, 130.6, 130.4, 130.2, 129.6, 129.3, 129.1, 113.8, 113.6, 82.2, 80.6, 72.6, 72.4, 71.3, 70.9, 68.2, 67.9, 55.2, 49.7, 49.4, 42.3, 41.5, 28.3, 28.1, 27.8, 27.6, 27.4, 27.3; HRMS (ES) found 412.2113, $C_{22}H_{31}NO_5Na$ requires (MNa) 412.2100.

Evidence that this product was a mixture of rotamers, rather than diastereomers, was obtained in two ways: firstly, reduction (DIBAL-H) gave the alcohol **18**, which was a single diastereomer by NMR spectroscopy; secondly, treatment of **19** with DBU gave recovered **19** together with a new aldehyde with two (rotameric) singlets in the ^{1}H NMR spectrum for the aldehyde CH at δ = 9.70 and 9.63.

Intermolecular cycloadducts 20. Sarcosine (36 mg, 0.4 mmol) and *N*-methylmaleimide (46 mg, 0.4 mmol) were added to the aldehyde **19** (73 mg, 0.19 mmol) in DMF (1 mL) and the mixture was heated at 120 °C. After 18 h, the mixture was cooled and was filtered through silica (rinsing with EtOAc). The solvent was evaporated to give the cycloadducts **20** as an oil; ^{1}H NMR (500 MHz, $CDCl_3$, mixture of 4 diastereoisomers) δ = 7.30–7.20 (m, 8H), 6.90–6.84 (m, 8H), 5.82–5.66 (m, 8H), 4.52–4.37 (m, 8H), 4.22–4.10 (m, 4H), 3.85–3.79 (m, 8H), 3.81–3.79 (m, 12H), 3.67–3.03 (m, 28H), 2.95–2.89 (m, 12H), 2.67–2.30 (m, 4H), 2.34–2.27 (m, 12H), 2.20–1.95 (m, 16H), 1.48–1.45 (m, 36H); HRMS (ES) found 528.3054, $C_{29}H_{42}N_3O_6$ requires (MH) 528.3074.

(2*S*,3*R*,*Z*)-*tert*-Butyl 3-(benzyloxymethyl)-2-formyl-3,4,7,8-tetrahydroazocine-1(2*H*)-carboxylate 21. Dess–Martin periodinane (254 mg, 0.6 mmol) was added to the alcohol (OBn equivalent of OPMB compound **18** – for its preparation and characterization, see ESI†) (189 mg, 0.53 mmol) in CH_2Cl_2 (1.5 mL) at 0 °C and the mixture was allowed to warm to room temperature. After 4 h, NaOH (1 M, 2.0 mL) was added and the mixture was extracted with Et_2O (3 × 10 mL). The organic layers were dried ($MgSO_4$) and evaporated and the residue was purified by column chromatography on silica, eluting with EtOAc–petrol (15 : 85), to give the aldehyde **21** (131 mg, 70%) as an oil; $[\alpha]_D^{20}$ −10.7 (2.1, CH_2Cl_2); ν_{max}/cm^{-1} 2930, 1730, 1710, 1680; ^{1}H NMR (500 MHz, $CDCl_3$, mixture of rotamers) δ = 9.53 (s, 0.5H), 9.78 (s, 0.5H), 7.28–7.19 (m, 5H), 5.83–5.65 (m, 2H), 4.57–4.52 (m, 1H), 4.43–4.34 (m, 1.5H), 4.11–4.07 (m, 0.5H), 3.78–3.76 (m, 0.5H), 3.67–3.65 (m, 0.5H), 3.63–3.62 (m, 0.5H), 3.45–3.44 (m, 0.5H), 3.16 (t, 0.5H, *J* 10 Hz), 3.09 (t, 0.5H, *J* 10 Hz), 2.67–2.37 (m, 4H), 2.14–1.97 (m, 2H), 1.37 (s, 4.5H), 1.25 (s, 4.5H); ^{13}C NMR (100 MHz, $CDCl_3$, mixture of rotamers) δ = 199.5, 198.6, 155.9, 154.8, 138.9, 138.5, 130.9, 130.4, 130.3, 129.6, 128.4, 128.3, 127.7, 127.6, 127.6, 127.4, 82.3, 80.7, 73.1, 72.8, 71.6, 71.2, 68.3, 68.0, 49.8, 49.4, 42.3, 41.5, 28.3, 28.2, 27.8, 27.6, 27.5, 27.4; HRMS (ES) found 360.2184, $C_{21}H_{30}NO_4$ requires (MH) 360.2175; *m*/*z* (ES) 384 (100%); 382 (95), 360 (20), 304 (100).

Cycloadduct 22a. $NaHCO_3$ (102 mg, 1.22 mmol) was added to the aldehyde **21** (97 mg, 0.27 mmol), and N-methylhydroxylamine·HCl (69 mg, 0.81 mmol) in EtOH (2.8 mL) and the mixture was heated in a sealed tube at 125 °C. After 4 h, the solvent was evaporated, H_2O (10 mL) was added and the mixture was extracted with EtOAc (3 × 8 mL). The organic layers were dried ($MgSO_4$) and the solvent was evaporated. Purification by column chromatography on silica, eluting with EtOAc–petrol (1 : 4), gave the cycloadduct **22a** (76 mg, 72%) as an oil; $[\alpha]_D^{20}$ 4.7 (1.8, CH_2Cl_2); ν_{max}/cm^{-1} 2950, 1680; ^{1}H NMR (500 MHz, $CDCl_3$, mixture of rotamers) δ = 7.38–7.29 (m, 5H), 4.56–4.48 (m, 2.5H), 4.41–4.39 (m, 1H), 4.24–4.23 (m, 0.5H), 3.83–3.73 (m, 1H), 3.70–3.65 (m, 0.5H), 3.55–3.37 (m, 3.5H), 3.21–3.14 (m, 1H), 2.72 (s, 1.5H), 2.71 (s, 1.5H), 2.36 (m, 1H), 1.99-1.86 (m, 1H), 1.76–1.66 (m, 3H), 1.48 (s, 4.5H), 1.43 (s, 4.5H); ^{13}C NMR (125 MHz, $CDCl_3$, mixture of rotamers) δ = 156.2, 155.8, 138.5, 138.3, 128.5, 128.4, 127.7, 127.6, 127.5, 79.4, 79.3, 77.7, 77.3, 74.2, 73.9, 73.8, 73.3, 73.2, 73.1, 59.8, 59.3, 49.4, 49.2, 48.7, 48.6, 47.6, 47.1, 39.6, 38.5, 29.1, 28.8, 28.6, 28.5, 25.6, 25.3; HRMS (ES) found 388.2373, $C_{22}H_{32}N_2O_4$ requires (M) 388.2362.

Amide product 23. TFA (3 mL, 0.4 mmol) was added to the cycloadduct **22a** (127 mg, 0.33 mmol) in CH_2Cl_2 (9 mL) at room temperature. After 45 min, the solvent was evaporated, toluene (20 mL) was added and the solvent was evaporated. Purification by column chromatography on silica, eluting with CH_2Cl_2–MeOH–NH_3 (9.7 : 0.3 : 0.1), gave the secondary amine (80 mg, 84%) as an oil; $[\alpha]_D^{22}$ 3.9 (2.5, CH_2Cl_2); ν_{max}/cm^{-1} 3410, 2950; ^{1}H NMR (500 MHz, C_6D_6) δ = 8.50 (br, 1H), 7.38–7.21 (m, 5H), 4.44 (d, 1H, *J* 12 Hz), 4.31 (d, 1H, *J* 12 Hz), 3.91 (d, 1H, *J* 7.5 Hz), 3.86 (dt, 1H, *J* 11, 2 Hz), 3.57 (ddd, 1H, *J* 14, 9.5. 6 Hz), 3.45 (dd, 1H, *J* 9, 5 Hz), 3.35 (t, 1H, *J* 7.5 Hz), 3.23 (dd, 1H, *J* 9, 5 Hz), 3.17 (dt, 1H, *J* 14, 6 Hz), 2.87–2.84 (m, 1H), 2.68–2.64 (m, 1H), 2.62 (s, 3H), 1.55–1.32 (m, 4H); ^{13}C NMR (125 MHz, C_6D_6) δ = 138.7, 128.3, 128.0, 127.8, 76.2, 73.2, 72.4, 72.3, 60.6, 49.9, 47.2, 42.5, 38.2, 26.6, 25.4; HRMS (ES) found 289.1915, $C_{17}H_{25}N_2O_2$ requires (MH) 289.1916. To this amine (60 mg, 0.21 mmol) in CH_2Cl_2 (1 mL) was added DMAP (13 mg, 0.11 mmol), 4-bromobenzoyl chloride (0.12 g, 0.53 mmol) and triethylamine (0.088 mL, 0.63 mmol) at room temperature. After 2.5 h, $NaHCO_3$ (10 mL) was added and the mixture was extracted with Et_2O (3 × 15 mL). The organic layers were dried ($MgSO_4$) and the solvent was evaporated to give the amide **23** (67 mg, 48%) as needles, which was recrystallized from EtOAc–Et_2O; m.p. 242–246 °C; ^{1}H NMR (500 MHz, $CDCl_3$, rotamers) δ = 8.42–8.33 (s, 1H), 7.69–7.56 (m, 4H), 7.40–7.22 (m, 7H), 7.13–7.06 (m, 2H), 4.61–4.15 (m, 4H), 3.89–3.44 (m, 2H), 3.21–3.16 (m, 1H), 3.05–3.00 (m, 1H), 2.90–2.55 (m, 1H), 2.49–2.41 (m, 1H), 2.16–2.04 (m, 2H), 1.65–1.55 (m, 1H), 1.31–1.19 (m, 2H), 0.90–0.82 (m, 1H); HRMS (ES) found 641.0679, $C_{30}H_{31}N_2O_4{}^{79}Br_2$ requires (MH) 641.0651; *m*/*z* (ES) 645 (50%), 643 (100), 641 (50).

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Notes and references

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