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# Asymmetric Synthesis of the Tetraponerine Alkaloids

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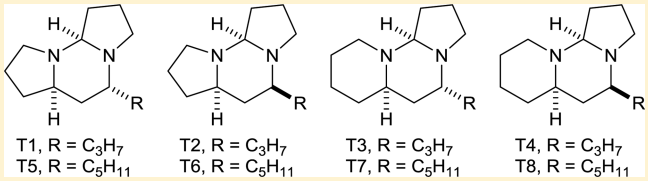
Supporting Information

**ABSTRACT:** The asymmetric syntheses of all eight tetraponerine alkaloids (T1−T8) were achieved using the diastereoselective conjugate additions of lithium amide reagents in the key stereodefining steps. Conjugate addition of either lithium (*R*)-*N*-allyl-*N*-(α-methylbenzyl)amide or lithium (*R*)-*N*-(but-3-en-1-yl)-*N*-(α-methylbenzyl)amide to *tert*-butyl sorbate was followed by ring-closing metathesis of the resultant *N*-alkenyl β-amino esters, reduction to the corresponding aldehydes, and reaction with *tert*-butyl (triphenylphosphoranylidene)-acetate. Subsequent conjugate addition of the requisite antipode of lithium *N*-benzyl-*N*-(α-methylbenzyl)amide to the resultant α,β-unsaturated esters gave a range of diamines for elaboration to T1−T8 via a sequence involving reduction of the ester moiety to give the corresponding aldehyde, olefination, tandem hydrogenation/hydrogenolysis, and cyclization upon reaction with 4-bromobutanal to give the tricyclic skeleton.




## INTRODUCTION

Tetraponerines 1−8 (which are also known as T1−T8, respectively) are a series of tricyclic aminals first isolated from the paralyzing venom of the New Guinean pseudomyrmecine ant *Tetraponera sp.*[1] These alkaloids represent the major constituents of the contact poison secreted by host ants as a defense against enemy colonies: when smeared with the contact poison, enemies display signs of paralysis and ultimately death, presumably by inhibition of nicotinic acetylcholine receptors.[2] The structures of the tetraponerine alkaloids are based on either a decahydrodipyrrolo[1,2-*a*:1′,2′-*c*]pyrimidine skeleton **1** (for tetraponerines 1, 2, 5 and 6) or a decahydro-5*H*-pyrido[1,2-*c*]pyrrolo[1,2-*a*]pyrimidine skeleton **2** (for tetraponerines 3, 4, 7, and 8), with a C(5)-alkyl substituent being present in all cases. Within each heterocyclic series, the alkaloids differ in their configurations at C(5) and also in the identity of the C(5)-alkyl substituent (Figure 1). (+)-Tetraponerine 8 is the only member of this family for which an X-ray crystal structure has been obtained to confirm both its gross structure and relative configuration.[1] The absolute configurations of tetraponerines 3−8 have been established by separate chemical syntheses and comparison of the specific rotations for the natural and synthetic material.[3−5] Synthetic samples of (+)-tetraponerine 1 and (+)-tetraponerine 2 have also been prepared,[5,6] although the absolute configurations of the natural materials have not been unambiguously established as only very small amounts were obtained from natural sources.[4,7] The unusual tricyclic aminal structure of the tetraponerine alkaloids, as well as their potent insecticidal activity, has meant that they have become popular targets for total synthesis. Since their isolation in 1987, there have been several syntheses of these alkaloids in both racemic[8] and enantiopure[3−6,9] form.[10,11] Herein, we report total syntheses of all eight tetraponerine alkaloids using our diastereoselective lithium amide conjugate addition methodology[12] in the key stereodefining steps.

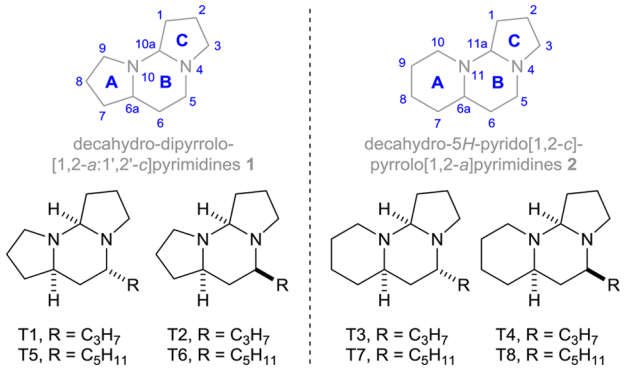



**Figure 1.** Structures of the tetraponerine alkaloids T1−T8.

Our divergent synthetic strategy toward the tetraponerine alkaloids involved two iterative lithium amide conjugate additions to install the requisite stereochemistry. In the first instance, conjugate addition of either lithium (*R*)-*N*-allyl-*N*-(α-methylbenzyl)amide (*R*)-**4** (*n* = 1) or lithium (*R*)-*N*-(but-3-en-1-yl)-*N*-(α-methylbenzyl)amide (*R*)-**5** (*n* = 2) to *tert*-butyl sorbate **3**,[13−15] followed by ring-closing metathesis of the resultant *N*-alkenyl β-amino ester **6** (*n* = 1 or 2) and homologation, would give the key α,β-unsaturated ester **7** (*n* = 1 or 2). Subsequent conjugate addition of the requisite antipode of lithium *N*-benzyl-*N*-(α-methylbenzyl)amide **8** to α,β-unsaturated ester **7** (*n* = 1 or 2) would then provide a range of diamines **9** and **10** (*n* = 1 or 2 in both cases) for elaboration. In each case, a sequence involving reduction of the ester moiety to the corresponding aldehyde, olefination, and tandem

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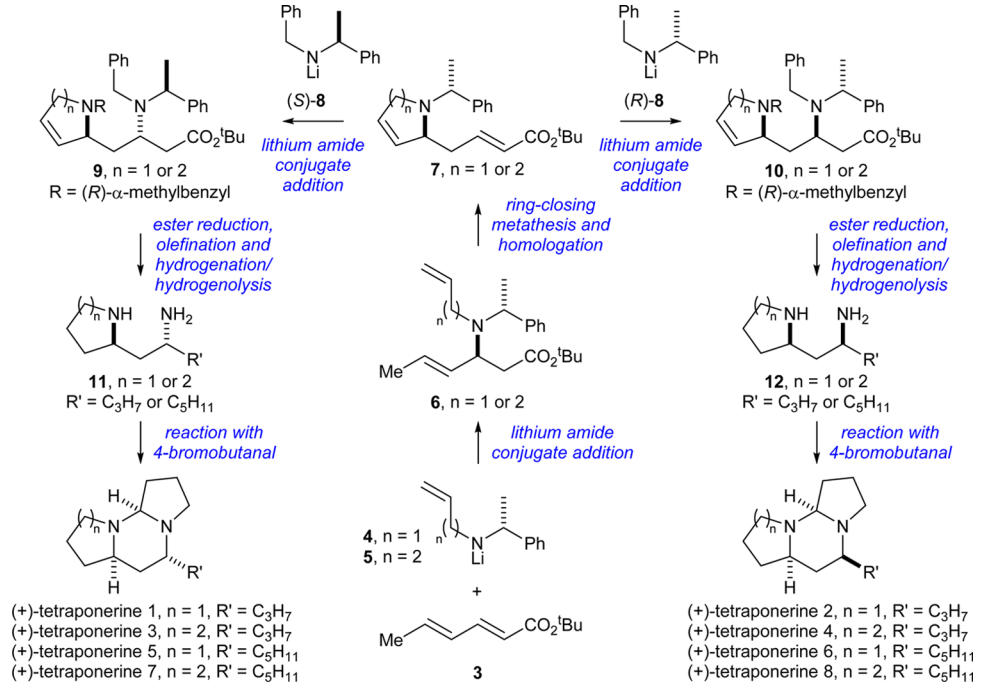


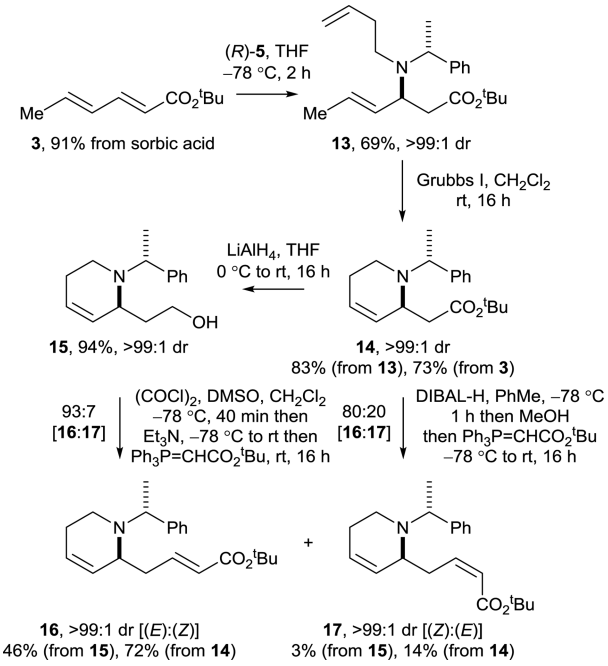

**Figure 2.** Proposed synthetic strategy to access all eight tetraponerine alkaloids.

hydrogenation/hydrogenolysis would produce the corresponding diamines **11** or **12** ($n$ = 1 or 2 in both cases), which have previously been converted into the tetraponerine alkaloids by Gonzalez-Gomez et al.[6,9d] upon reaction with 4-bromobutanal (Figure 2). As part of their study, Gonzalez-Gomez et al. proposed that the configuration at the aminal functionality within each of the tetraponerine alkaloids is susceptible to equilibration via the corresponding iminium ion and that the natural products may therefore possess the most thermodynamically favorable relative configurations with respect to epimerization at the aminal center.

## RESULTS AND DISCUSSION

The tetraponerine alkaloids based upon a decahydro-5*H*-pyrido[1,2-*c*]pyrrolo[1,2-*a*]pyrimidine skeleton **2** (i.e., tetraponerines 3, 4, 7, and 8) were targeted initially. Tetrahydropyridine **14** was prepared via a known sequence of reactions,[13,14] involving conjugate addition of lithium (*R*)-*N*-(but-3-en-1-yl)-*N*-(α-methylbenzyl)amide (*R*)-**5** to *tert*-butyl sorbate **3**,[16] which gave β-amino ester **13** as a single diastereoisomer (>99:1 dr) in 69% yield. Subsequent ring-closing metathesis of **13** gave tetrahydropyridine **14** in 83% yield.[13,14] A superior overall yield of **14** from *tert*-butyl sorbate **3** was obtained by omitting the purification of the intermediate β-amino ester **13**; following this sequence, tetrahydropyridine **14** was isolated in 73% yield (from **3**) and >99:1 dr. Reduction of **14** with $LiAlH_4$ gave the corresponding alcohol **15** in 94% yield as a single diastereoisomer. Swern oxidation of primary alcohol **15** followed by Wittig reaction of the resultant aldehyde with $Ph_3P{=}CHCO_2{}^tBu$ gave a 93:7 mixture of diastereoisomeric products **16** and **17**, respectively. Purification of the crude reaction mixture gave the major product **16** in 46% yield and >99:1 dr [(*E*):(*Z*)], and the minor product **17**, in 3% yield and >99:1 dr [(*Z*):(*E*)]. However, a superior yield of **16** was obtained from the reduction of β-amino ester **14** with DIBAL-H followed by in situ Wittig reaction of the intermediate aldehyde with $Ph_3P{=}CHCO_2{}^tBu$, which gave an 80:20 mixture of **16** and **17**, respectively, from which **16** was isolated in 72% yield and >99:1 dr [(*E*):(*Z*)], and **17** was isolated in 14% yield and >99:1 dr [(*Z*):(*E*)] (Scheme 1).

**Scheme 1. Preparation of Tetrahydropyridine 16**




The inherent level of substrate control offered by chiral α,β-unsaturated ester **16** upon reaction with a lithium amide reagent was probed upon conjugate addition of lithium *N*-isopropyl-*N*-benzylamide **18**, which we have previously employed as an achiral model for the conjugate addition of either antipode of enantiopure lithium *N*-benzyl-*N*-(α-methylbenzyl)amide **8**.[17] Reaction of **16** with the achiral



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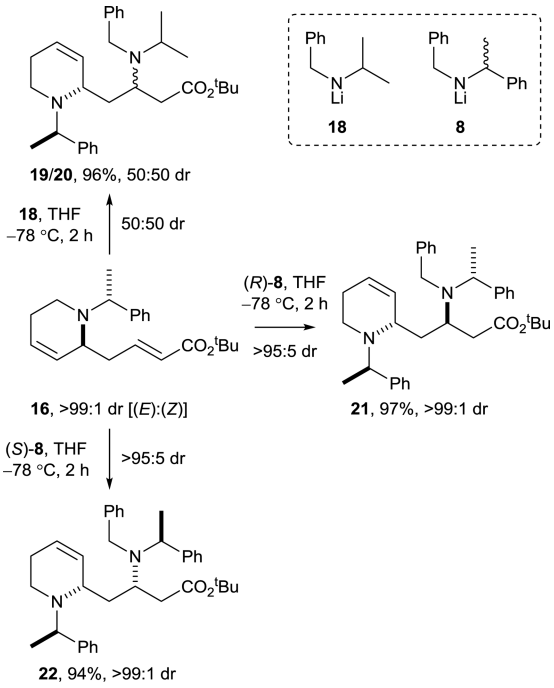
lithium amide reagent **18** gave a 50:50 mixture of the diastereoisomeric $\beta$-amino ester adducts **19** and **20**, which were isolated in 96% combined yield. This result suggests that $\alpha,\beta$-unsaturated ester **16** elicits essentially no diastereoselectivity in the conjugate addition reaction, and is consistent with the low levels of substrate control observed upon conjugate addition of lithium amides to substrates bearing remote stereogenic centers.[18] The conjugate addition of lithium (*R*)-*N*-benzyl-*N*-($\alpha$-methylbenzyl)amide (*R*)-**8** to $\alpha,\beta$-unsaturated ester **16** gave $\beta$-amino ester **21** in >95:5 dr, and conjugate addition of lithium (*S*)-*N*-benzyl-*N*-($\alpha$-methylbenzyl)amide (*S*)-**8** to **16** gave $\beta$-amino ester **22** in >95:5 dr. Following purification of the crude reaction mixtures, **21** was isolated in 97% yield and >99:1 dr, and **22** was isolated in 94% yield and >99:1 dr (Scheme 2). The configurations of the newly formed

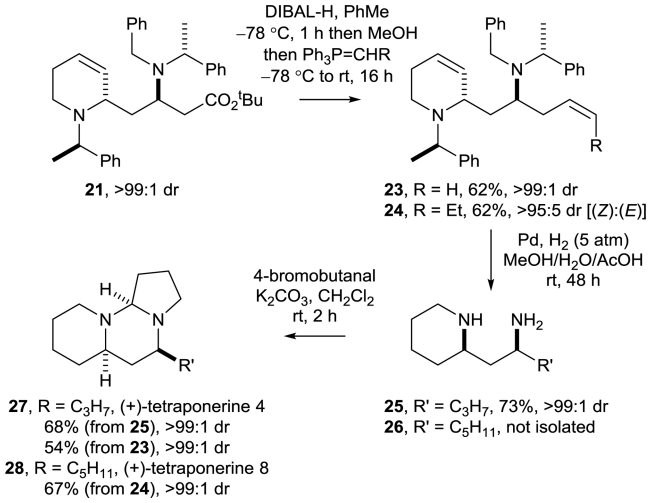
**Scheme 2. Conjugate Additions to 16**




stereogenic centers within **21** and **22** were assigned on the assumption that conjugate addition proceeds under the dominant stereocontrol of the lithium amide reagent **8** (given the total lack of substrate control observed upon conjugate addition of lithium *N*-isopropyl-*N*-benzylamide **18** to $\alpha,\beta$-unsaturated ester **16**), and is consistent with the formation of **21** and **22** as single diastereoisomers in both cases. These stereochemical assignments were later confirmed upon derivatization to the target tetraponerine alkaloids.

The elaboration of **21** to (+)-tetraponerine 4 (**27**) was achieved via reduction of the ester moiety within **21** with DIBAL-H followed by Wittig reaction of the resultant aldehyde with $Ph_3P{=}CH_2$, which gave olefin **23** in 62% yield and >99:1 dr. Tandem Pd-mediated hydrogenation/hydrogenolysis of **23** in a mixture of MeOH, $H_2O$, and AcOH gave diamine **25** in 73% isolated yield and >99:1 dr. Finally, reaction of **25** with 4-bromobutanal and $K_2CO_3$ in $CH_2Cl_2$, according to the literature protocol,[6,9d] gave (+)-tetraponerine 4 (**27**) in 68% yield and >99:1 dr. The spectroscopic data and specific rotation for this sample of (+)-tetraponerine 4 (**27**) were in good agreement with literature values {$[\alpha]_D^{25}$ +90.8 (*c* 1.0 in $CHCl_3$); lit.[4] for a sample isolated from the natural source $[\alpha]_D^{25}$ +94 (*c* 0.2 in $CHCl_3$); lit.[9b] $[\alpha]_D^{25}$ +96 (*c* 2.0 in $CHCl_3$)}, thereby confirming the assigned configurations of the synthetic precursors **21**, **23**, and **25**. Repetition of this hydrogenation/hydrogenolysis and ring-closure reaction sequence, but omitting the purification of the intermediate diamine **25**, gave (+)-tetraponerine 4 (**27**) in 54% overall yield (from **23**), representing a marginal improvement over the stepwise protocol (i.e., 50% overall yield from **23**). (+)-Tetraponerine 8 (**28**) was also prepared from **21** in a directly analogous manner: one-pot reduction/Wittig reaction of **21** gave olefin **24** in 62% yield and >95:5 dr [(*Z*):(*E*)].[19] Subsequent tandem hydrogenation/hydrogenolysis of **24** gave diamine **26** [although in this case only it was necessary to resubject the hydrogenation/hydrogenolysis reaction using $Pd(OH)_2/C$ as the catalyst to effect complete *N*-debenzylation]. Diamine **26** was then immediately converted into (+)-tetraponerine 8 (**28**) upon treatment with 4-bromobutanal.[6,9d] Following purification of the crude reaction mixture, (+)-tetraponerine 8 (**28**) was isolated as a single diastereoisomer (>99:1 dr) in 67% yield from **24** (Scheme 3). The spectroscopic data, melting point,

**Scheme 3. Preparation of (+)-Tetraponerine 4 and (+)-Tetraponerine 8**




and specific rotation for this sample of (+)-tetraponerine 8 (**28**) were all in good agreement with literature values {mp 38–40 °C; lit.[5] mp 40 °C; $[\alpha]_D^{25}$ +93.0 (*c* 1.0 in $CHCl_3$); lit.[4] for a sample isolated from the natural source $[\alpha]_D^{20}$ +102 (*c* 0.2 in $CHCl_3$); lit.[9b] $[\alpha]_D^{20}$ +101 (*c* 2.0 in $CHCl_3$)}, thereby confirming the assigned configurations of the synthetic precursors **21**, **24**, and **26**. The asymmetric syntheses of (+)-tetraponerine 4 (**27**) and (+)-tetraponerine 8 (**28**) were therefore achieved in 15.5% and 19.3% overall yield, respectively, in eight steps from commercially available starting materials.

Elaboration of the diastereoisomeric substrate **22** to (+)-tetraponerine 3 (**33**) and (+)-tetraponerine 7 (**34**) was also evaluated. Reduction of **22** with DIBAL-H followed by Wittig reaction of the resultant aldehyde with the requisite ylid reagent $Ph_3P{=}CHR$ gave either **29** (R = H) or **30** (R = Et); after chromatographic purification of the crude reaction mixtures, **29** was isolated in 54% yield as a single diastereoisomer and **30** was isolated in 47% yield and >95:5 dr [(*Z*):(*E*)].[20] Tandem hydrogenation/hydrogenolysis of **29** and **30** gave the corresponding diamines **31** and **32**, which were immediately reacted with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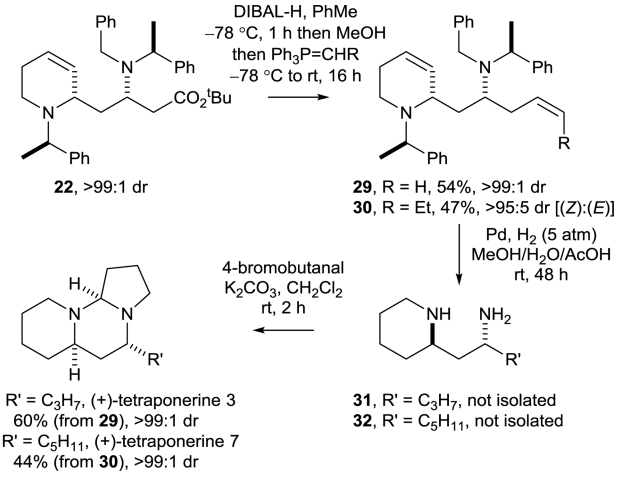
4-bromobutanal[6,9d] to give (+)-tetraponerine 3 (**33**) and (+)-tetraponerine 7 (**34**) in 60% and 44% yield, respectively, as single diastereoisomers (>99:1 dr) in each case (Scheme 4).

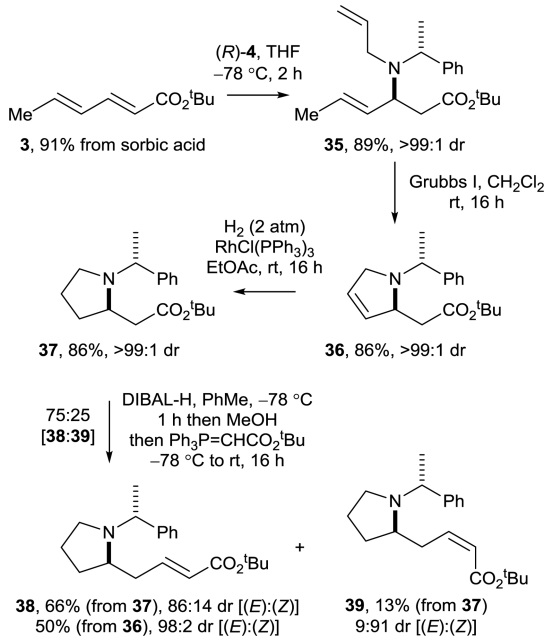
**Scheme 4. Preparation of (+)-Tetraponerine 3 and (+)-Tetraponerine 7**




The spectroscopic data and specific rotations for these samples of (+)-tetraponerine 3 (**33**) and (+)-tetraponerine 7 (**34**) were in good agreement with literature values {for (+)-tetraponerine 3 (**33**): $[\alpha]_D^{25}$ +30.9 (*c* 1.0 in $CHCl_3$); lit.[4] for a sample isolated from the natural source $[\alpha]_D^{20}$ +27 (*c* 0.07 in $CHCl_3$); lit.[5] $[\alpha]_D^{20}$ +31 (*c* 3.1 in $CHCl_3$); lit.[9d] $[\alpha]_D^{20}$ +35 (*c* 0.49 in $CHCl_3$); for (+)-tetraponerine 7 (**34**): $[\alpha]_D^{25}$ +30.4 (*c* 0.8 in $CHCl_3$); lit.[4] for a sample isolated from the natural source $[\alpha]_D^{20}$ +30 (*c* 0.22 in $CHCl_3$); lit.[9b] $[\alpha]_D^{20}$ +29.5 (*c* 2.2 in $CHCl_3$)}, thereby confirming the assigned configurations of the synthetic precursors **22** and **29**–**32**. The asymmetric syntheses of (+)-tetraponerine 3 (**33**) and (+)-tetraponerine 7 (**34**) were therefore achieved in 14.6% and 9.3% overall yield, respectively, in eight steps from commercially available starting materials.

The remaining tetraponerine alkaloids in the series, based on a decahydrodipyrrolo[1,2-*a*:1′,2′-*c*]pyrimidine scaffold **1** (i.e., tetraponerines 1, 2, 5, and 6), were targeted next. Dihydropyrrole **36** was prepared via a known sequence of reactions,[13,15] involving conjugate addition of lithium (*R*)-*N*-allyl-*N*-(α-methylbenzyl)amide (*R*)-**4** to *tert*-butyl sorbate **3**,[16] which gave β-amino ester **35** in 89% yield as a single diastereoisomer (>99:1 dr). Subsequent ring-closing metathesis of **35** gave dihydropyrrole **36** in 86% yield and >99:1 dr.[13,15] In this case, it was found that hydrogenation of **36** with Wilkinson's catalyst $[RhCl(PPh_3)_3]$[13,15a,b] to give pyrrolidine **37** was necessary to avoid oxidative side reactions, leading to various pyrrole containing species, in the subsequent steps.[21] Reduction of the ester moiety within pyrrolidine **37** with DIBAL-H followed by in situ Wittig reaction of the corresponding aldehyde with $Ph_3P{=}CHCO_2{}^tBu$ gave a 75:25 mixture of **38** and **39**, respectively. Following purification of the crude reaction mixture, an 86:14 mixture of **38** and **39**, respectively, was isolated in 66% combined yield in addition to a 9:91 mixture of **38** and **39** in 13% combined yield. Upon repetition of the reaction sequence, hydrogenation of dihydropyrrole **36** followed by immediate reduction of the crude reaction mixture with DIBAL-H and Wittig reaction of the resultant aldehyde gave **38** in 50% yield (from **36**) and 98:2 dr (Scheme 5).

**Scheme 5. Preparation of Pyrrolidine 38**




The inherent level of substrate control offered by α,β-unsaturated ester **38** (98:2 dr [(*E*):(*Z*)]) was probed upon conjugate addition of lithium *N*-isopropyl-*N*-benzylamide **18**, which gave a 50:50 mixture of the diastereoisomeric β-amino ester adducts **40** and **41**. Following purification of the crude reaction mixture, **40** and **41** were isolated as a 50:50 mixture in 70% combined yield. This result suggests that α,β-unsaturated ester **38** elicits essentially no diastereoselectivity in the conjugate addition reaction, as was also the case for the homologous tetrahydropyridine containing substrate **16**, and is again consistent with the low levels of substrate control observed upon conjugate addition of lithium amides to other substrates bearing remote stereogenic centers.[18] The conjugate addition of lithium (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amide (*R*)-**8** to α,β-unsaturated ester **38** (98:2 dr [(*E*):(*Z*)]) gave β-amino ester **42** in 98% yield and >99:1 dr, whereas conjugate addition of lithium (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amide (*S*)-**8** to **38** (98:2 dr [(*E*):(*Z*)]) gave β-amino ester **43** in 92% isolated yield and >99:1 dr (Scheme 6). The configurations of the newly formed stereogenic centers within the conjugate addition products **42** and **43** were assigned, as before, on the assumption that conjugate addition proceeds under the dominant stereocontrol of the lithium amide reagent in both cases; these assignments were later confirmed upon derivatization to the target alkaloids. Conjugate addition of lithium amide (*R*)-**8** to an 86:14 mixture of (*E*)-**38** and (*Z*)-**39**, respectively, gave an 86:14 mixture of β-amino ester **42** and a species which was tentatively assigned as the corresponding β,γ-unsaturated derivative **44**; there was no evidence of either (*E*)-**38** or (*Z*)-**39** in the $^1H$ NMR spectrum of the crude reaction mixture. As β-amino ester **42** and β,γ-unsaturated ester **44** were only partially separable upon attempted chromatographic purification, this result confirmed that it was necessary to enrich the diastereoisomeric purity of the α,β-unsaturated ester prior to attempting the conjugate addition reaction.

Reduction of **42** with DIBAL-H followed by Wittig reaction of the resultant aldehyde with the requisite ylid reagent $Ph_3P{=}CHR$ gave either **45** (R = H) or **46** (R = Et); after



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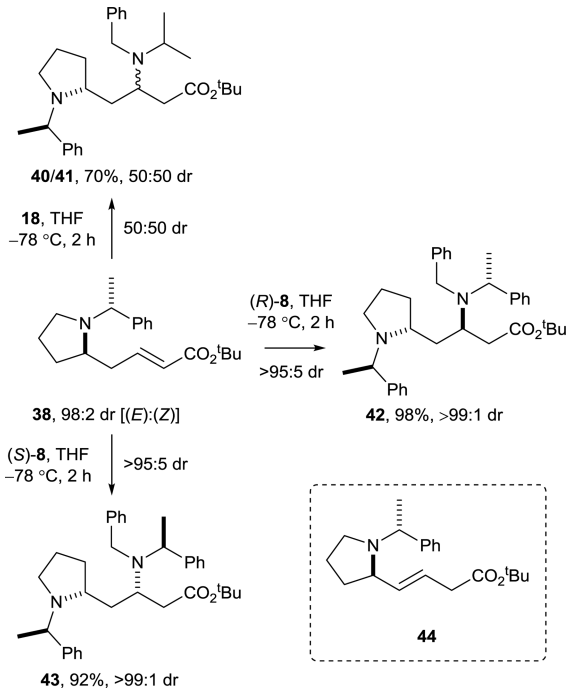
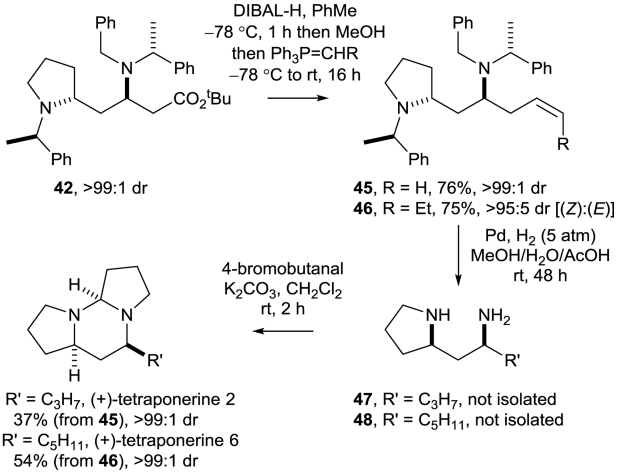
**Scheme 6. Conjugate Additions to 38**




chromatographic purification of the crude reaction mixtures, **45** was isolated in 76% yield and >99:1 dr, and **46** was isolated in 75% yield and >95:5 dr [(*Z*):(*E*)].[20] Tandem hydrogenation/hydrogenolysis of **45** and **46** gave the corresponding diamines **47** and **48**, which were immediately reacted with 4-bromobutanal[6,9d] to give (+)-tetraponerine 2 (**49**) and (+)-tetraponerine 6 (**50**) in 37% and 54% yield, respectively, as single diastereoisomers (>99:1 dr) in each case (Scheme 7).

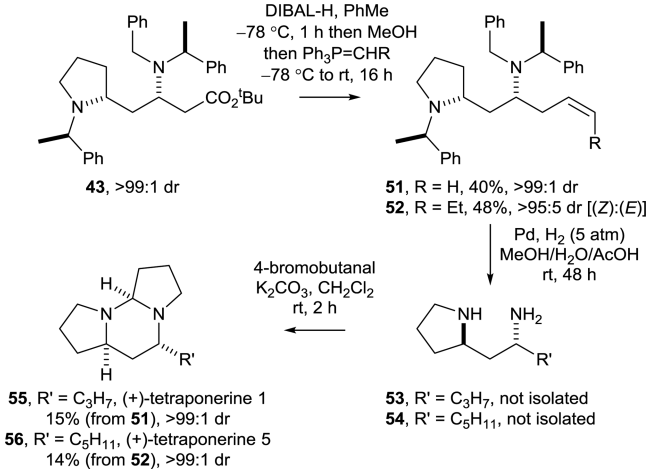
**Scheme 7. Preparation of (+)-Tetraponerine 2 and (+)-Tetraponerine 6**




For (+)-tetraponerine 2 (**49**), the specific rotation was consistent with literature values {$[\alpha]_D^{25}$ +44.2 (*c* 1.0 in $CHCl_3$); lit.[5] $[\alpha]_D^{20}$+36 (*c* 1.79 in $CHCl_3$); lit.[6] $[\alpha]_D^{20}$ +47 (*c* 0.232 in $CHCl_3$)}; however, for (+)-tetraponerine 6 (**50**) the specific rotations of our synthetic samples were consistently larger than literature values {$[\alpha]_D^{25}$ +66.3 (*c* 1.0 in $CHCl_3$); lit.[4] for a sample isolated from the natural source $[\alpha]_D^{20}$ +35 (*c* 0.15 in $CHCl_3$); lit.[6] $[\alpha]_D^{20}$ +40 (*c* 0.75 in $CHCl_3$)}. Despite this discrepancy,[22] the spectroscopic data for both samples of (+)-tetraponerine 2 (**49**) and (+)-tetraponerine 6 (**50**) were in good agreement with literature values, thereby confirming the assigned configurations of the synthetic precursors **42** and **45**–**48**. The asymmetric syntheses of (+)-tetraponerine 2 (**49**) and (+)-tetraponerine 6 (**50**) were therefore achieved in 9.6% and 13.8% overall yield, respectively, in nine steps from commercially available starting materials.

Reduction of the diastereoisomeric substrate **43** with DIBAL-H followed by Wittig reaction of the resultant aldehyde with the requisite ylid reagent $Ph_3P{=}CHR$ gave either **51** (R = H) or **52** (R = Et); after chromatographic purification of the crude reaction mixtures, **51** was isolated in 40% yield as a single diastereoisomer and **52** was isolated in 48% yield and >95:5 dr [(*Z*):(*E*)].[20] Tandem hydrogenation/hydrogenolysis of **51** and **52** gave the corresponding diamines **53** and **54**, which were immediately reacted with 4-bromobutanal[6,9d] to give (+)-tetraponerine 1 (**55**) and (+)-tetraponerine 5 (**56**) in 15% and 14% yield, respectively, as single diastereoisomers (>99:1 dr) in each case (Scheme 8). The spectroscopic data and specific rotations for

**Scheme 8. Preparation of (+)-Tetraponerine 1 and (+)-Tetraponerine 5**




these samples of (+)-tetraponerine 1 (**55**) and (+)-tetraponerine 5 (**56**) were in good agreement with literature values {for (+)-tetraponerine 1 (**55**): $[\alpha]_D^{25}$ +14.4 (*c* 0.13 in $CHCl_3$); lit.[5] $[\alpha]_D^{20}$ +11 (*c* 0.14 in $CHCl_3$); lit.[6] $[\alpha]_D^{20}$ +14 (*c* 0.498 in $CHCl_3$); for (+)-tetraponerine 5 (**56**): $[\alpha]_D^{25}$ +12.4 (*c* 0.13 in $CHCl_3$); lit.[4] for a sample isolated from the natural source $[\alpha]_D^{20}$ +10 (*c* 0.2 in $CHCl_3$); lit.[5] $[\alpha]_D^{20}$ +10 (*c* 0.24 in $CHCl_3$); lit.[6] $[\alpha]_D^{20}$ +14 (*c* 1.6 in $CHCl_3$)}, thereby confirming the assigned configurations of the synthetic precursors **43** and **51**–**54**. The asymmetric syntheses of (+)-tetraponerine 1 (**55**) and (+)-tetraponerine 5 (**56**) were therefore achieved in 1.9% and 2.2% overall yield, respectively, in nine steps from commercially available starting materials.

## CONCLUSION

In conclusion, the conjugate addition of either lithium (*R*)-*N*-allyl-*N*-(α-methylbenzyl)amide or lithium (*R*)-*N*-(but-3-en-1-yl)-*N*-(α-methylbenzyl)amide to *tert*-butyl sorbate was followed by ring-closing metathesis of the resultant *N*-alkenyl β-amino esters and homologation. Subsequent conjugate addition of the requisite antipode of lithium *N*-benzyl-*N*-(α-methylbenzyl)-amide to the resultant α,β-unsaturated esters gave a range of diamines for elaboration to all eight tetraponerine alkaloids (T1–T8) via a sequence involving reduction of the ester



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moiety to the corresponding aldehyde, olefination, tandem hydrogenation/hydrogenolysis, and reaction with 4-bromobutanal to give the tricyclic skeleton. In each case, the target alkaloids were isolated enantiomerically pure as single diastereoisomers in nine steps or fewer from commercially available sorbic acid.

## EXPERIMENTAL SECTION

**General Experimental Details.** All reactions involving organometallic or other moisture-sensitive reagents were carried out under a nitrogen atmosphere using standard vacuum line techniques and glassware that was flame-dried and cooled under nitrogen before use. Solvents were dried according to the procedure outlined by Grubbs and co-workers.[23] BuLi was purchased as a solution in hexanes and titrated against diphenylacetic acid before use. All other reagents were used as supplied without prior purification. Organic layers were dried over $Na_2SO_4$. Thin layer chromatography was performed on aluminum plates coated with 60 $F_{254}$ silica. Plates were visualized using UV light (254 nm), 1% aq $KMnO_4$, or Dragendorff's reagent. Flash column chromatography was performed on Kieselgel 60 silica. Melting points are uncorrected. Specific rotations are reported in $10^{-1}$ deg $cm^2$ $g^{-1}$, and concentrations in g/100 mL. IR spectra were recorded using an ATR module. Selected characteristic peaks are reported in $cm^{-1}$. NMR spectra were recorded in the deuterated solvent stated. Spectra were recorded at rt unless otherwise stated. The field was locked by external referencing to the relevant deuteron resonance. $^1H-^1H$ COSY, $^1H-^{13}C$ HMQC, and $^1H-^{13}C$ HMBC analyses were used to establish atom connectivity. Accurate mass measurements were run on a TOF spectrometer internally calibrated with polyalanine.

***tert*-Butyl (*E*,*E*)-Hexa-2,4-dienoate [*tert*-Butyl Sorbate] 3.** Condensed isobutylene (180 mL) at −78 °C was added to a stirred solution of sorbic acid (30.0 g, 268 mmol) and conc aq $H_2SO_4$ (3.00 mL) in $CH_2Cl_2$ (600 mL) at 0 °C, and the resultant mixture was allowed to warm to rt and stirred at rt for 48 h. The reaction mixture was washed with satd aq $NaHCO_3$ (5 × 300 mL), and the combined aqueous washings were extracted with $CH_2Cl_2$ (2 × 300 mL). The combined organic extracts were washed with brine (500 mL), then dried, and concentrated in vacuo to give **3** as a pale yellow oil (41.1 g, 91%, >99:1 dr);[13] $\delta_H$ (400 MHz, $CDCl_3$) 1.48 (9H, s, $CMe_3$), 1.84 (3H, d, *J* 5.9, C(6)$H_3$), 5.70 (1H, d, *J* 15.4, C(2)*H*), 6.04−6.21 (2H, m, C(4)*H*, C(5)*H*), 7.15 (1H, dd, *J* 15.4, 10.0, C(3)*H*).

***tert*-Butyl (3*S*,α*R*,*E*)-3-[*N*-(But-3′-en-1′-yl)-*N*-(α-methylbenzyl)amino]hex-4-enoate 13.** BuLi (2.3 M in hexanes, 2.00 mL, 4.61 mmol) was added dropwise to a stirred solution of (*R*)-*N*-(but-3-en-1-yl)-*N*-(α-methylbenzyl)amine (833 mg, 4.76 mmol, >99:1 er) in THF (5 mL) at −78 °C, and the resultant mixture was stirred at −78 °C for 30 min. A solution of **3** (500 mg, 2.97 mmol, >99:1 dr) in THF (2 mL) at −78 °C was added via cannula, and the resultant mixture was stirred at −78 °C for 2 h. Satd aq $NH_4Cl$ (2 mL) was added, and the reaction mixture was allowed to warm to rt and then concentrated in vacuo. The residue was partitioned between $CH_2Cl_2$ (10 mL) and 10% citric acid (10 mL), and the organic layer was washed with satd aq $NaHCO_3$ (10 mL) and brine (10 mL), then dried, and concentrated in vacuo to give **13** in >95:5 dr. Purification via flash column chromatography (eluent 30−40 °C petrol/$Et_2O$, 20:1) gave **13** as a pale yellow oil (708 mg, 69%, >99:1 dr);[13] $[\alpha]_D^{25}$ −15.4 (*c* 2.0 in $CHCl_3$); {lit.[14] $[\alpha]_D^{20}$ −14.6 (*c* 1.0 in $CHCl_3$)}; $\delta_H$ (400 MHz, $CDCl_3$) 1.36 (3H, d, *J* 6.7, C(α)*Me*), 1.40 (9H, s, $CMe_3$), 1.69 (3H, d, *J* 5.0, C(6)$H_3$), 1.96−2.08 (2H, m, C(2′)$H_2$), 2.28 (1H, dd, *J* 14.1, 8.2, C(2)$H_A$), 2.40 (1H, dd, *J* 14.1, 6.6, C(2)$H_B$), 2.44−2.58 (2H, m, C(1′)$H_2$), 3.75−3.81 (1H, m, C(3)*H*), 3.93 (1H, q, *J* 6.7, C(α)*H*), 4.86−4.94 (2H, m, C(4′)$H_2$), 5.45−5.58 (2H, m, C(4)*H*, C(5)*H*), 5.64 (1H, ddt, *J* 17.0, 10.3, 6.8, C(3′)*H*), 7.17−7.23 (1H, m, *Ph*), 7.25−7.30 (2H, m, *Ph*), 7.32−7.37 (2H, m, *Ph*).

***tert*-Butyl (2′*S*,α*R*)-2-[*N*(1′)-(α-Methylbenzyl)-1′,2′,5′,6′-tetrahydropyridin-2′-yl]acetate 14.** *Method A (from 13).* Grubbs I catalyst (301 mg, 0.366 mmol) was added to a stirred, degassed solution of **13** (3.14 g, 9.14 mmol, >99:1 dr) in anhydrous $CH_2Cl_2$ (EtOH stabilized, 300 mL) at rt. The resultant mixture was stirred at rt for 16 h and then concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/$Et_2O$/$NH_4OH$, 100:10:1) gave **14** as a pale yellow oil (2.30 g, 83% from **13**, >99:1 dr);[13] $[\alpha]_D^{25}$ +41.5 (*c* 1.0 in $CHCl_3$); {lit.[13] $[\alpha]_D^{25}$ +41.8 (*c* 1.5 in $CHCl_3$)}; $\delta_H$ (400 MHz, $CDCl_3$) 1.38 (3H, d, *J* 6.6, C(α)*Me*), 1.48 (9H, s, $CMe_3$), 1.66−1.75 (1H, m, C(5′)$H_A$), 2.04−2.16 (1H, m, C(5′)$H_B$), 2.37 (1H, dd, *J* 14.2, 6.8, C(2)$H_A$), 2.43−2.50 (1H, m, C(6′)$H_A$), 2.59 (1H, dd, *J* 14.2, 7.3, C(2)$H_B$), 2.84 (1H, ddd, *J* 13.9, 9.5, 4.7, C(6′)$H_B$), 3.70−3.77 (1H, m, C(2′)*H*), 3.89 (1H, q, *J* 6.6, C(α)*H*), 5.62−5.67 (1H, m, C(3′)*H*), 5.78−5.85 (1H, m, C(4′)*H*), 7.20−7.34 (5H, m, *Ph*).

*Method B (from 3): Step 1.* BuLi (2.3 M in hexanes, 20.0 mL, 46.1 mmol) was added dropwise to a stirred solution of (*R*)-*N*-(but-3-en-1-yl)-*N*-(α-methylbenzyl)amine (8.33 g, 47.6 mmol, >99:1 er) in THF (70 mL) at −78 °C, and the resultant mixture was stirred at −78 °C for 30 min. A solution of **3** (5.00 g, 29.7 mmol, >99:1 dr) in THF (10 mL) at −78 °C was then added, and the resultant mixture was stirred at −78 °C for 2 h. Satd aq $NH_4Cl$ (20 mL) was added, and the reaction mixture was allowed to warm to rt and then concentrated in vacuo. The residue was partitioned between $CH_2Cl_2$ (50 mL) and 10% citric acid (50 mL), and the organic layer was washed with satd aq $NaHCO_3$ (50 mL) and brine (50 mL), then dried, and concentrated in vacuo to give **13** in >95:5 dr.

*Method B (from 3): Step 2.* Grubbs I catalyst (854 mg, 1.04 mmol) was added to a stirred, degassed solution of the residue of **13** from the previous step in anhydrous $CH_2Cl_2$ (EtOH stabilized, 900 mL) at rt. The resultant solution was stirred at rt for 16 h and then concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/$Et_2O$/$NH_4OH$, 100:10:1) gave **14** as a pale yellow oil (6.55 g, 73% from **3**, >99.1 dr); $[\alpha]_D^{25}$ +44.8 (*c* 0.8 in $CHCl_3$).

**(2′*S*,α*R*)-2-[*N*(1′)-(α-Methylbenzyl)-1′,2′,5′,6′-tetrahydropyridin-2′-yl]ethan-1-ol 15.** $LiAlH_4$ (2.4 M in THF, 3.18 mL, 7.63 mmol) was added to a stirred solution of **14** (2.30 g, 7.63 mmol, >99:1 dr) in THF (70 mL) at 0 °C. The resultant mixture was allowed to warm to rt and stirred at rt for 16 h. 2.0 M aq NaOH (7 mL) was then added, and the resultant mixture was stirred at rt for 3 h. The reaction mixture was filtered through Celite (eluent $CH_2Cl_2$) and then concentrated in vacuo to give **15** as a pale yellow oil (1.66 g, 94%, >99:1 dr); $[\alpha]_D^{25}$ −3.9 (*c* 1.0 in $CHCl_3$); $\nu_{max}$ (ATR) 3393 (O−H), 3026, 2970, 2839, (C−H), 1454 (C=C); $\delta_H$ (400 MHz, $CDCl_3$) 1.49 (3H, d, *J* 6.6, C(α)*Me*), 1.73−1.88 (2H, m, C(2)$H_A$, C(5′)$H_A$), 1.88−1.97 (1H, m, C(2)$H_B$), 2.04−2.14 (1H, m, C(5′)$H_B$), 2.34 (1H, app dt, *J* 13.4, 4.5, C(6′)$H_A$), 3.02 (1H, ddd, *J* 13.4, 8.9, 4.7, C(6′)$H_B$), 3.59−3.66 (1H, m, C(2′)*H*), 3.85−3.96 (2H, m, C(1)$H_2$), 4.05 (1H, q, *J* 6.6, C(α)*H*), 5.50−5.56 (1H, m, C(3′)*H*), 5.84−5.97 (1H, m, C(4′)*H*), 6.36 (1H, br s, O*H*), 7.24−7.39 (5H, m, *Ph*); $\delta_C$ (100 MHz, $CDCl_3$) 21.3, 21.4 (C(5′), C(α)*Me*), 32.9 (C(2)), 40.0 (C(6′)), 56.2 (C(2′)), 57.6 (C(α)), 63.0 (C(1)), 126.4 (C(4′)), 127.4 (*p*-*Ph*), 127.8, 128.5 (*o*,*m*-*Ph*), 128.5 (C(3′)), 142.6 (*i*-*Ph*); *m*/*z* (ESI$^+$) 232 ([M + H]$^+$, 100%); HRMS (ESI$^+$) *m*/*z*: [M + H]$^+$ Calcd for $C_{15}H_{22}NO^+$ 232.1696; Found 232.1696.

***tert*-Butyl (2′*S*,α*R*,*E*)-4-[*N*(1′)-(α-Methylbenzyl)-1′,2′,5′,6′-tetrahydropyridin-2′-yl]but-2-enoate 16 and *tert*-Butyl (2′*S*,α*R*,*Z*)-4-[*N*(1′)-(α-methylbenzyl)-1′,2′,5′,6′-tetrahydropyridin-2′-yl]but-2-enoate 17.** *Method A (from 15).* DMSO (0.61 mL, 8.65 mmol) was added to a stirred solution of $(COCl)_2$ (0.37 mL, 4.32 mmol) in $CH_2Cl_2$ (50 mL) at −78 °C. After 20 min, **15** (500 mg, 2.16 mmol, >99:1 dr) was added, the resultant mixture was stirred at −78 °C for 40 min, and then $Et_3N$ (1.81 mL, 13.0 mmol) was added. The reaction mixture was allowed to warm to rt, $Ph_3P{=}CHCO_2{}^tBu$ (814 mg, 2.16 mmol) was added, and the resultant mixture was stirred at rt for 16 h. Satd aq $K_2CO_3$ (300 mL) was then added and the reaction mixture was extracted with $CH_2Cl_2$ (3 × 300 mL). The combined organic extracts were washed with brine (500 mL), then dried and concentrated in vacuo to give a 93:7 mixture of **16** and **17**, respectively. Purification via flash column chromatography (eluent 30−40 °C petrol/$Et_2O$/$NH_4OH$, 100:10:1) gave **17** as a pale yellow oil (19 mg, 3%, >99:1 dr); $[\alpha]_D^{25}$ +57.4 (*c* 1.0 in $CHCl_3$); $\nu_{max}$ (ATR) 2975, 2931 (C−H), 1712 (C=O), 1639 (C=C); $\delta_H$ (400 MHz, $CDCl_3$) 1.34 (3H, d, *J* 6.8, C(α)*Me*), 1.47 (9H, s, $CMe_3$), 1.84−1.94 (1H, m, C(5′)$H_A$), 1.96−2.05 (1H, m, C(5′)$H_B$), 2.23 (1H,



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ddd, $J$ 12.1, 7.2, 5.7, C(6′)$H_A$), 2.65−2.73 (1H, m, C(4)$H_A$), 2.92 (1H, app dt, $J$ 12.1, 5.6, C(6′)$H_B$), 3.16−3.26 (2H, m, C(4)$H_B$, C(2′)$H$), 4.00 (1H, q, $J$ 6.8, C(α)$H$), 5.46−5.51 (1H, m, C(3′)$H$), 5.73 (1H, d, $J$ 11.4, C(2)$H$), 5.73−5.78 (1H, m, C(4′)$H$), 6.30 (1H, app dt, $J$ 11.4, 7.5, C(3)$H$), 7.17−7.34 (5H, m, *Ph*); $\delta_C$ (100 MHz, $CDCl_3$) 20.9 (C(α)*Me*), 24.3 (*C*(5′)), 28.4 (C*Me*$_3$), 32.1 (*C*(4)), 40.8 (*C*(6′)), 54.9 (*C*(2′)), 57.1 (*C*(α)), 80.1 (*C*Me$_3$), 122.0 (*C*(2)), 126.5 (*C*(4′)), 126.9 (*p-Ph*), 128.1, 128.1 (*o,m-Ph*), 130.1 (*C*(3′)), 142.6 (*i-Ph*), 146.7 (*C*(3)), 166.4 (*C*(1)); $m/z$ (ESI$^+$) 328 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $m/z$: [M + H]$^+$ Calcd for $C_{21}H_{30}NO_2^+$ 328.2271; Found 328.2273. Further elution gave **16** as a yellow oil (322 mg, 46%, >99:1 dr); $[\alpha]_D^{25}$ +65.9 ($c$ 1.0 in $CHCl_3$); $\nu_{max}$ (ATR) 2979, 2932 (C−H), 1713 (C═O), 1651 (C═C); $\delta_H$ (400 MHz, $CDCl_3$) 1.38 (3H, d, $J$ 6.7, C(α)*Me*), 1.49 (9H, s, C*Me*$_3$), 1.82−1.93 (1H, m, C(5′)$H_A$), 2.03−2.15 (1H, m, C(5′)$H_B$), 2.36−2.55 (3H, m, C(4)$H_2$, C(6′)$H_A$), 2.88 (1H, ddd, $J$ 12.7, 7.8, 4.8, C(6′)$H_B$), 3.23−3.31 (1H, m, C(2′)$H$), 3.95 (1H, q, $J$ 6.7, C(α)$H$), 5.53−5.58 (1H, m, C(3′)$H$), 5.77 (1H, d, $J$ 15.5, C(2)$H$), 5.77−5.83 (1H, m, C(4′)$H$), 6.90 (1H, ddd, $J$ 15.5, 8.0, 6.7, C(3)$H$), 7.21−7.35 (5H, m, *Ph*); $\delta_C$ (100 MHz, $CDCl_3$) 21.4 (C(α)*Me*), 23.9 (*C*(5′)), 28.3 (C*Me*$_3$), 35.9 (*C*(4)), 40.7 (*C*(6′)), 54.6 (*C*(2′)), 57.9 (*C*(α)), 80.1 (*C*Me$_3$), 124.3 (*C*(2)), 126.5 (*C*(4′)), 127.0 (*p-Ph*), 127.9, 128.3 (*o,m-Ph*), 129.5 (*C*(3′)), 143.4 (*i-Ph*), 145.9 (*C*(3)), 166.1 (*C*(1)); $m/z$ (ESI$^+$) 328 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $m/z$: [M + H]$^+$ Calcd for $C_{21}H_{30}NO_2^+$ 328.2271; Found 328.2271.

*Method B (from **14**).* DIBAL-H (1.0 M in PhMe, 7.30 mL, 7.30 mmol) was added dropwise to a stirred solution of **14** (2.00 g, 6.64 mmol, >99:1 dr) in PhMe (20 mL) at −78 °C, and the resultant mixture was stirred at −78 °C for 1 h. MeOH (1.34 mL, 33.2 mmol) and $Ph_3P$═$CHCO_2{}^tBu$ (2.50 g, 6.64 mmol) were added sequentially, and the resultant mixture was allowed to warm to rt and stirred at rt for 16 h. The reaction mixture was then concentrated in vacuo to give an 80:20 mixture of **16** and **17**, respectively. Purification via flash column chromatography (eluent 30−40 °C petrol/$Et_2O$/$NH_4OH$, 100:10:1) gave **17** as a pale yellow oil (313 mg, 14%, >99:1 dr); $[\alpha]_D^{25}$ +60.2 ($c$ 0.5 in $CHCl_3$). Further elution gave **16** as a yellow oil (1.57 g, 72%, >99:1 dr); $[\alpha]_D^{25}$ +63.4 ($c$ 1.0 in $CHCl_3$).

***tert*-Butyl (3*R*,2′*S*,α*R*)-3-[*N*-Benzyl-*N*-isopropylamino]-4-[*N*(1′)-(α-methylbenzyl)-1′,2′,5′,6′-tetrahydropyridin-2′-yl]-butanoate and *tert*-Butyl (3*S*,2′*S*,α*R*)-3-[*N*-Benzyl-*N*-isopropylamino]-4-[*N*(1′)-(α-methylbenzyl)-1′,2′,5′,6′-tetrahydropyridin-2′-yl]butanoate 19 and 20.** BuLi (2.3 M in hexanes, 0.44 mL, 1.00 mmol) was added dropwise to a stirred solution of *N*-benzyl-*N*-isopropylamine (155 mg, 1.04 mmol) in THF (2 mL) at −78 °C, and the resultant mixture was stirred at −78 °C for 30 min. A solution of **16** (212 mg, 0.647 mmol, >99:1 dr) in THF (1 mL) at −78 °C was added via cannula, and the resultant mixture was stirred at −78 °C for 2 h. Satd aq $NH_4Cl$ (0.5 mL) was added, and the reaction mixture was allowed to warm to rt and then was concentrated in vacuo. The residue was partitioned between $CH_2Cl_2$ (10 mL) and 10% citric acid (10 mL), and the organic layer was washed with satd aq $NaHCO_3$ (10 mL) and brine (10 mL), then dried, and concentrated in vacuo to give a 50:50 mixture of **19** and **20** as a colorless oil (296 mg, 96%). Data for **19**: $\delta_H$ (400 MHz, $CDCl_3$) 1.05−1.11 (6H, m, NCH*Me*$_2$), 1.35 (3H, d, $J$ 6.5, C(α)*Me*), 1.36−1.63 (2H, m, C(4)$H_A$, C(5′)$H_A$), 1.50 (9H, s, C*Me*$_3$), 1.84−1.98 (1H, m, C(4)$H_B$), 2.04−2.17 (1H, m, C(5′)$H_B$), 2.42−2.57 (3H, m, C(2)$H_2$, C(6′)$H_A$), 2.72−2.84 (1H, m, C(6′)$H_B$), 2.91−3.02 (1H, m, NC*H*Me$_2$), 3.32−3.43 (1H, m, C(2′)$H$), 3.52−3.61 (1H, m, C(3)$H$), 3.65 (1H, d, $J$ 14.5, NC$H_AH_B$Ph), 3.73 (1H, d, $J$ 14.5, NC$H_AH_B$Ph), 3.84 (1H, q, $J$ 6.5, C(α)$H$), 5.33−5.43 (1H, m, C(3′)$H$), 5.69−5.79 (1H, m, C(4′)$H$), 7.19−7.43 (10H, m, *Ph*). Data for **20**: $\delta_H$ (400 MHz, $CDCl_3$) 1.05−1.11 (6H, m, NCH*Me*$_2$), 1.35 (3H, d, $J$ 6.5, C(α)*Me*), 1.36−1.63 (2H, m, C(4)$H_A$, C(5′)$H_A$), 1.46 (9H, s, C*Me*$_3$), 1.68 (1H, app dt, $J$ 14.2, 5.2, C(4)$H_B$), 2.04−2.17 (1H, m, C(5′)$H_B$), 2.29 (1H, dd, $J$ 13.7, 6.2, C(2)$H_A$), 2.40−2.57 (2H, m, C(2)$H_B$, C(6′)$H_A$), 2.72−2.84 (1H, m, C(6′)$H_B$), 2.91−3.02 (1H, m, NC*H*Me$_2$), 3.32−3.43 (1H, m, C(2′)$H$), 3.52−3.61 (1H, m, C(3)$H$), 3.66 (2H, s, NC$H_2$Ph), 3.84 (1H, q, $J$ 6.5, C(α)$H$), 5.49−5.55 (1H, m, C(3′)$H$), 5.69−5.79 (1H, m, C(4′)$H$), 7.19−7.43 (10H, m, *Ph*). Data for mixture of **19** and **20**: $\nu_{max}$ (ATR) 3024, 2967, 2931, 2837 (C−H), 1724 (C═O), 1602 (C═C); $\delta_C$ (100 MHz, $CDCl_3$) 20.2, 20.4, 20.8, 20.9, 21.1, 21.8, 22.7, 23.0, 28.3, 28.3, 36.5, 37.4, 39.8, 39.9, 40.2, 40.4, 47.8, 49.3, 49.4, 50.0, 51.2, 51.9, 52.4, 53.9, 58.0, 58.2, 80.0, 80.1, 125.4, 125.7, 126.6, 126.6, 126.8, 126.8, 127.5, 127.6, 128.1, 128.1, 128.3, 128.3, 128.5, 129.0, 129.8, 130.2, 141.8, 142.3, 145.9, 146.2, 172.3, 172.6; $m/z$ (ESI$^+$) 477 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $m/z$: [M + H]$^+$ Calcd for $C_{31}H_{45}N_2O_2^+$ 477.3476; Found 477.3471.

***tert*-Butyl (3*R*,2′*S*,α*R*,α′*R*)-3-[*N*-Benzyl-*N*-(α-methylbenzyl)-amino]-4-[*N*(1′)-(α′-methylbenzyl)-1′,2′,5′,6′-tetrahydropyridin-2′-yl]butanoate 21.** BuLi (2.3 M in hexanes, 0.58 mL, 1.33 mmol) was added dropwise to a stirred solution of (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (289 mg, 1.37 mmol, >99:1 er) in THF (2 mL) at −78 °C, and the resultant mixture was stirred at −78 °C for 30 min. A solution of **16** (280 mg, 0.855 mmol, >99:1 dr) in THF (1 mL) at −78 °C was added, and the resultant mixture was stirred at −78 °C for 2 h. Satd aq $NH_4Cl$ (0.5 mL) was added, and the reaction mixture was allowed to warm to rt and then concentrated in vacuo. The residue was partitioned between $CH_2Cl_2$ (5 mL) and 10% citric acid (5 mL), and the organic layer was washed with satd aq $NaHCO_3$ (5 mL) and brine (5 mL), then dried, and concentrated in vacuo to give **21** in >95:5 dr. Purification via flash column chromatography (eluent 30−40 °C petrol/$Et_2O$/$NH_4OH$, 100:10:1) gave **21** as a pale yellow oil (449 mg, 97%, >99:1 dr); $[\alpha]_D^{25}$ +23.8 ($c$ 1.0 in $CHCl_3$); $\nu_{max}$ (ATR) 3025, 2973, 2931, 2837 (C−H), 1722 (C═O), 1618 (C═C); $\delta_H$ (400 MHz, $CDCl_3$) 1.28 (3H, d, $J$ 6.8, C(α′)*Me*), 1.29 (3H, d, $J$ 6.9, C(α)*Me*), 1.32 (9H, s, C*Me*$_3$), 1.39−1.50 (2H, m, C(4)$H_A$, C(5′)$H_A$), 1.90−2.00 (1H, m, C(4)$H_B$), 2.06 (1H, dd, $J$ 14.1, 7.7, C(2)$H_A$), 2.03−2.19 (1H, m, C(5′)$H_B$), 2.18 (1H, dd, $J$ 14.1, 5.4, C(2)$H_B$), 2.48 (1H, app dd, $J$ 13.8, 5.3, C(6′)$H_A$), 2.81 (1H, ddd, $J$ 13.8, 11.0, 4.7, C(6′)$H_B$), 3.47−3.59 (2H, m, C(3)$H$, C(2′)$H$), 3.58 (1H, d, $J$ 14.7, NC$H_AH_B$Ph), 3.83 (1H, d, $J$ 14.7, NC$H_AH_B$Ph), 3.84 (1H, q, $J$ 6.8, C(α′)$H$), 3.92 (1H, q, $J$ 6.9, C(α)$H$), 5.40−5.47 (1H, m, C(3′)$H$), 5.71−5.77 (1H, m, C(4′)$H$), 7.17−7.43 (15H, m, *Ph*); $\delta_C$ (100 MHz, $CDCl_3$) 20.5 (C(α)*Me*), 20.9 (*C*(5′)), 22.9 (C(α′)*Me*), 28.2 (C*Me*$_3$), 38.3, 38.5 (*C*(2), *C*(4)), 40.3 (*C*(6′)), 50.4 (NC$H_2$Ph), 50.9 (*C*(2′)), 52.7 (*C*(3)), 58.2 (*C*(α′)), 58.6 (*C*(α)), 80.1 (*C*Me$_3$), 125.7 (*C*(4′)), 126.6, 126.8, 127.0 (*p-Ph*), 127.6, 128.2, 128.2, 128.3, 128.3, 128.6 (*o,m-Ph*), 129.6 (*C*(3′)), 142.1, 144.2, 146.2 (*i-Ph*), 172.1 (*C*(1)); $m/z$ (ESI$^+$) 539 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $m/z$: [M + H]$^+$ Calcd for $C_{36}H_{47}N_2O_2^+$ 539.3632; Found 539.3648.

***tert*-Butyl (3*S*,2′*S*,α*S*,α′*R*)-3-[*N*-Benzyl-*N*-(α-methylbenzyl)-amino]-4-[*N*(1′)-(α′-methylbenzyl)-1′,2′,5′,6′-tetrahydropyridin-2′-yl]butanoate 22.** BuLi (2.3 M in hexanes, 0.64 mL, 1.47 mmol) was added dropwise to a stirred solution of (*S*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (318 mg, 1.51 mmol, >99:1 er) in THF (2 mL) at −78 °C, and the resultant mixture was stirred at −78 °C for 30 min. A solution of **16** (308 mg, 0.941 mmol, >99:1 dr) in THF (1 mL) at −78 °C was added, and the resultant mixture was stirred at −78 °C for 2 h. Satd aq $NH_4Cl$ (0.5 mL) was added, and the reaction mixture was allowed to warm to rt and then concentrated in vacuo. The residue was partitioned between $CH_2Cl_2$ (5 mL) and 10% citric acid (5 mL), and the organic layer was washed with satd aq $NaHCO_3$ (5 mL) and brine (5 mL), then dried, and concentrated in vacuo to give **22** in >95:5 dr. Purification via flash column chromatography (eluent 30−40 °C petrol/$Et_2O$/$NH_4OH$, 100:10:1) gave **22** as a pale yellow oil (476 mg, 94%, >99:1 dr); $[\alpha]_D^{25}$ +68.1 ($c$ 1.0 in $CHCl_3$); $\nu_{max}$ (ATR) 3064, 3025, 2973, 2932 (C−H), 1722 (C═O), 1609 (C═C); $\delta_H$ (400 MHz, $CDCl_3$) 1.28 (3H, d, $J$ 6.6, C(α′)*Me*), 1.40 (3H, d, $J$ 6.9, C(α)*Me*), 1.44 (9H, s, C*Me*$_3$), 1.55−1.73 (3H, m, C(4)$H_2$, C(5′)$H_A$), 2.03−2.14 (1H, m, C(5′)$H_B$), 2.17 (1H, dd, $J$ 14.4, 6.6, C(2)$H_A$), 2.30 (1H, dd, $J$ 14.4, 6.6, C(2)$H_B$), 2.41 (1H, app dd, $J$ 13.7, 3.5, C(6′)$H_A$), 2.76 (1H, ddd, $J$ 13.7, 10.4, 4.8, C(6′)$H_B$), 3.28−3.35 (1H, m, C(2′)$H$), 3.55−3.63 (1H, m, C(3)$H$), 3.63 (1H, d, $J$ 15.0, NC$H_AH_B$Ph), 3.76 (1H, d, $J$ 15.0, NC$H_AH_B$Ph), 3.82 (1H, q, $J$ 6.6, C(α′)$H$), 4.01 (1H, q, $J$ 6.9, C(α)$H$), 5.55−5.61 (1H, m, C(3′)$H$), 5.71−5.77 (1H, m, C(4′)$H$), 7.17−7.39 (15H, m, *Ph*); $\delta_C$ (100 MHz, $CDCl_3$) 19.6 (C(α)*Me*), 21.5 (*C*(5′)), 22.5 (C(α′)*Me*), 28.3 (C*Me*$_3$), 36.6 (*C*(4)), 39.8, 39.9 (*C*(2), *C*(6′)), 49.8 (NC$H_2$Ph), 52.9 (*C*(2′)), 54.3 (*C*(3)), 58.1 (*C*(α′)), 58.9 (*C*(α)), 80.0 (*C*Me$_3$), 125.3 (*C*(4′)),



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126.6, 126.8, 126.9 (*p-Ph*), 127.7, 128.1, 128.2, 128.3, 128.3, 128.5 (*o,m-Ph*), 130.4 (*C*(3′)), 141.9, 143.9, 145.7 (*i-Ph*), 172.3 (*C*(1)); *m/z* (ESI$^+$) 539 ([M + H]$^+$, 100%); HRMS (ESI$^+$) *m/z*: [M + H]$^+$ Calcd for $C_{36}H_{47}N_2O_2^+$ 539.3632; Found 539.3631.

**(2*S*,2′*S*,α*R*,α′*R*)-1-[*N*(1′)-(α-Methylbenzyl)-1′,2′,5′,6′-tetrahydropyridin-2′-yl]-2-[*N*-benzyl-*N*-(α′-methylbenzyl)-amino]pent-4-ene 23.** DIBAL-H (1.0 M in PhMe, 0.20 mL, 0.20 mmol) was added dropwise to a stirred solution of **21** (100 mg, 0.19 mmol, >99:1 dr) in PhMe (2 mL) at −78 °C, and the resultant mixture was stirred at −78 °C for 1 h. MeOH (38 μL, 0.93 mmol) and $Ph_3P{=}CH_2$ (0.31 M in PhMe/THF, 6.58 mL, 2.04 mmol)[24] were added sequentially, and the resultant mixture was allowed to warm to rt, stirred at rt for 16 h, and then concentrated in vacuo. The residue was dissolved in $Et_2O$ (10 mL), and the resultant solution was filtered through a short plug of Celite (eluent $Et_2O$) and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/$Et_2O$/$NH_4OH$, 100:5:1) gave **23** as a colorless oil (54 mg, 62%, >99:1 dr); $[\alpha]_D^{25}$ +28.2 (*c* 1.0 in $CHCl_3$); $\nu_{max}$ (ATR) 3358, 2961 (C−H), 1596 (C=C); $\delta_H$ (400 MHz, $CDCl_3$) 1.26 (3H, d, *J* 6.4, C(α)*Me*), 1.37 (3H, d, *J* 6.9, C(α′)*Me*), 1.46−1.57 (2H, m, C(1)$H_A$, C(5′)$H_A$), 1.89−2.01 (2H, m, C(3)$H_A$, C(1)$H_B$), 2.05−2.16 (2H, m, C(3)$H_B$, C(5′)$H_B$), 2.49 (1H, app dd, *J* 14.0, 5.2, C(6′)$H_A$), 2.86 (1H, ddd, *J* 14.0, 11.2, 4.6, C(6′)$H_B$), 3.12 (1H, app quintet, *J* 6.4, C(2)*H*), 3.38−3.46 (1H, m, C(2′)*H*), 3.73 (1H, d, *J* 14.7, NC$H_A$H$_B$Ph), 3.82 (1H, q, *J* 6.4, C(α)*H*), 3.84 (1H, d, *J* 14.7, NCH$_A$$H_B$Ph), 3.96 (1H, q, *J* 6.9, C(α′)*H*), 4.85−4.93 (2H, m, C(5)$H_2$), 5.46−5.52 (1H, m, C(3′)*H*), 5.59 (1H, ddt, *J* 17.0, 10.2, 7.0, C(4)*H*), 5.72−5.79 (1H, m, C(4′)*H*), 7.18−7.34 (11H, m, *Ph*), 7.36−7.41 (2H, m, *Ph*), 7.42−7.46 (2H, m, *Ph*); $\delta_C$ (100 MHz, $CDCl_3$) 17.9 (C(α′)*Me*), 20.6 (*C*(5′)), 22.9 (C(α)*Me*), 36.4 (*C*(3)), 37.9 (*C*(1)), 40.2 (*C*(6′)), 50.3 ($NCH_2Ph$), 51.3 (*C*(2′)), 53.8 (*C*(2)), 57.3 (*C*(α′)), 58.1 (*C*(α)), 115.3 (*C*(5)), 125.5 (*C*(4′)), 126.5, 126.6, 126.6 (*p-Ph*), 127.4, 127.9, 128.1, 128.2, 128.2, 128.5 (*o,m-Ph*), 130.0 (*C*(3′)), 137.9 (*C*(4)), 142.2, 144.7, 146.1 (*i-Ph*); *m/z* (ESI$^+$) 465 ([M + H]$^+$, 100%); HRMS (ESI$^+$) *m/z*: [M + H]$^+$ Calcd for $C_{33}H_{41}N_2^+$ 465.3264; Found 465.3258.

**(2*S*,2′*S*,α*R*,α′*R*,*Z*)-1-[*N*(1′)-(α-Methylbenzyl)-1′,2′,5′,6′-tetrahydropyridin-2′-yl]-2-[*N*-benzyl-*N*-(α′-methylbenzyl)amino]-hept-4-ene 24.** DIBAL-H (1.0 M in PhMe, 0.53 mL, 0.53 mmol) was added dropwise to a stirred solution of **21** (260 mg, 0.483 mmol, >99:1 dr) in PhMe (4 mL) at −78 °C, and the resultant mixture was stirred at −78 °C for 1 h. MeOH (98 μL, 2.41 mmol) and $Ph_3P{=}CHCH_2CH_3$ (0.31 M in PhMe/THF, 15.6 mL, 4.83 mmol)[25] were added sequentially, and the resultant mixture was allowed to warm to rt, stirred at rt for 16 h, and then concentrated in vacuo. The residue was dissolved in $Et_2O$ (20 mL), and the resultant solution was filtered through a short plug of Celite (eluent $Et_2O$) and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/$Et_2O$/$NH_4OH$, 100:5:1) gave **24** as a pale yellow oil (148 mg, 62%, >95:5 dr [(*Z*):(*E*)]); $[\alpha]_D^{25}$ +36.5 (*c* 1.0 in $CHCl_3$); $\nu_{max}$ (ATR) 3024, 2931, 2838 (C−H), 1580, 1493, 1453 (C=C); $\delta_H$ (400 MHz, $CDCl_3$) 0.91 (3H, t, *J* 7.5, C(7)$H_3$), 1.26 (3H, d, *J* 6.4, C(α′)*Me*), 1.36 (3H, d, *J* 6.9, C(α)*Me*), 1.46−1.58 (2H, m, C(1)$H_A$, C(5′)$H_A$), 1.89−2.16 (6H, m, C(1)$H_B$, C(3)$H_2$, C(6)$H_2$, C(5′)$H_B$), 2.49 (1H, dd, *J* 14.0, 5.2, C(6′)$H_A$), 2.87 (1H, ddd, *J* 14.0, 11.2, 4.7, C(6′)$H_B$), 3.06 (1H, app quintet, *J* 6.4, C(2)*H*), 3.40−3.47 (1H, m, C(2′)*H*), 3.73 (1H, d, *J* 14.8, NC$H_A$H$_B$Ph), 3.81 (1H, q, *J* 6.4, C(α′)*H*), 3.86 (1H, d, *J* 14.8, NCH$_A$$H_B$Ph), 3.98 (1H, q, *J* 6.9, C(α)*H*), 5.10−5.19 (1H, m, C(4)*H*), 5.25−5.33 (1H, m, C(5)*H*), 5.44−5.50 (1H, m, C(3′)*H*), 5.71−5.78 (1H, m, C(4′)*H*), 7.19−7.35 (11H, m, *Ph*), 7.37−7.41 (2H, m, *Ph*), 7.42−7.46 (2H, m, *Ph*); $\delta_C$ (100 MHz, $CDCl_3$) 14.3 (*C*(7)), 18.5 (C(α)*Me*), 20.8 (*C*(5′)), 20.9 (*C*(6)), 23.0 (C(α′)*Me*), 29.6 (*C*(3)), 38.3 (*C*(1)), 40.3 (*C*(6′)), 50.5 ($NCH_2Ph$), 51.6 (*C*(2′)), 54.5 (*C*(2)), 57.7 (*C*(α)), 58.2 (*C*(α′)), 125.5 (*C*(4′)), 126.5, 126.7, 126.7 (*p-Ph*), 127.6 (*o,m-Ph*), 128.0 (*C*(4)), 128.0, 128.2, 128.3, 128.3, 128.6 (*o,m-Ph*), 130.2 (*C*(3′)), 131.9 (*C*(5)), 142.6, 145.2, 146.3 (*i-Ph*); *m/z* (ESI$^+$) 493 ([M + H]$^+$, 100%); HRMS (ESI$^+$) *m/z*: [M + H]$^+$ Calcd for $C_{35}H_{45}N_2^+$ 493.3577; Found 493.3568.

**(2*S*,2′*R*)-1-(Piperidin-2′-yl)-2-aminopentane 25.** Palladium black (15 mg, 20% w/w) was added to a stirred, degassed solution of **23** (75 mg, 0.16 mmol) in MeOH/$H_2O$/AcOH (10:1:1, 2 mL). The resultant mixture was stirred under an atmosphere of $H_2$ (5 atm) at rt for 48 h. The reaction mixture was then filtered through a short plug of Celite (eluent MeOH/$H_2O$/AcOH, 10:1:1) and concentrated in vacuo. Purification via flash column chromatography (eluent $CHCl_3$/MeOH/$NH_4OH$ 10:1:1) gave **25** as a colorless oil (20 mg, 73%, >99:1 dr); $[\alpha]_D^{25}$ −3.3 (*c* 1.0 in $CHCl_3$); $\nu_{max}$ (ATR) 3292 (N−H), 2930, 2860 (C−H); $\delta_H$ (400 MHz, $CDCl_3$) 0.89 (3H, t, *J* 6.9, C(5)$H_3$), 1.02−1.13 (1H, m, C(3′)$H_A$), 1.17−1.46 (8H, m, C(1)$H_2$, C(3)$H_2$, C(4)$H_2$, C(4′)$H_A$, C(5′)$H_A$), 1.53−1.68 (2H, m, C(3′)$H_B$, C(4′)$H_B$), 1.72−1.80 (1H, m, C(5′)$H_B$), 2.55−2.66 (2H, m, C(2′)*H*, C(6′)$H_A$), 2.75−2.82 (1H, m, C(2)*H*), 3.01−3.07 (1H, m, C(6′)$H_B$); $\delta_C$ (100 MHz, $CDCl_3$) 14.3 (*C*(5)), 19.2 (*C*(4)), 25.0 (*C*(5′)), 26.7 (*C*(4′)), 33.4 (*C*(3′)), 42.1 (*C*(3)), 45.5 (*C*(1)), 47.1 (*C*(6′)), 49.9 (*C*(2)), 56.1 (*C*(2′)); *m/z* (ESI$^+$) 171 ([M + H]$^+$, 100%); HRMS (ESI$^+$) *m/z*: [M + H]$^+$ Calcd for $C_{10}H_{23}N_2^+$ 171.1856; Found 171.1856.

**(5*S*,6a*R*,11a*S*)-5-Propyldecahydro-5*H*-pyrido[1,2-*c*]pyrrolo-[1,2-*a*]pyrimidine [(+)-Tetraponerine 4] 27.** *Method A (from **25**).* $K_2CO_3$ (88 mg, 0.63 mmol) and 4-bromobutanal (64 mg, 0.42 mmol) were added to a stirred solution of **25** (36 mg, 0.21 mmol, >99:1 dr) in $CH_2Cl_2$ (2 mL) at rt, and the resultant mixture was stirred at rt for 2 h. $H_2O$ (2 mL) and satd aq $NaHCO_3$ (10 mL) were added, and the resultant mixture was extracted with $CH_2Cl_2$ (3 × 5 mL), then dried, and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/$Me_2CO$/$NH_4OH$, 100:10:1) gave (+)-tetraponerine 4 (**27**) as a colorless oil (32 mg, 68% from **25**, >99:1 dr); $[\alpha]_D^{25}$ +90.8 (*c* 1.0 in $CHCl_3$); {lit.[4] for a sample isolated from the natural source $[\alpha]_D^{20}$ +94 (*c* 0.2 in $CHCl_3$); lit.[9b] $[\alpha]_D^{20}$ +96 (*c* 2.0 in $CHCl_3$)}; $\nu_{max}$ (ATR) 2933, 2855, 2793 (C−H);[26] $\delta_H$ (400 MHz, $C_6D_6$) 0.89 (3H, t, *J* 7.1, C(3′)$H_3$), 1.13−1.29 (2H, m, C(9)$H_A$, C(2′)$H_A$), 1.30−1.56 (9H, m, C(2)$H_A$, C(6)$H_2$, C(7)$H_2$, C(8)$H_A$, C(1′)$H_2$, C(2′)$H_B$), 1.59−1.77 (7H, m, C(1)$H_2$, C(2)$H_B$, C(6a)*H*, C(8)$H_B$, C(9)$H_B$, C(10)$H_A$), 2.02 (1H, dd, *J* 16.3, 8.6, C(3)$H_A$), 2.11 (1H, ddd, *J* 14.6, 7.4, 3.6, C(5)*H*), 2.31 (1H, dd, *J* 7.8, 5.6, C(11a)*H*), 2.80−2.85 (1H, m, C(10)$H_B$), 3.13 (1H, app td, *J* 8.6, 2.2, C(3)$H_B$); $\delta_C$ (100 MHz, $C_6D_6$) 14.8 (*C*(3′)), 18.7 (*C*(2′)), 20.2 (*C*(2)), 25.1 (*C*(9)), 26.3 (*C*(8)), 29.7 (*C*(1)), 33.0 (*C*(7)), 36.9 (*C*(1′)), 38.0 (*C*(6)), 49.0 (*C*(3)), 51.6 (*C*(10)), 61.1 (*C*(5)), 62.7 (*C*(6a)), 85.6 (*C*(11a)); *m/z* (ESI$^+$) 223 ([M + H]$^+$, 100%); HRMS (ESI$^+$) *m/z*: [M + H]$^+$ Calcd for $C_{14}H_{27}N_2^+$ 223.2169; Found 223.2169.

*Method B (from **23**).* Palladium black (24 mg, 20% w/w) was added to a stirred, degassed solution of **23** (121 mg, 0.26 mmol, >99:1 dr) in MeOH/$H_2O$/AcOH (10:1:1, 2 mL). The resultant mixture was stirred under an atmosphere of $H_2$ (5 atm) at rt for 48 h. The reaction mixture was then filtered through a short plug of Celite (eluent MeOH/$H_2O$/AcOH, 10:1:1) and concentrated in vacuo. The residue was dissolved in $CH_2Cl_2$ (2 mL), and then $K_2CO_3$ (108 mg, 0.78 mmol) and 4-bromobutanal (79 mg, 0.52 mmol) were added to the resultant solution. The reaction mixture was stirred at rt for 2 h, and then $H_2O$ (2 mL) and satd aq $NaHCO_3$ (10 mL) were added. The reaction mixture was then extracted with $CH_2Cl_2$ (3 × 5 mL), and the combined organic extracts were dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/$Me_2CO$/$NH_4OH$, 100:10:1) gave (+)-tetraponerine 4 (**27**) as a colorless oil (31 mg, 54% from **23**, >99:1 dr); $[\alpha]_D^{25}$ +88.6 (*c* 1.0 in $CHCl_3$).

**(5*S*,6a*R*,11a*S*)-5-Pentyldecahydro-5*H*-pyrido[1,2-*c*]pyrrolo-[1,2-*a*]pyrimidine [(+)-Tetraponerine 8] 28.** Palladium black (26 mg, 20% w/w) was added to a stirred, degassed solution of **24** (130 mg, 0.26 mmol, >95:5 dr) in MeOH/$H_2O$/AcOH (10:1:1, 2 mL). The resultant mixture was stirred under an atmosphere of $H_2$ (5 atm) at rt for 48 h. The reaction mixture was then filtered through a short plug of Celite (eluent MeOH/$H_2O$/AcOH, 10:1:1) and concentrated in vacuo. The residue was dissolved in MeOH/$H_2O$/AcOH (10:1:1, 2 mL), and the resultant solution was degassed. $Pd(OH)_2$/C (65 mg, 50% w/w) was added, and the resultant mixture was stirred under an atmosphere of $H_2$ (5 atm) at rt for 24 h. The reaction mixture was then filtered through a short plug of Celite (eluent MeOH/$H_2O$/AcOH, 10:1:1) and concentrated in vacuo. The residue was dissolved in $CH_2Cl_2$ (2 mL), and then $K_2CO_3$ (110 mg,


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0.792 mmol) and 4-bromobutanal (80 mg, 0.53 mmol) were added to the resultant solution. The reaction mixture was stirred at rt for 2 h, and then $H_2O$ (2 mL) and satd aq $NaHCO_3$ (10 mL) were added. The reaction mixture was then extracted with $CH_2Cl_2$ (3 × 5 mL), and the combined organic extracts were dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/$Me_2CO$/$NH_4OH$, 100:10:1) gave (+)-tetraponerine 8 (**28**) as a white solid (44 mg, 67% from **24**, >99:1 dr); mp 38−40 °C; {lit.[5] mp 40 °C}; $[\alpha]_D^{25}$ +93.0 (*c* 1.0 in $CHCl_3$); {lit.[4] for a sample isolated from the natural source $[\alpha]_D^{20}$ +102 (*c* 0.2 in $CHCl_3$); lit.[9b] $[\alpha]_D^{20}$ +101 (*c* 2.0 in $CHCl_3$)}; $\nu_{max}$ (ATR) 2931, 2857, 2780 (C−H);[26] $\delta_H$ (400 MHz, $C_6D_6$) 0.90 (3H, t, *J* 7.0, C(5′)$H_3$), 1.16−1.67 (17H, m, C(2)$H_A$, C(6)$H_2$, C(7)$H_2$, C(8)$H_2$, C(9)$H_2$, C(1′)$H_2$, C(2′)$H_2$, C(3′)$H_2$, C(4′)$H_2$), 1.68−1.78 (5H, m, C(1)$H_2$, C(2)$H_B$, C(6a)*H*, C(10)$H_A$), 2.04 (1H, app dd, *J* 16.3, 8.5, C(3)$H_A$), 2.12 (1H, app ddd, *J* 14.6, 7.3, 3.6, C(5)*H*), 2.31 (1H, dd, *J* 7.9, 5.7, C(11a)*H*), 2.81−2.86 (1H, m, C(10)$H_B$), 3.15 (1H, app td, *J* 8.5, 2.2, C(3)$H_B$); $\delta_C$ (100 MHz, $C_6D_6$) 14.4 (*C*(5′)), 20.2 (*C*(2)), 23.2 (*C*(4′)), 25.2 (*C*(9)), 25.2 (*C*(2′)), 26.3 (*C*(8)), 29.7 (*C*(1)), 32.8 (*C*(3′)), 33.0 (*C*(7)), 34.6 (*C*(1′)), 38.0 (*C*(6)), 49.0 (*C*(3)), 51.6 (*C*(10)), 61.4 (*C*(5)), 62.7 (*C*(6a)), 85.6 (*C*(11a)); *m*/*z* ($ESI^+$) 251 ([M + H]$^+$, 100%); HRMS ($ESI^+$) *m*/*z*: [M + H]$^+$ Calcd for $C_{16}H_{31}N_2^+$ 251.2482; Found 251.2472.

**(2*R*,2′*S*,α*S*,α′*R*)-1-[*N*(1′)-(α-Methylbenzyl)-1′,2′,5′,6′-tetrahydropyridin-2′-yl]-2-[*N*-benzyl-*N*-(α′-methylbenzyl)-amino]pent-4-ene 29.** DIBAL-H (1.0 M in PhMe, 0.78 mL, 0.78 mmol) was added dropwise to a stirred solution of **22** (383 mg, 0.711 mmol, >99:1 dr) in PhMe (6 mL) at −78 °C, and the resultant mixture was stirred at −78 °C for 1 h. MeOH (144 μL, 3.55 mmol) and $Ph_3P{=}CH_2$ (0.31 M in PhMe/THF, 22.9 mL, 7.11 mmol)[24] were added sequentially, and the resultant mixture was allowed to warm to rt, stirred at rt for 16 h, and then was concentrated in vacuo. The residue was dissolved in $Et_2O$ (30 mL), and the resultant solution was filtered through a short plug of Celite (eluent $Et_2O$) and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/$Et_2O$/$NH_4OH$, 100:5:1) gave **29** as a pale yellow oil (180 mg, 54%, >99:1 dr); $[\alpha]_D^{25}$ +52.5 (*c* 1.0 in $CHCl_3$); $\nu_{max}$ (ATR) 3061, 3025, 2933, 2836 (C−H), 1601, 1492, 1452 (C=C); $\delta_H$ (400 MHz, $CDCl_3$) 1.26 (3H, d, *J* 6.6, C(α)*Me*), 1.34 (3H, d, *J* 6.9, C(α′)*Me*), 1.58−1.76 (3H, d, C(1)$H_2$, C(5′)$H_A$), 1.90−1.99 (1H, m, C(3)$H_A$), 2.00−2.15 (2H, m, C(3)$H_B$, C(5′)$H_B$), 2.46 (1H, ddd, *J* 13.4, 5.4, 2.6, C(6′)$H_A$), 2.83 (1H, ddd, *J* 13.4, 9.9, 4.7, C(6′)$H_B$), 2.93 (1H, app quintet, *J* 6.2, C(2)*H*), 3.24−3.30 (1H, m, C(2′)*H*), 3.73 (1H, d, *J* 14.8, NC$H_A$$H_B$Ph), 3.81 (1H, d, *J* 14.8, NC$H_A$$H_B$Ph), 3.82 (1H, q, *J* 6.6, C(α)*H*), 3.96 (1H, q, *J* 6.9, C(α′)*H*), 4.86−4.88 (1H, m, C(5)$H_A$), 4.89−4.92 (1H, m, C(5)$H_B$), 5.54−5.65 (2H, m, C(4)*H*, C(3′)*H*), 5.72−5.77 (1H, m, C(4′)*H*), 7.18−7.37 (13H, m, *Ph*), 7.42−7.46 (2H, m, *Ph*); $\delta_C$ (100 MHz, $CDCl_3$) 18.2 (C(α′)*Me*), 22.2 (*C*(5′)), 22.5 (C(α)*Me*), 36.8 (*C*(1)), 37.1 (*C*(3)), 40.1 (*C*(6′)), 50.1 ($NCH_2Ph$), 53.1 (*C*(2′)), 55.1 (*C*(2)), 57.6 (*C*(α′)), 58.3 (*C*(α)), 115.2 (*C*(5)), 125.2 (*C*(4′)), 126.6, 126.8, 126.8 (*p-Ph*), 127.7, 128.1, 128.3, 128.3, 128.3, 128.5 (*o,m-Ph*), 130.6 (*C*(3′)), 138.1 (*C*(4)), 142.3, 144.4, 145.5 (*i-Ph*); *m*/*z* ($ESI^+$) 465 ([M + H]$^+$, 100%); HRMS ($ESI^+$) *m*/*z*: [M + H]$^+$ Calcd for $C_{33}H_{41}N_2^+$ 465.3264; Found 465.3259.

**(2*R*,2′*S*,α*S*,α′*R*,*Z*)-1-[*N*(1′)-(α-Methylbenzyl)-1′,2′,5′,6′-tetrahydropyridin-2′-yl]-2-[*N*-benzyl-*N*-(α′-methylbenzyl)-amino]hept-4-ene 30.** DIBAL-H (1.0 M in PhMe, 0.77 mL, 0.77 mmol) was added dropwise to a stirred solution of **22** (377 mg, 0.700 mmol, >99:1 dr) in PhMe (6 mL) at −78 °C, and the resultant mixture was stirred at −78 °C for 1 h. MeOH (142 μL, 3.50 mmol) and $Ph_3P{=}CHCH_2CH_3$ (0.31 M in PhMe/THF, 22.6 mL, 7.00 mmol)[25] were added sequentially, and the resultant mixture was allowed to warm to rt, stirred at rt for 16 h, and then concentrated in vacuo. The residue was dissolved in $Et_2O$ (30 mL), and the resultant solution was filtered through a short plug of Celite (eluent $Et_2O$) and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/$Et_2O$/$NH_4OH$, 100:5:1) gave **30** as a pale yellow oil (162 mg, 47%, >95:5 dr [(*Z*):(*E*)]); $[\alpha]_D^{25}$ +59.2 (*c* 1.0 in $CHCl_3$); $\nu_{max}$ (ATR) 2970 (C−H), 1493, 1453 (C=C); $\delta_H$ (400 MHz, $CDCl_3$) 0.90 (3H, t, *J* 7.5, C(7)$H_3$), 1.26 (3H, d, *J* 6.6, C(α)*Me*), 1.34 (3H, d, *J* 6.9, C(α′)*Me*), 1.60−1.80 (3H, m, C(1)$H_2$, C(5′)$H_A$), 1.91 (2H, app quintet, *J* 7.5, C(6)$H_2$), 1.97 (2H, app t, *J* 6.8, C(3)$H_2$), 2.04−2.15 (1H, m, C(5′)$H_B$), 2.47 (1H, ddd, *J* 13.1, 5.3, 3.1, C(6′)$H_A$), 2.80−2.92 (2H, m, C(2)*H*, C(6′)$H_B$), 3.20−3.26 (1H, m, C(2′)*H*), 3.73 (1H, d, *J* 14.8, NC$H_A$$H_B$Ph), 3.81 (1H, d, *J* 14.8, NC$H_A$$H_B$Ph), 3.83 (1H, q, *J* 6.6, C(α)*H*), 3.98 (1H, q, *J* 6.9, C(α′)*H*), 5.12−5.19 (1H, m, C(4)*H*), 5.25−5.32 (1H, m, C(5)*H*), 5.56−5.61 (1H, m, C(3′)*H*), 5.71−5.77 (1H, m, C(4′)*H*), 7.17−7.44 (15H, m, *Ph*); $\delta_C$ (100 MHz, $CDCl_3$) 14.3 (*C*(7)), 18.3 (C(α′)*Me*), 20.9 (*C*(6)), 22.3 (C(α)*Me*), 22.6 (*C*(5′)), 30.0 (*C*(3)), 36.8 (*C*(1)), 40.2 (*C*(6′)), 50.0 ($NCH_2Ph$), 53.2 (*C*(2′)), 55.5 (*C*(2)), 57.6 (*C*(α′)), 58.2 (*C*(α)), 125.1 (*C*(4′)), 126.6, 126.7, 126.8 (*p-Ph*), 127.8, 128.0 (*o,m-Ph*), 128.1 (*C*(4)), 128.2, 128.2, 128.3, 128.5 (*o,m-Ph*), 130.8 (*C*(3′)), 131.8 (*C*(5)), 142.4, 144.7, 145.2 (*i-Ph*); *m*/*z* ($ESI^+$) 493 ([M + H]$^+$, 100%); HRMS ($ESI^+$) *m*/*z*: [M + H]$^+$ Calcd for $C_{35}H_{45}N_2^+$ 493.3577; Found 493.3565.

**(5*R*,6a*R*,11a*S*)-5-Propyldecahydro-5*H*-pyrido[1,2-*c*]pyrrolo-[1,2-*a*]pyrimidine [(+)-Tetraponerine 3] 33.** Palladium black (23 mg, 20% w/w) was added to a stirred, degassed solution of **29** (115 mg, 0.25 mmol, >99:1 dr) in MeOH/$H_2O$/AcOH (10:1:1, 2 mL). The resultant mixture was stirred under an atmosphere of $H_2$ (5 atm) at rt for 48 h. The reaction mixture was then filtered through a short plug of Celite (eluent MeOH/$H_2O$/AcOH, 10:1:1) and concentrated in vacuo. The residue was dissolved in $CH_2Cl_2$ (2 mL), then $K_2CO_3$ (102 mg, 0.741 mmol) and 4-bromobutanal (75 mg, 0.49 mmol) were added to the resultant solution. The reaction mixture was stirred at rt for 2 h, then $H_2O$ (2 mL) and satd aq $NaHCO_3$ (10 mL) were added. The reaction mixture was then extracted with $CH_2Cl_2$ (3 × 5 mL) and the combined organic extracts were dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/$Me_2CO$/$NH_4OH$, 100:10:1) gave (+)-tetraponerine 3 (**33**) as a colorless oil (33 mg, 60% from **29**, >99:1 dr); $[\alpha]_D^{25}$ +30.9 (*c* 1.0 in $CHCl_3$); {lit.[4] for a sample isolated from the natural source $[\alpha]_D^{20}$ +27 (*c* 0.07 in $CHCl_3$); lit.[5] $[\alpha]_D^{20}$ +31 (*c* 3.1 in $CHCl_3$); lit.[9d] $[\alpha]_D^{20}$ +35 (*c* 0.49 in $CHCl_3$)}; $\nu_{max}$ (ATR) 2954, 2928, 2859, 2802 (C−H);[26] $\delta_H$ (400 MHz, $C_6D_6$) 0.95 (3H, t, *J* 7.2, C(3′)$H_3$), 1.09 (1H, app dt, *J* 12.7, 1.9, C(6)$H_A$), 1.15−1.28 (1H, m, C(9)$H_A$), 1.27−1.48 (5H, m, C(7)$H_2$, C(1′)$H_A$, C(2′)$H_2$), 1.48−1.84 (9H, m, C(1)$H_2$, C(2)$H_2$, C(8)$H_2$, C(9)$H_B$, C(10)$H_A$, C(1′)$H_B$), 1.91 (1H, ddd, *J* 12.7, 11.9, 5.3, C(6)$H_B$), 1.99−2.07 (1H, m, C(6a)*H*), 2.72−2.86 (3H, m, C(3)$H_A$, C(5)*H*, C(10)$H_B$), 3.17 (1H, app q, *J* 7.5, C(3)$H_B$), 3.30 (1H, app t, *J* 3.5, C(11a)*H*); $\delta_C$ (100 MHz, $C_6D_6$) 14.5 (*C*(3′)), 20.7 (*C*(2′)), 22.2 (*C*(2)), 25.3 (*C*(9)), 26.6 (*C*(8)), 30.6 (*C*(1)), 32.2 (*C*(6)), 33.4 (*C*(1′)), 34.3 (*C*(7)), 50.6 (*C*(3)), 51.0 (*C*(10)), 53.0 (*C*(5)), 56.7 (*C*(6a)), 75.4 (*C*(11a)); *m*/*z* ($ESI^+$) 223 ([M + H]$^+$, 100%); HRMS ($ESI^+$) *m*/*z*: [M + H]$^+$ Calcd for $C_{14}H_{27}N_2^+$ 223.2169; Found 223.2168.

**(5*R*,6a*R*,11a*S*)-5-Pentyldecahydro-5*H*-pyrido[1,2-*c*]pyrrolo-[1,2-*a*]pyrimidine [(+)-Tetraponerine 7] 34.** Palladium black (22 mg, 20% w/w) was added to a stirred, degassed solution of **30** (108 mg, 0.22 mmol, >95:5 dr) in MeOH/$H_2O$/AcOH (10:1:1, 2 mL). The resultant mixture was stirred under an atmosphere of $H_2$ (5 atm) at rt for 48 h. The reaction mixture was then filtered through a short plug of Celite (eluent MeOH/$H_2O$/AcOH, 10:1:1) and concentrated in vacuo. The residue was dissolved in $CH_2Cl_2$ (2 mL), and then $K_2CO_3$ (91 mg, 0.66 mmol) and 4-bromobutanal (66 mg, 0.44 mmol) were added to the resultant solution. The reaction mixture was stirred at rt for 2 h, and then $H_2O$ (2 mL) and satd aq $NaHCO_3$ (10 mL) were added. The reaction mixture was then extracted with $CH_2Cl_2$ (3 × 5 mL), and the combined organic extracts were dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/$Me_2CO$/$NH_4OH$, 100:10:1) gave (+)-tetraponerine 7 (**34**) as a colorless oil (24 mg, 44% from **30**, >99:1 dr); $[\alpha]_D^{25}$ +30.4 (*c* 0.8 in $CHCl_3$); {lit.[4] for a sample isolated from the natural source $[\alpha]_D^{20}$ +30 (*c* 0.22 in $CHCl_3$); lit.[9b] $[\alpha]_D^{20}$ +29.5 (*c* 2.2 in $CHCl_3$)}; $\nu_{max}$ (ATR) 2928, 2856, 2790 (C−H);[26] $\delta_H$ (400 MHz, $C_6D_6$) 0.93 (3H, t, *J* 6.9, C(5′)$H_3$), 1.13 (1H, app dt, *J* 12.9, 1.9, C(6)$H_A$), 1.17−1.86 (19H, m, C(1)$H_2$, C(2)$H_2$, C(7)$H_2$, C(8)$H_2$, C(9)$H_2$, C(10)$H_A$, C(1′)$H_2$, C(2′)$H_2$, C(3′)$H_2$, C(4′)$H_2$), 1.93 (1H, ddd, *J* 12.9, 11.9, 5.4, C(6)$H_B$), 2.02−2.09 (1H, m,


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C(6a)*H*), 2.74−2.86 (3H, m, C(3)$H_A$, C(5)*H*, C(10)$H_B$), 3.15−3.21 (1H, m, C(3)$H_B$), 3.33 (1H, app t, *J* 3.6, C(11a)*H*); $\delta_C$ (100 MHz, $C_6D_6$) 14.4 (*C*(5′)), 22.2 (*C*(2)), 23.2 (*C*(4′)), 25.3 (*C*(8)), 26.6 (*C*(9)), 27.4 (*C*(2′)), 30.6 (*C*(1)), 31.1 (*C*(1′)), 32.3 (*C*(6)), 32.5 (*C*(3′)), 34.3 (*C*(7)), 50.7 (*C*(3)), 51.0 (*C*(10)), 53.3 (*C*(5)), 56.7 (*C*(6a)), 75.5 (*C*(11a)); *m*/*z* (ESI$^+$) 251 ([M + H]$^+$, 100%); HRMS (ESI$^+$) *m*/*z*: [M + H]$^+$ Calcd for $C_{16}H_{31}N_2^+$ 251.2482; Found 251.2480.

***tert*-Butyl (3*S*,α*R*,*E*)-3-[*N*-Allyl-*N*-(α-methylbenzyl)amino]-hex-4-enoate 35.** BuLi (2.30 M in hexanes, 14.0 mL, 32.3 mmol) was added dropwise to a stirred solution of (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (5.36 g, 33.3 mmol, >99:1 er) in THF (30 mL) at −78 °C, and the resultant mixture was stirred at −78 °C for 30 min. A solution of **3** (3.50 g, 20.8 mmol, >99:1 dr) in THF (10 mL) at −78 °C was added dropwise via cannula, and the resultant mixture was stirred at −78 °C for 2 h. Satd aq $NH_4Cl$ (10 mL) was added, and the reaction mixture was allowed to warm to rt and then concentrated in vacuo. The residue was partitioned between $CH_2Cl_2$ (100 mL) and 10% aq citric acid (100 mL), and the organic layer was washed with satd aq $NaHCO_3$ (100 mL) and brine (100 mL), then dried, and concentrated in vacuo to give **35** in >95:5 dr. Purification via flash column chromatography (eluent 30−40 C petrol/EtOAc, 20:1) gave **35** as a pale yellow oil (6.10 g, 89%, >99:1 dr);[15b] $[\alpha]_D^{25}$ −3.5 (*c* 2.0 in $CHCl_3$); {lit.[15c] $[\alpha]_D^{20}$ −4.7 (*c* 1.0 in $CHCl_3$)}; $\delta_H$ (400 MHz, $CDCl_3$) 1.36 (3H, d, *J* 6.8, C(α)*Me*), 1.40 (9H, s, *CMe*$_3$), 1.69 (3H, d, *J* 5.3, C(6)$H_3$), 2.26 (1H, dd, *J* 14.2, 8.4, C(2)$H_A$), 2.40 (1H, dd, *J* 14.2, 6.4, C(2)$H_B$), 3.10−3.14 (2H, m, C(1′)$H_2$), 3.78−3.85 (1H, m, C(3)*H*), 4.00 (1H, q, *J* 6.8, C(α)*H*), 4.99 (1H, dd, *J* 10.3, 1.6, C(3′)$H_A$), 5.07 (1H, dd, *J* 17.0, 1.6, C(3′)$H_B$), 5.43−5.58 (2H, m, C(4)*H*, C(5)*H*), 5.77 (1H, ddt, *J* 17.0, 10.3, 6.3, C(2′)*H*), 7.17−7.22 (1H, m, *Ph*), 7.25−7.31 (2H, m, *Ph*), 7.35−7.39 (2H, m, *Ph*).

***tert*-Butyl (2′*S*,α*R*)-2-[*N*(1′)-(α-Methylbenzyl)-2′,5′-dihydro-1*H*-pyrrol-2′-yl]acetate 36.** Grubbs I catalyst (230 mg, 0.36 mmol) was added to a stirred, degassed solution of **35** (3.00 g, 9.11 mmol, >99:1 dr) in anhydrous $CH_2Cl_2$ (EtOH stabilized, 300 mL) at rt. The resultant mixture was stirred at rt for 16 h and then concentrated in vacuo. The residue was dissolved in $CH_2Cl_2$ (80 mL), and then $P(CH_2OH)_3$ (4.52 g, 36.4 mmol) and $Et_3N$ (2.54 mL, 18.2 mmol) were added sequentially. The resultant mixture was stirred at rt for 5 min, then excess silica gel (10 g) was added, and the resultant mixture was stirred at rt for 12 h before being concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/$Et_2O$/$NH_4OH$, 100:10:1) gave **36** as a pale yellow oil (2.25 g, 86%, >99:1 dr);[15a] $[\alpha]_D^{25}$ +99.0 (*c* 1.0 in $CHCl_3$); {lit.[15b] for *ent*-**36**: $[\alpha]_D^{24}$ −132.0 (*c* 0.99 in $CHCl_3$)}; $\delta_H$ (400 MHz, $CDCl_3$) 1.43 (3H, d, *J* 6.7, C(α)*Me*), 1.46 (9H, s, *CMe*$_3$), 2.33 (1H, dd, *J* 14.5, 8.9, C(2)$H_A$), 2.59 (1H, dd, *J* 14.5, 4.0, C(2)$H_B$), 3.34−3.41 (1H, m, C(5′)$H_A$), 3.57−3.63 (1H, m, C(5′)$H_B$), 3.85 (1H, q, *J* 6.7, C(α)*H*), 4.10−4.18 (1H, m, C(2′)*H*), 5.68−5.76 (2H, m, C(3′)*H*, C(4′)*H*), 7.19−7.34 (5H, m, *Ph*).

***tert*-Butyl (*R*,*R*)-2-[*N*(1′)-(α-Methylbenzyl)pyrrolidin-2′-yl]-acetate 37.** $RhCl(PPh_3)_3$ (100 mg, 0.11 mmol) was added to a degassed solution of **36** (1.00 g, 3.48 mmol, >99:1 dr) in EtOAc (5 mL), and the resultant mixture was stirred under $H_2$ (2 atm) at rt for 16 h. The reaction mixture was then filtered through Celite (eluent EtOAc) and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/$Et_2O$, 10:1) gave **37** as a colorless oil (860 mg, 86%, >99:1 dr);[15b] $[\alpha]_D^{25}$ +57.0 (*c* 1.0 in $CHCl_3$); {lit.[15b] for *ent*-**37**: $[\alpha]_D^{23}$ −56.1 (*c* 1.6 in $CHCl_3$)}; $\delta_H$ (400 MHz, $CDCl_3$) 1.44 (3H, d, *J* 6.8, C(α)*Me*), 1.44 (9H, s, *CMe*$_3$), 1.55−1.64 (2H, m, C(3′)$H_A$, C(4′)$H_A$), 1.65−1.77 (1H, m, C(4′)$H_B$), 1.79−1.89 (1H, m, C(3′)$H_B$), 2.18 (1H, dd, *J* 14.2, 9.9, C(2)$H_A$), 2.39 (1H, td, *J* 8.8, 6.9, C(5′)$H_A$), 2.58 (1H, dd, *J* 14.2, 3.5, C(2)$H_B$), 2.76−2.82 (1H, m, C(5′)$H_B$), 3.00−3.09 (1H, m, C(2′)*H*), 3.76 (1H, q, *J* 6.8, C(α)*H*), 7.21−7.35 (5H, m, *Ph*).

***tert*-Butyl (*R*,*R*,*E*)-4-[*N*(1′)-(α-Methylbenzyl)pyrrolidin-2′-yl]-but-2-enoate 38.** *Method A (from 37).* DIBAL-H (1.0 M in PhMe, 0.57 mL, 0.57 mmol) was added dropwise to a stirred solution of **37** (151 mg, 0.522 mmol, >99:1 dr) in PhMe (2 mL) at −78 °C, and the resultant mixture was stirred at −78 °C for 1 h. MeOH (0.11 mL, 2.61 mmol) and $Ph_3P{=}CHCO_2{}^tBu$ (196 mg, 0.522 mmol) were added sequentially, and the resultant mixture was allowed to warm to rt and stirred at rt for 16 h. The reaction mixture was then concentrated in vacuo to give a 75:25 mixture of **38** and **39**, respectively. Purification via flash column chromatography (eluent 30−40 °C petrol/$Et_2O$/$NH_4OH$, 100:20:1) gave a 9:91 mixture of **38** and **39**, respectively, as a pale yellow oil (22 mg, 13%). Data for **39**: $\delta_H$ (400 MHz, $CDCl_3$) 1.44 (3H, d, *J* 6.8, C(α)*Me*), 1.46−1.60 (2H, m, C(3′)$H_A$, C(4′)$H_A$), 1.50 (9H, s, *CMe*$_3$), 1.65−1.77 (2H, m, C(3′)$H_B$, C(4′)$H_B$), 2.37 (1H, app q, *J* 8.2, C(5′)$H_A$), 2.65−2.79 (2H, m, C(4)$H_A$, C(2′)*H*), 2.84−2.90 (1H, m, C(5′)$H_B$), 2.94−3.03 (1H, m, C(4)$H_B$), 3.87 (1H, q, *J* 6.8, C(α)*H*), 5.75 (1H, dt, *J* 11.6, 1.7, C(2)*H*), 6.18 (1H, dt, *J* 11.6, 7.2, C(3)*H*), 7.21−7.37 (5H, m, *Ph*); $\delta_C$ (100 MHz, $CDCl_3$) 22.0 (C(α)*Me*), 22.6 (*C*(4′)), 28.4 (*CMe*$_3$), 29.9 (*C*(3′)), 32.6 (*C*(4)), 49.0 (*C*(5′)), 58.9 (*C*(2′)), 59.2 (*C*(α)), 80.1 (*CMe*$_3$), 122.5 (*C*(2)), 126.9 (*p*-*Ph*), 128.1, 128.2 (*o*,*m*-*Ph*), 142.4 (*i*-*Ph*), 146.2 (*C*(3)), 166.2 (*C*(1)). Data for mixture: $\nu_{max}$ (ATR) 2972, 2873 (C−H), 1713 (C═O), 1651 (C═C); *m*/*z* (ESI$^+$) 316 ([M + H]$^+$, 100%); HRMS (ESI$^+$) *m*/*z*: [M + H]$^+$ Calcd for $C_{20}H_{30}NO_2^+$ 316.2271; Found 316.2269. Further elution (eluent 30−40 °C petrol/$Et_2O$/$NH_4OH$, 100:20:1) gave an 86:14 mixture of **38** and **39**, respectively, as a colorless oil (108 mg, 66%).

*Method B (from 36): Step 1.* $RhCl(PPh_3)_3$ (320 mg, 0.348 mmol) was added to a degassed solution of **36** (5.00 g, 17.4 mmol) in EtOAc (100 mL), and the resultant mixture was stirred under $H_2$ (2 atm) at rt for 16 h. The reaction mixture was then filtered through Celite (eluent EtOAc) and concentrated in vacuo to give **37**.

*Method B (from 36): Step 2.* DIBAL-H (1.0 M in PhMe, 19.1 mL, 19.1 mmol) was added dropwise to a stirred solution of the residue of **37** from the previous step in PhMe (70 mL) at −78 °C, and the resultant mixture was stirred at −78 °C for 1 h. MeOH (3.57 mL, 87.0 mmol) and $Ph_3P{=}CHCO_2{}^tBu$ (6.55 g, 17.4 mmol) were added sequentially, and the resultant mixture was allowed to warm to rt and stirred at rt for 16 h. The reaction mixture was then concentrated in vacuo to give a 75:25 mixture of **38** and **39**, respectively. Purification via exhaustive flash column chromatography (eluent 30−40 °C petrol/$Et_2O$/$NH_4OH$, 100:20:1) gave **38** as a pale yellow oil (2.76 g, 50% from **36**, 98:2 dr); $[\alpha]_D^{25}$ +82.7 (*c* 1.0 in $CHCl_3$); $\nu_{max}$ (ATR) 2972, 2873 (C−H), 1713 (C═O); $\delta_H$ (400 MHz, $CDCl_3$) 1.44 (3H, d, *J* 6.8, C(α)*Me*), 1.48 (9H, s, *CMe*$_3$), 1.48−1.81 (4H, m, C(3′)$H_2$, C(4′)$H_2$), 2.18 (1H, app dt, *J* 14.2, 9.0, C(4)$H_A$), 2.40 (1H, app td, *J* 8.7, 7.2, C(5′)$H_A$), 2.50 (1H, dddd, *J* 14.2, 7.0, 3.3, 1.5, C(4)$H_B$), 2.70−2.78 (1H, m, C(2′)*H*), 2.80−2.86 (1H, m, C(5′)$H_B$), 3.80 (1H, q, *J* 6.8, C(α)*H*), 5.76 (1H, dt, *J* 15.6, 1.5, C(2)*H*), 6.83 (1H, app dt, *J* 15.6, 7.0, C(3)*H*), 7.21−7.34 (5H, m, *Ph*); $\delta_C$ (100 MHz, $CDCl_3$) 22.2 (C(α)*Me*), 22.7 (*C*(4′)), 28.3 (*CMe*$_3$), 30.2 (*C*(3′)), 37.6 (*C*(4)), 49.9 (*C*(5′)), 58.7 (*C*(2′)), 60.3 (*C*(α)), 80.2 (*CMe*$_3$), 124.4 (*C*(2)), 127.0 (*p*-*Ph*), 128.0, 128.2 (*o*,*m*-*Ph*), 142.9 (*i*-*Ph*), 145.9 (*C*(3)), 166.1 (*C*(1)); *m*/*z* (ESI$^+$) 316 ([M + H]$^+$, 100%); HRMS (ESI$^+$) *m*/*z*: [M + H]$^+$ Calcd for $C_{20}H_{30}NO_2^+$ 316.2271; Found 316.2270.

***tert*-Butyl (*R*,*R*,*R*)-3-[*N*-Benzyl-*N*-isopropylamino]-4-[*N*(1′)-(α-methylbenzyl)pyrrolidin-2′-yl]butanoate and *tert*-Butyl (3*S*,2′*R*,α*R*)-3-[*N*-Benzyl-*N*-isopropylamino]-4-[*N*(1′)-(α-methyl-benzyl)pyrrolidin-2′-yl]butanoate 40 and 41.** BuLi (2.3 M in hexanes, 0.11 mL, 0.253 mmol) was added dropwise to a stirred solution of *N*-benzyl-*N*-isopropylamine (38 mg, 0.25 mmol) in THF (0.5 mL) at −78 °C, and the resultant mixture was stirred at −78 °C for 30 min. A solution of **38** (50 mg, 0.159 mmol, 98:2 dr [(*E*):(*Z*)]) in THF (0.5 mL) at −78 °C was added via cannula, and the resultant mixture was stirred at −78 °C for 2 h. Satd aq $NH_4Cl$ (0.2 mL) was added, and the reaction mixture was allowed to warm to rt and then concentrated in vacuo. The residue was partitioned between $CH_2Cl_2$ (5 mL) and 10% citric acid (5 mL), and the organic layer was washed with satd aq $NaHCO_3$ (5 mL) and brine (5 mL), then dried, and concentrated in vacuo to give a 50:50 mixture of **40** and **41**. Purification via flash column chromatography (eluent 30−40 °C petrol/$Et_2O$/$NH_4OH$, 100:20:1) gave a 50:50 mixture of **40** and **41** as a colorless oil (52 mg, 70%). Data for **40**: $\delta_H$ (400 MHz, $CDCl_3$) 0.96−1.06 (6H, m, NCH*Me*$_2$), 1.07−1.31 (2H, m, C(4)$H_A$, C(3′)$H_A$), 1.34−1.41 (1H, m, C(3′)$H_B$), 1.39 (3H, d, *J* 6.7, C(α)*Me*), 1.45 (9H,



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s, C$Me_3$), 1.48−1.62 (2H, m, C(4′)$H_2$), 1.87 (1H, ddd, $J$ 13.5, 10.2, 3.8, C(4)$H_B$), 2.10−2.18 (1H, m, C(2)$H_A$), 2.33−2.42 (1H, m, C(5′)$H_A$), 2.64 (1H, dd, $J$ 13.8, 3.8, C(2)$H_B$), 2.70 (1H, ddd, $J$ 9.2, 7.4, 3.7, C(5′)$H_B$), 2.87−2.97 (2H, m, C(2′)$H$, NC$H$Me$_2$), 3.11 (1H, app tt, $J$ 14.5, 3.8, C(3)$H$), 3.43 (1H, d, $J$ 14.1, NC$H_A$H$_B$Ph), 3.70 (1H, d, $J$ 14.1, NCH$_A$$H_B$Ph), 3.74 (1H, q, $J$ 6.7, C($\alpha$)$H$), 7.17−7.40 (10H, m, $Ph$). Data for **41**: $\delta_H$ (400 MHz, $CDCl_3$) 0.96−1.06 (6H, m, NCH$Me_2$), 1.45 (3H, d, $J$ 6.9, C($\alpha$)$Me$), 1.45 (9H, s, C$Me_3$), 1.46−1.63 (3H, m, C(4)$H_A$, C(3′)$H_A$, C(4′)$H_A$), 1.67−1.87 (3H, m, C(4)$H_B$, C(3′)$H_B$, C(4′)$H_B$), 2.10−2.18 (1H, m, C(2)$H_A$), 2.27−2.43 (3H, m, C(2)$H_B$, C(2′)$H$, C(5′)$H_A$), 2.82−2.97 (2H, m, C(5′)$H_B$, NC$H$Me$_2$), 3.22−3.29 (1H, m, C(3)$H$), 3.62 (1H, d, $J$ 14.6, NC$H_A$H$_B$Ph), 3.75 (1H, d, $J$ 14.6, NCH$_A$$H_B$Ph), 3.84 (1H, q, $J$ 6.9, C($\alpha$)$H$), 7.17−7.40 (10H, m, $Ph$). Data for mixture of **40** and **41**: $\nu_{max}$ (ATR) 3026, 2966, 2932, 2871 (C−H), 1724 (C═O); $\delta_C$ (100 MHz, $CDCl_3$) 18.8, 19.8, 21.4, 21.7, 22.5, 22.8, 22.9, 23.0, 28.2, 28.2, 29.6, 30.5, 37.4, 37.8, 39.2, 40.0, 46.8, 48.7, 48.9, 49.1, 49.3, 50.4, 52.6, 52.9, 57.5, 58.2, 59.4, 61.0, 80.1, 80.2, 126.6, 126.6, 126.7, 127.0, 127.9, 128.0, 128.0, 128.1, 128.1, 128.2, 128.6, 129.0, 141.1, 141.8, 142.1, 144.2, 172.4, 172.4; $m/z$ (ESI$^+$) 465 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $m/z$: [M + H]$^+$ Calcd for $C_{30}H_{45}N_2O_2^+$ 465.3476; Found 465.3475.

***tert*-Butyl (*R*,*R*,*R*,*R*)-3-[*N*-Benzyl-*N*-(α-methylbenzyl)amino]-4-[*N*(1′)-(α′-methylbenzyl)pyrrolidin-2′-yl]butanoate 42.** *Method A.* BuLi (2.3 M in hexanes, 0.85 mL, 1.96 mmol) was added dropwise to a stirred solution of (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)-amine (429 mg, 2.03 mmol, >99:1 er) in THF (3 mL) at −78 °C, and the resultant mixture was stirred at −78 °C for 30 min. A solution of **38** (400 mg, 1.27 mmol, 98:2 dr [(*E*):(*Z*)]) in THF (2 mL) at −78 °C was added, and the resultant mixture was stirred at −78 °C for 2 h. Satd aq $NH_4Cl$ (1 mL) was added, and the reaction mixture was allowed to warm to rt and then concentrated in vacuo. The residue was partitioned between $CH_2Cl_2$ (10 mL) and 10% citric acid (10 mL), and the organic layer was washed with satd aq $NaHCO_3$ (10 mL) and brine (10 mL), then dried, and concentrated in vacuo to give **42** in >95:5 dr. Purification via flash column chromatography (eluent 30−40 °C petrol/$Et_2O$/$NH_4OH$, 100:20:1) gave **42** as a pale yellow oil (655 mg, 98%, >99:1 dr); $[\alpha]_D^{25}$ +45.1 ($c$ 1.0 in $CHCl_3$); $\nu_{max}$ (ATR) 3027, 2971, 2932, 2872 (C−H), 1723 (C═O); $\delta_H$ (400 MHz, $CDCl_3$) 1.13 (1H, ddd, $J$ 13.7, 10.9, 2.7, C(4)$H_A$), 1.32 (3H, d, $J$ 7.0, C($\alpha$)$Me$), 1.38 (3H, obsc d, C($\alpha'$)$Me$), 1.40 (9H, s, C$Me_3$), 1.42−1.50 (1H, m, C(3′)$H_A$), 1.53−1.74 (3H, m, C(3′)$H_B$, C(4′)$H_2$), 1.75−1.83 (2H, m, C(2)$H_2$), 1.92 (1H, ddd, $J$ 13.7, 10.8, 2.7, C(4)$H_B$), 2.42 (1H, app q, $J$ 8.1, C(5′)$H_A$), 2.73−2.79 (1H, m, C(5′)$H_B$), 3.10−3.18 (1H, m, C(2′)$H$), 3.34−3.41 (1H, m, C(3)$H$), 3.44 (1H, d, $J$ 14.8, NC$H_A$H$_B$Ph), 3.73−3.81 (2H, m, C($\alpha$)$H$, C($\alpha'$)$H$), 3.87 (1H, d, $J$ 14.8, NCH$_A$$H_B$Ph), 7.16−7.40 (15H, m, $Ph$); $\delta_C$ (100 MHz, $CDCl_3$) 20.8 (C($\alpha$)$Me$), 23.0 (C($\alpha'$)$Me$), 23.1 (C(4′)), 28.2 (C$Me_3$), 29.8 (C(3′)), 37.9 (C(2)), 38.8 (C(4)), 50.4 (NC$H_2$Ph), 50.7 (C(5′)), 51.8 (C(3)), 57.1 (C($\alpha$)), 57.5 (C(2′)), 61.0 (C($\alpha'$)), 80.1 (C$Me_3$), 126.7, 126.8, 127.1 (*p*-*Ph*), 127.9, 128.2, 128.2, 128.3, 128.4, 128.5 (*o*,*m*-*Ph*), 141.1, 142.5, 144.2 (*i*-*Ph*), 172.1 (C(1)); $m/z$ (ESI$^+$) 527 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $m/z$: [M + H]$^+$ Calcd for $C_{35}H_{47}N_2O_2^+$ 527.3632; Found 527.3626.

*Method B.* BuLi (2.3 M in hexanes, 0.22 mL, 0.50 mmol) was added dropwise to a stirred solution of (*R*)-*N*-benzyl-*N*-(α-methylbenzyl)amine (109 mg, 0.52 mmol, >99:1 er) in THF (2 mL) at −78 °C, and the resultant mixture was stirred at −78 °C for 30 min. A solution of **38** and **39** (102 mg, 0.32 mmol, 86:14 dr [(*E*):(*Z*)]) in THF (1 mL) at −78 °C was added, and the resultant mixture was stirred at −78 °C for 2 h. Satd aq $NH_4Cl$ (0.5 mL) was added, and the reaction mixture was allowed to warm to rt and then concentrated in vacuo. The residue was partitioned between $CH_2Cl_2$ (5 mL) and 10% citric acid (5 mL), and the organic layer was washed with satd aq $NaHCO_3$ (5 mL) and brine (5 mL), then dried, and concentrated in vacuo to give an 86:14 mixture of **42** and **44**, respectively. Purification via flash column chromatography (eluent 30−40 °C petrol/$Et_2O$/$NH_4OH$, 100:20:1) gave a 90:10 mixture of **42** and **44**, respectively, as a pale yellow oil (143 mg). Data for **44**: $\delta_H$ (400 MHz, $CDCl_3$) [selected peaks] 2.28−2.36 (1H, m, C(5′)$H_A$) 2.85−2.95 (2H, m, C(2′)$H$, C(5′)$H_B$), 2.99 (1H, dd, $J$ 15.9, 6.9, C(2)$H_A$), 3.05 (1H, dd, $J$ 15.9, 6.9, C(2)$H_B$), 5.52 (1H, dd, $J$ 15.5, 8.3, C(4)$H$), 5.65 (1H, app dt, $J$ 15.5, 6.9, C(3)$H$); $m/z$ (ESI$^+$) 527 ([M(**42**) + H]$^+$, 100%); 316 ([M(**44**) + H]$^+$, 32%).

***tert*-Butyl (3*S*,2′*R*,α*S*,α′*R*)-3-[*N*-Benzyl-*N*-(α-methylbenzyl)-amino]-4-[*N*(1′)-(α′-methylbenzyl)pyrrolidin-2′-yl]butanoate 43.** BuLi (2.3 M in hexanes, 0.85 mL, 1.97 mmol) was added dropwise to a stirred solution of (*S*)-*N*-benzyl-*N*-(α-methlbenzyl)amine (429 mg, 2.03 mmol, >99:1 er) in THF (3 mL) at −78 °C, and the resultant mixture was stirred at −78 °C for 30 min. A solution of **38** (400 mg, 1.27 mmol, 98:2 dr [(*E*):(*Z*)]) in THF (2 mL) at −78 °C was added, and the resultant mixture was stirred at −78 °C for 2 h. Satd aq $NH_4Cl$ (1 mL) was added, and the reaction mixture was allowed to warm to rt and then concentrated in vacuo. The residue was partitioned between $CH_2Cl_2$ (10 mL) and 10% citric acid (10 mL), and the organic layer was washed with satd aq $NaHCO_3$ (10 mL) and brine (10 mL), then dried, and concentrated in vacuo to give **43** in >95:5 dr. Purification via flash column chromatography (eluent 30−40 °C petrol/$Et_2O$/$NH_4OH$, 100:20:1) gave **43** as a pale yellow oil (615 mg, 92%, >99:1 dr); $[\alpha]_D^{25}$ +72.8 ($c$ 1.0 in $CHCl_3$); $\nu_{max}$ (ATR) 3027, 2972, 2932, 2801 (C−H), 1725 (C═O); $\delta_H$ (400 MHz, $CDCl_3$) 1.34 (3H, d, $J$ 6.9, C($\alpha$)$Me$), 1.38 (9H, s, C$Me_3$), 1.42 (3H, d, $J$ 6.9, C($\alpha'$)$Me$), 1.41−1.47 (1H, m, C(3′)$H_A$), 1.52−1.78 (4H, m, C(4)$H_A$, C(3′)$H_B$, C(4′)$H_2$), 1.84 (1H, ddd, $J$ 13.0, 9.8, 2.5, C(4)$H_B$), 1.93 (1H, dd, $J$ 15.1, 6.6, C(2)$H_A$), 2.10 (1H, dd, $J$ 15.1, 5.8, C(2)$H_B$), 2.32−2.47 (2H, m, C(2′)$H$, C(5′)$H_A$), 2.79−2.85 (1H, m, C(5′)$H_B$), 3.31−3.39 (1H, m, C(3)$H$), 3.62 (1H, d, $J$ 14.8, NC$H_A$H$_B$Ph), 3.75 (1H, d, $J$ 14.8, NCH$_A$$H_B$Ph), 3.80 (1H, q, $J$ 6.9, C($\alpha'$)$H$), 3.91 (1H, q, $J$ 6.9, C($\alpha$)$H$), 7.17−7.40 (15H, m, $Ph$); $\delta_C$ (100 MHz, $CDCl_3$) 19.8 (C($\alpha$)$Me$), 21.9 (C($\alpha'$)$Me$), 22.7 (C(4′)), 28.2 (C$Me_3$), 30.9 (C(3′)), 38.8 (C(4)), 39.0 (C(2)), 49.2 (C(5′)), 50.4 (NC$H_2$Ph), 53.4 (C(3)), 58.2 (C(2′)), 58.6 (C($\alpha$)), 59.8 (C($\alpha'$)), 80.1 (C$Me_3$), 126.6, 126.9, 127.0 (*p*-*Ph*), 128.1, 128.1, 128.1, 128.2, 128.2, 128.5 (*o*,*m*-*Ph*), 141.8, 142.5, 144.1 (*i*-*Ph*), 172.1 (C(1)); $m/z$ (ESI$^+$) 527 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $m/z$: [M + H]$^+$ Calcd for $C_{35}H_{47}N_2O_2^+$ 527.3632; Found 527.3627.

**(2*S*,2′*R*,α*R*,α′*R*)-1-[*N*(1′)-(α-Methylbenzyl)pyrrolidin-2′-yl]-2-[*N*-benzyl-*N*-(α′-methylbenzyl)amino]pent-4-ene 45.** DIBAL-H (1.0 M in PhMe, 0.59 mL, 0.59 mmol) was added dropwise to a stirred solution of **42** (284 mg, 0.539 mmol, >99:1 dr) in PhMe (5 mL) at −78 °C, and the resultant mixture was stirred at −78 °C for 1 h. MeOH (109 μL, 2.70 mmol) and $Ph_3P$═$CH_2$ (0.31 M suspension in PhMe/THF 17.4 mL, 5.39 mmol)[24] were added sequentially, and the resultant mixture was allowed to warm to rt and stirred at rt for 16 h and then concentrated in vacuo. The residue was dissolved in $Et_2O$ (40 mL), and the resultant solution was filtered through a short plug of Celite (eluent $Et_2O$) and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/$Et_2O$/$NH_4OH$, 100:10:1) gave **45** as a colorless oil (185 mg, 76%, >99:1 dr); $[\alpha]_D^{25}$ +76.9 ($c$ 1.0 in $CHCl_3$); $\nu_{max}$ (ATR) 3026, 2970, 2933, 2870, 2803 (C−H), 1638, 1601, 1493, 1452 (C═C); $\delta_H$ (400 MHz, $CDCl_3$) 1.21−1.31 (2H, m, C(1)$H_A$, C(3′)$H_A$), 1.27 (3H, d, $J$ 7.0, C($\alpha'$)$Me$), 1.37 (3H, d, $J$ 6.8, C($\alpha$)$Me$), 1.48−1.72 (4H, m, C(3)$H_A$, C(3′)$H_B$, C(4′)$H_2$), 1.72−1.80 (1H, m, C(3)$H_B$), 1.85 (1H, ddd, $J$ 13.7, 9.9, 3.3, C(1)$H_B$), 2.36 (1H, app q, $J$ 8.2, C(5′)$H_A$), 2.73−2.81 (2H, m, C(2)$H$, C(5′)$H_B$), 2.99−3.08 (1H, m, C(2′)$H$), 3.57 (1H, d, $J$ 15.0, NC$H_A$H$_B$Ph), 3.79 (1H, q, $J$ 6.8, C($\alpha$)$H$), 3.83 (1H, q, $J$ 7.0, C($\alpha'$)$H$), 3.92 (1H, d, $J$ 15.0, NCH$_A$$H_B$Ph), 4.81 (1H, d, $J$ 17.1, C(5)$H_A$), 4.87 (1H, d, $J$ 10.3, C(5)$H_B$), 5.46−5.57 (1H, m, C(4)$H$), 7.16−7.36 (13H, m, $Ph$), 7.39−7.43 (2H, m, $Ph$); $\delta_C$ (100 MHz, $CDCl_3$) 20.8 (C($\alpha'$)$Me$), 22.7 (C($\alpha$)$Me$), 22.9 (C(4′)), 30.3 (C(3′)), 35.9 (C(3)), 37.6 (C(1)), 50.1 (C(5′)), 50.4 (NC$H_2$Ph), 55.0 (C(2)), 57.4 (C($\alpha'$)), 57.9 (C(2′)), 60.5 (C($\alpha$)), 116.1 (C(5)), 126.6, 126.8, 127.0 (*p*-*Ph*), 128.1, 128.1, 128.1, 128.2, 128.4, 128.4 (*o*,*m*-*Ph*), 137.4 (C(4)), 141.8, 143.6, 143.7 (*i*-*Ph*); $m/z$ (ESI$^+$) 453 ([M + H]$^+$, 100%); HRMS (ESI$^+$) $m/z$: [M + H]$^+$ Calcd for $C_{32}H_{41}N_2^+$ 453.3264; Found 453.3259.

**(2*S*,2′*R*,α*R*,α′*R*,*Z*)-1-[*N*(1′)-(α-Methylbenzyl)pyrrolidin-2′-yl]-2-[*N*-benzyl-*N*-(α′-methylbenzyl)amino]hept-4-ene 46.** DIBAL-H (1.0 M in PhMe, 0.53 mL, 0.53 mmol) was added dropwise to a stirred solution of **42** (255 mg, 0.484 mmol, >99:1 dr) in PhMe



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(5 mL) at −78 °C, and the resultant mixture was stirred at −78 °C for 1 h. MeOH (98 μL, 2.42 mmol) and $Ph_3P{=}CHCH_2CH_3$ (0.31 M suspension in PhMe/THF 15.6 mL, 4.84 mmol)[25] were added sequentially, and the resultant mixture was allowed to warm to rt and stirred at rt for 16 h and then concentrated in vacuo. The residue was dissolved in $Et_2O$ (40 mL), and the resultant solution was filtered through a short plug of Celite (eluent $Et_2O$) and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/$Et_2O$/$NH_4OH$, 100:10:1) gave **46** as a colorless oil (174 mg, 75%, >95:5 dr [(*Z*):(*E*)]); $[\alpha]_D^{25}$ +78.7 (*c* 1.0 in $CHCl_3$); $\nu_{max}$ (ATR) 3061, 3026, 2966, 2932, 2872 (C−H), 1602, 1493, 1453 (C═C); $\delta_H$ (400 MHz, $CDCl_3$) 0.90 (3H, t, *J* 7.5, C(7)$H_3$), 1.16−1.30 (2H, m, C(1)$H_A$, C(3′)$H_A$), 1.27 (3H, d, *J* 7.0, C(α′)*Me*), 1.38 (3H, d, *J* 6.8, C(α)*Me*), 1.51−1.65 (3H, m, C(3′)$H_B$, C(4′)$H_2$), 1.72−1.95 (5H, m, C(1)$H_B$, C(3)$H_2$, C(6)$H_2$), 2.39 (1H, app q, *J* 7.9, C(5′)$H_A$), 2.69−2.81 (2H, m, C(2)*H*, C(5′)$H_B$), 2.98−3.06 (1H, m, C(2′)*H*), 3.60 (1H, d, *J* 15.1, NC$H_A$$H_B$Ph), 3.80 (1H, q, *J* 6.8, C(α)*H*), 3.86 (1H, q, *J* 7.0, C(α′)*H*), 3.96 (1H, d, *J* 15.1, NC$H_A$$H_B$Ph), 5.03−5.12 (1H, m, C(4)*H*), 5.24−5.32 (1H, m, C(5)*H*), 7.18−7.37 (13H, m, *Ph*), 7.40−7.43 (2H, m, *Ph*); $\delta_C$ (100 MHz, $CDCl_3$) 14.3 (*C*(7)), 20.8 (*C*(6)), 21.1 (C(α′)*Me*), 22.6 (C(α)*Me*), 22.8 (*C*(4′)), 28.7 (*C*(3)), 30.2 (*C*(3′)), 37.5 (*C*(1)), 50.0 (*C*(5′)), 50.5 ($NCH_2$Ph), 55.8 (*C*(2)), 57.8 (*C*(α′)), 57.8 (*C*(2′)), 60.3 (*C*(α)), 126.5, 126.8, 126.9 (*p*-*Ph*), 127.5 (*C*(4)), 128.0, 128.1, 128.1, 128.2, 128.3, 128.4 (*o*,*m*-*Ph*), 132.5 (*C*(5)), 142.1, 143.7, 144.3 (*i*-*Ph*); *m*/*z* (ESI$^+$) 481 ([M + H]$^+$, 100%); HRMS (ESI$^+$) *m*/*z*: [M + H]$^+$ Calcd for $C_{34}H_{45}N_2^+$ 481.3577; Found 481.3574.

**(5*S*,6a*R*,10a*S*)-5-Propyldecahydrodipyrrolo[1,2-*a*:1′,2′-*c*]-pyrimidine [(+)-Tetraponerine 2] 49.** Palladium black (37 mg, 20% w/w) was added to a stirred, degassed solution of **45** (183 mg, 0.404 mmol, >99:1 dr) in MeOH/$H_2O$/AcOH (10:1:1, 2 mL). The resultant mixture was stirred under an atmosphere of $H_2$ (5 atm) at rt for 48 h. The reaction mixture was then filtered through a short plug of Celite (eluent MeOH/$H_2O$/AcOH, 10:1:1) and concentrated in vacuo. The residue was dissolved in $CH_2Cl_2$ (2 mL), and then $K_2CO_3$ (168 mg, 1.21 mmol) and 4-bromobutanal (123 mg, 0.81 mmol) were added to the resultant solution. The reaction mixture was stirred at rt for 2 h, and then $H_2O$ (2 mL) and satd aq $NaHCO_3$ (10 mL) were added. The reaction mixture was then extracted with $CH_2Cl_2$ (3 × 5 mL), and the combined organic extracts were dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/$Me_2CO$/$NH_4OH$, 100:10:1) gave (+)-tetraponerine 2 (**49**) as a colorless oil (31 mg, 37% from **45**, >99:1 dr); $[\alpha]_D^{25}$ +44.2 (*c* 1.0 in $CHCl_3$); {lit.[5] $[\alpha]_D^{20}$ +36 (*c* 1.79 in $CHCl_3$); lit.[6] $[\alpha]_D^{20}$ +47 (*c* 0.232 in $CHCl_3$)}; $\nu_{max}$ (ATR) 2957, 2931, 2871, 2786 (C−H);[26] $\delta_H$ (400 MHz, $C_6D_6$) 0.92 (3H, t, *J* 7.2, C(3′)$H_3$), 1.27−1.83 (14H, m, C(1)$H_2$, C(2)$H_2$, C(6)$H_2$, C(7)$H_2$, C(8)$H_2$, C(1′)$H_2$, C(2′)$H_2$), 1.83−1.97 (2H, m, C(9)$H_A$, C(6a)*H*), 2.29−2.36 (1H, m, C(3)$H_A$), 2.39−2.46 (1H, m, C(5)*H*), 2.86 (1H, app t, *J* 5.3, C(10a)*H*), 2.93 (1H, app td, *J* 8.5, 2.5, C(9)$H_B$), 3.01−3.07 (1H, m, C(3)$H_B$); $\delta_C$ (100 MHz, $C_6D_6$) 14.7 (*C*(3′)), 19.3 (*C*(2′)), 21.0 (*C*(2)), 21.3 (*C*(8)), 29.3 (*C*(1)), 30.6 (*C*(7)), 33.4 (*C*(6)), 37.0 (*C*(1′)), 45.8 (*C*(3)), 49.2 (*C*(9)), 59.4 (*C*(5)), 64.2 (*C*(6a)), 83.4 (*C*(10a)); *m*/*z* (ESI$^+$) 209 ([M + H]$^+$, 100%); HRMS (ESI$^+$) *m*/*z*: [M + H]$^+$ Calcd for $C_{13}H_{25}N_2^+$ 209.2012; Found 209.2012.

**(5*S*,6a*R*,10a*S*)-5-Pentyldecahydrodipyrrolo[1,2-*a*:1′,2′-*c*]-pyrimidine [(+)-Tetraponerine 6] 50.** Palladium black (31 mg, 20% w/w) was added to a stirred, degassed solution of **46** (155 mg, 0.322 mmol, >95:5 dr [(*E*):(*Z*)]) in MeOH/$H_2O$/AcOH (10:1:1, 2 mL). The resultant mixture was stirred under an atmosphere of $H_2$ (5 atm) at rt for 48 h. The reaction mixture was then filtered through a short plug of Celite (eluent MeOH/$H_2O$/AcOH, 10:1:1) and concentrated in vacuo. The residue was dissolved in $CH_2Cl_2$ (2 mL), and then $K_2CO_3$ (134 mg, 0.97 mmol) and 4-bromobutanal (98 mg, 0.65 mmol) were added to the resultant solution. The reaction mixture was stirred at rt for 2 h, and then $H_2O$ (2 mL) and satd aq $NaHCO_3$ (10 mL) were added. The reaction mixture was then extracted with $CH_2Cl_2$ (3 × 5 mL), and the combined organic extracts were dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/$Me_2CO$/$NH_4OH$, 100:10:1) gave (+)-tetraponerine 6 (**50**) as a pale yellow oil (41 mg, 54% from **46**, >99:1 dr); $[\alpha]_D^{25}$ +66.3 (*c* 1.0 in $CHCl_3$); {lit.[4] for a sample isolated from the natural source $[\alpha]_D^{20}$ +35 (*c* 0.15 in $CHCl_3$); lit.[6] $[\alpha]_D^{20}$ +40 (*c* 0.75 in $CHCl_3$)}; $\nu_{max}$ (ATR) 2955, 2928, 2857, 2785 (C−H);[26] $\delta_H$ (400 MHz, $C_6D_6$) 0.91 (3H, t, *J* 7.0, C(5′)$H_3$), 1.23−1.54 (11H, m, C(6)$H_2$, C(7)$H_A$, C(8)$H_A$, C(1′)$H_A$, C(2′)$H_2$, C(3′)$H_2$, C(4′)$H_2$), 1.54−1.98 (9H, m, C(1)$H_2$, C(2)$H_2$, C(6a)*H*, C(7)$H_B$, C(8)$H_B$, C(9)$H_A$, C(1′)$H_B$), 2.31−2.38 (1H, m, C(3)$H_A$), 2.39−2.46 (1H, m, C(5)*H*), 2.87 (1H, app t, *J* 5.3, C(10a)*H*), 2.94 (1H, app td, *J* 8.5, 2.5, C(9)$H_B$), 3.03−3.10 (1H, m, C(3)$H_B$); $\delta_C$ (100 MHz, $C_6D_6$) 14.4 (*C*(5′)), 21.0 (*C*(2)), 21.3 (*C*(8)), 23.2 (*C*(4′)), 25.9 (*C*(2′)), 29.3 (*C*(1)), 30.6 (*C*(7)), 32.7 (*C*(3′)), 33.5 (*C*(6)), 34.8 (*C*(1′)), 45.9 (*C*(3)), 49.2 (*C*(9)), 59.7 (*C*(5)), 64.2 (*C*(6a)), 83.5 (*C*(10a)); *m*/*z* (ESI$^+$) 237 ([M + H]$^+$, 100%); HRMS (ESI$^+$) *m*/*z*: [M + H]$^+$ Calcd for $C_{15}H_{29}N_2^+$ 237.2325; Found 237.2326.

**(2*R*,2′*R*,α*S*,α′*R*)-1-[*N*(1′)-(α-Methylbenzyl)pyrrolidin-2′-yl]-2-[*N*-benzyl-*N*-(α′-methylbenzyl)amino]pent-4-ene 51.** DIBAL-H (1.0 M in PhMe, 0.65 mL, 0.65 mmol) was added dropwise to a stirred solution of **43** (200 mg, 0.380 mmol, >99:1 dr) in PhMe (5 mL) at −78 °C, and the resultant mixture was stirred at −78 °C for 1 h. MeOH (46 μL, 1.1 mmol) and $Ph_3P{=}CH_2$ (0.31 M suspension in PhMe/THF, 6.1 mL, 1.9 mmol)[24] were added sequentially, and the resultant mixture was allowed to warm to rt, stirred at rt for 16 h, and then concentrated in vacuo. The residue was dissolved in $Et_2O$ (40 mL), and the resultant solution was filtered through a short plug of Celite (eluent $Et_2O$) and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/$Et_2O$/$NH_4OH$, 100:20:1) gave **51** as a colorless oil (68 mg, 40%, >99:1 dr); $[\alpha]_D^{25}$ +56.3 (*c* 1.0 in $CHCl_3$); $\nu_{max}$ (ATR) 3026, 2968, 2932, 2872 (C−H), 1638, 1602, 1493, 1452 (C═C); $\delta_H$ (400 MHz, $CDCl_3$) 1.31 (3H, d, *J* 6.9, C(α)*Me*), 1.43 (3H, d, *J* 6.8, C(α′)*Me*), 1.42−1.48 (1H, m, C(3′)$H_A$), 1.52−1.76 (4H, m, C(1)$H_A$, C(3′)$H_B$, C(4′)$H_2$), 1.82−1.90 (2H, m, C(1)$H_B$, C(3)$H_A$), 1.99−2.08 (1H, m, C(3)$H_B$), 2.36−2.48 (2H, m, C(2′)*H*, C(5′)$H_A$), 2.62−2.70 (1H, m, C(2)*H*), 2.81−2.87 (1H, m, C(5′)$H_B$), 3.74 (1H, d, *J* 14.7, NC$H_A$$H_B$Ph), 3.79 (1H, d, *J* 14.7, NC$H_A$$H_B$Ph), 3.83 (1H, q, *J* 6.8, C(α′)*H*), 3.97 (1H, q, *J* 6.9, C(α)*H*), 4.80−4.86 (2H, m, C(5)$H_2$), 5.52 (1H, ddt, *J* 15.8, 11.4, 7.0, C(4)*H*), 7.16−7.35 (13H, m, *Ph*), 7.39−7.43 (2H, m, *Ph*); $\delta_C$ (100 MHz, $CDCl_3$) 17.9 (C(α)*Me*), 21.9 (C(α′)*Me*), 22.4 (*C*(4′)), 30.5 (*C*(3′)), 36.7 (*C*(3)), 37.6 (*C*(1)), 48.8 (*C*(5′)), 50.2 ($NCH_2$Ph), 55.4 (*C*(2)), 57.1 (*C*(α)), 58.5 (*C*(2′)), 59.3 (*C*(α′)), 115.3 (*C*(5)), 126.6, 126.7, 127.0 (*p*-*Ph*), 128.0, 128.0, 128.1, 128.2, 128.3, 128.5 (*o*,*m*-*Ph*), 138.1 (*C*(4)), 142.1, 142.3, 144.8 (*i*-*Ph*); *m*/*z* (ESI$^+$) 453 ([M + H]$^+$, 100%); HRMS (ESI$^+$) *m*/*z*: [M + H]$^+$ Calcd for $C_{32}H_{41}N_2^+$ 453.3264; Found 453.3259.

**(2*R*,2′*R*,α*S*,α′*R*,*Z*)-1-[*N*(1′)-(α-Methylbenzyl)pyrrolidin-2′-yl]-2-[*N*-benzyl-*N*-(α′-methylbenzyl)amino]hept-4-ene 52.** DIBAL-H (1.0 M in PhMe, 1.0 mL, 1.0 mmol) was added dropwise to a stirred solution of **43** (242 mg, 0.459 mmol, >99:1 dr) in PhMe (5 mL) at −78 °C, and the resultant mixture was stirred at −78 °C for 1 h. MeOH (93 μL, 2.3 mmol) and $Ph_3P{=}CHCH_2CH_3$ (0.31 M suspension in PhMe/THF, 14.8 mL, 4.59 mmol)[25] were added sequentially, and the resultant mixture was allowed to warm to rt, stirred at rt for 16 h, and then concentrated in vacuo. The residue was dissolved in $Et_2O$ (40 mL), and the resultant solution was filtered through a short plug of Celite (eluent $Et_2O$) and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/$Et_2O$/$NH_4OH$, 100:20:1) gave **52** as a pale yellow oil (106 mg, 48%, >95:5 dr [(*Z*):(*E*)]); $[\alpha]_D^{25}$ +53.9 (*c* 1.0 in $CHCl_3$); $\nu_{max}$ (ATR) 3025, 2964, 2932, 2872 (C−H), 1602, 1493, 1453 (C═C); $\delta_H$ (400 MHz, $CDCl_3$) 0.86 (3H, t, *J* 7.5, C(7)$H_3$), 1.32 (3H, d, *J* 6.8, C(α)*Me*), 1.41−1.47 (1H, m, C(1)$H_A$), 1.44 (3H, d, *J* 6.8, C(α′)*Me*), 1.53−1.77 (4H, m, C(1)$H_B$, C(3′)$H_A$, C(4′)$H_2$), 1.79−1.92 (4H, m, C(3)$H_A$, C(6)$H_2$, C(3′)$H_B$), 1.93−2.03 (1H, m, C(3)$H_B$), 2.36−2.45 (2H, m, C(2′)*H*, C(4′)$H_A$), 2.58−2.66 (1H, m, C(2)*H*), 2.84 (1H, ddd, *J* 9.1, 7.8, 2.4, C(4′)$H_B$), 3.73 (1H, d, *J* 14.8, NC$H_A$$H_B$Ph), 3.77 (1H, d, *J* 14.8, NC$H_A$$H_B$Ph), 3.85 (1H, q, *J* 6.8, C(α′)*H*), 3.99 (1H, q, *J* 6.8, C(α)*H*), 5.09 (1H, app dtt, *J* 10.8, 6.8, 1.4, C(4)*H*), 5.23 (1H, app dtt, *J* 10.8, 7.1, 1.6, C(5)*H*), 7.15−7.41 (15H, m, *Ph*); $\delta_C$ (100 MHz, $CDCl_3$) 14.2 (*C*(7)), 18.0 (C(α)*Me*),


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20.9 (*C*(6)), 21.9 (C(α′)*Me*), 22.4 (*C*(4′)), 29.7 (*C*(3)), 30.6 (*C*(1)), 37.4 (*C*(3′)), 48.7 (*C*(5′)), 50.1 ($NCH_2Ph$), 55.9 (*C*(2)), 57.0 (*C*(α)), 58.6 (*C*(2′)), 59.2 (*C*(α′)), 126.6, 126.6, 127.0 (*p-Ph*), 128.0, 128.1 (*o,m-Ph*), 128.2 (*C*(4)), 128.2, 128.2, 128.3, 128.6 (*o,m-Ph*), 131.7 (*C*(5)), 142.2, 142.3, 145.0 (*i-Ph*); *m/z* ($ESI^+$) 481 ($[M + H]^+$, 100%); HRMS ($ESI^+$) *m/z*: $[M + H]^+$ Calcd for $C_{34}H_{45}N_2^+$ 481.3577; Found 481.3571.

**(5*R*,6a*R*,10a*S*)-5-Propyldecahydrodipyrrolo[1,2-*a*:1′,2′-*c*]-pyrimidine [(+)-Tetraponerine 1] 55.** Palladium black (29 mg, 20% w/w) was added to a stirred, degassed solution of **51** (145 mg, 0.320 mmol, >99:1 dr) in $MeOH/H_2O/AcOH$ (10:1:1, 2 mL). The resultant mixture was stirred under an atmosphere of $H_2$ (5 atm) at rt for 48 h. The reaction mixture was then filtered through a short plug of Celite (eluent $MeOH/H_2O/AcOH$, 10:1:1) and concentrated in vacuo. The residue was dissolved in $CH_2Cl_2$ (2 mL), and then $K_2CO_3$ (133 mg, 0.96 mmol) and 4-bromobutanal (96 mg, 0.64 mmol) were added to the resultant solution. The reaction mixture was stirred at rt for 2 h, and then $H_2O$ (2 mL) and satd aq $NaHCO_3$ (10 mL) were added. The reaction mixture was then extracted with $CH_2Cl_2$ (3 × 5 mL), and the combined organic extracts were dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/$Me_2CO/NH_4OH$, 100:10:1) gave (+)-tetraponerine 1 (**55**) as a colorless oil (10 mg, 15% from **51**, >99:1 dr); $[\alpha]_D^{25}$ +14.4 (*c* 0.13 in $CHCl_3$); {lit.[5] $[\alpha]_D^{20}$ +11 (*c* 0.14 in $CHCl_3$); lit.[6] $[\alpha]_D^{20}$ +14 (*c* 0.498 in $CHCl_3$)}; $\nu_{max}$ (ATR) 2927, 2801 (C−H);[26] $\delta_H$ (400 MHz, $C_6D_6$) 0.96 (3H, t, *J* 7.3, C(3′)$H_3$), 1.23−1.45 (6H, m, C(1)$H_A$, C(6)$H_A$, C(7)$H_A$, C(8)$H_A$, C(1′)$H_A$, C(2′)$H_A$), 1.49−1.69 (3H, m, C(7)$H_B$, C(8)$H_B$, C(2′)$H_B$), 1.69−1.91 (6H, m, C(1)$H_B$, C(2)$H_2$, C(6)$H_B$, C(9)$H_A$, C(1′)$H_B$), 1.91−2.02 (1H, m, C(6a)*H*), 2.82−2.91 (3H, m, C(3)$H_A$, C(5)*H*, C(9)$H_B$), 3.21 (1H, app q, *J* 7.7, C(3)$H_B$), 3.48, (1H, app t, *J* 2.3, C(10a)*H*); $\delta_H$ (400 MHz, $CDCl_3$) 0.90 (3H, t, *J* 7.3, C(3′)$H_3$), 1.24−1.43 (3H, m, C(7)$H_A$, C(2′)$H_2$), 1.43−1.96 (12H, m, C(1)$H_2$, C(2)$H_2$, C(6)$H_2$, C(7)$H_B$, C(8)$H_2$, C(9)$H_A$, C(1′)$H_2$), 2.00−2.10 (1H, m, C(6a)*H*), 2.82 (1H, td, *J* 7.9, 3.0, C(3)$H_A$), 2.91−3.01 (2H, m, C(5)*H*, C(9)$H_B$), 3.08 (1H, app q, *J* 7.9, C(3)$H_B$), 3.39 (1H, app d, *J* 3.7, C(10a)*H*); $\delta_C$ (100 MHz, $C_6D_6$) 14.5 (*C*(3′)), 20.4 (*C*(8)), 20.8 (*C*(2′)), 22.0 (*C*(2)), 30.1, 30.1 (*C*(1), *C*(6)), 31.6 (*C*(7)), 35.4 (*C*(1′)), 50.0 (*C*(9)), 51.0 (*C*(3)), 53.7 (*C*(5)), 58.3 (*C*(6a)), 76.5 (*C*(10a)); $\delta_C$ (100 MHz, $CDCl_3$) 14.3 (*C*(3′)), 20.1 (*C*(8)), 20.6 (*C*(2′)), 21.3 (*C*(2)), 29.4 (*C*(6)), 29.7 (*C*(1)), 31.0 (*C*(7)), 34.0 (*C*(1′)), 50.1 (*C*(9)), 50.3 (*C*(3)), 53.6 (*C*(5)), 58.3 (*C*(6a)), 76.9 (*C*(10a));[27] *m/z* ($ESI^+$) 209 ($[M + H]^+$, 100%); HRMS ($ESI^+$) *m/z*: $[M + H]^+$ Calcd for $C_{13}H_{25}N_2^+$ 209.2012; Found 209.2013.

**(5*R*,6a*R*,10a*S*)-5-Pentyldecahydrodipyrrolo[1,2-*a*:1′,2′-*c*]-pyrimidine [(+)-Tetraponerine 5] 56.** Palladium black (31 mg, 20% w/w) was added to a stirred, degassed solution of **52** (154 mg, 0.330 mmol) in $MeOH/H_2O/AcOH$ (10:1:1, 2 mL). The resultant mixture was stirred under an atmosphere of $H_2$ (5 atm) at rt for 48 h. The reaction mixture was then filtered through a short plug of Celite (eluent $MeOH/H_2O/AcOH$, 10:1:1) and concentrated in vacuo. The residue was dissolved in $CH_2Cl_2$ (2 mL), and then $K_2CO_3$ (137 mg, 0.99 mmol) and 4-bromobutanal (99 mg, 0.66 mmol) were added to the resultant solution. The reaction mixture was stirred at rt for 2 h, and then $H_2O$ (2 mL) and satd aq $NaHCO_3$ (10 mL) were added. The reaction mixture was then extracted with $CH_2Cl_2$ (3 × 5 mL), and the combined organic extracts were dried and concentrated in vacuo. Purification via flash column chromatography (eluent 30−40 °C petrol/$Me_2CO/NH_4OH$, 100:10:1) gave (+)-tetraponerine 5 (**56**) as a colorless oil (11 mg, 14% from **52**, >99:1 dr); $[\alpha]_D^{25}$ +12.4 (*c* 0.13 in $CHCl_3$); {lit.[4] for a sample isolated from the natural source $[\alpha]_D^{20}$ +10 (*c* 0.2 in $CHCl_3$); lit.[5] $[\alpha]_D^{20}$ +10 (*c* 0.24 in $CHCl_3$); lit.[6] $[\alpha]_D^{20}$ +14 (*c* 1.6 in $CHCl_3$)}; $\nu_{max}$ (ATR) 2980, 2930, 2794 (C−H);[26] $\delta_H$ (400 MHz, $C_6D_6$) 0.93 (3H, t, *J* 6.8, C(5′)$H_3$), 1.28−1.46 (10H, m, C(1)$H_A$, C(6)$H_A$, C(7)$H_A$, C(8)$H_A$, C(1′)$H_A$, C(2′)$H_A$, C(3′)$H_2$, C(4′)$H_2$), 1.50−1.69 (3H, m, C(7)$H_B$, C(8)$H_B$, C(2′)$H_B$), 1.69−1.92 (6H, m, C(1)$H_B$, C(2)$H_2$, C(6)$H_B$, C(9)$H_A$, C(1′)$H_B$), 1.94−2.01 (1H, m, C(6a)*H*), 2.83−2.92 (3H, m, C(3)$H_A$, C(5)*H*, C(9)$H_B$), 3.23 (1H, app q, *J* 7.8, C(3)$H_B$), 3.51 (1H, app t, *J* 2.1, C(10a)*H*); $\delta_H$ (400 MHz, $CDCl_3$) 0.88 (3H, t, *J* 6.8, C(5′)$H_3$), 1.22−1.42 (7H, m, C(7)$H_A$, C(2′)$H_2$, C(3′)$H_2$, C(4′)$H_2$), 1.43−1.96 (12H, m, C(1)$H_2$, C(2)$H_2$, C(6)$H_2$, C(7)$H_B$, C(8)$H_2$, C(9)$H_A$, C(1′)$H_2$), 2.01−2.10 (1H, m, C(6a)*H*), 2.82 (1H, app td, *J* 8.0, 2.8, C(3)$H_A$), 2.89−3.01 (2H, m, C(5)*H*, C(9)$H_B$), 3.08 (1H, app q, *J* 8.0, C(3)$H_B$), 3.39 (1H, app d, *J* 3.5, C(10a)*H*); $\delta_C$ (100 MHz, $C_6D_6$) 14.4 (*C*(5′)), 20.4 (*C*(8)), 22.0 (*C*(2)), 23.2 (*C*(4′)), 27.5 (*C*(2′)), 30.1, 30.2 (*C*(1), *C*(6)), 31.6 (*C*(7)), 32.5 (*C*(3′)), 33.2 (*C*(1′)), 50.0 (*C*(9)), 51.1 (*C*(3)), 54.1 (*C*(5)), 58.3 (*C*(6a)), 76.5 (*C*(10a)); $\delta_C$ (100 MHz, $CDCl_3$) 14.3 (*C*(5′)), 20.2 (*C*(8)), 21.3 (*C*(2)), 22.8 (*C*(4′)), 27.2 (*C*(2′)), 29.4 (*C*(6)), 29.7 (*C*(1)), 31.0 (*C*(7)), 31.7 (*C*(1′)), 32.1 (*C*(3′)), 50.0 (*C*(9)), 50.3 (*C*(3)), 53.9 (*C*(5)), 58.3 (*C*(6a)), 76.8 (*C*(10a));[27] *m/z* ($ESI^+$) 237 ($[M + H]^+$, 100%); HRMS ($ESI^+$) *m/z*: $[M + H]^+$ Calcd for $C_{15}H_{29}N_2^+$ 237.2325; Found 237.2324.

## ■ ASSOCIATED CONTENT

### Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.7b00837.

Copies of $^1H$ and $^{13}C$ NMR spectra (PDF)

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### Notes

The authors declare no competing financial interest.

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(20) The (*Z*)-configurations of the C═C double bonds within **30**, **46**, and **52** were assigned by analogy to that within (*Z*)-**24** in the absence of authentic samples of the corresponding (*E*)-diastereoisomers.

(21) Oxidation of *ent*-**36** to give the corresponding pyrrole was previously noted upon attempted Pd-mediated tandem hydrogenation/hydrogenolysis; see ref 15a.

(22) As (+)-tetraponerine 2 (**49**) and (+)-tetraponerine 6 (**50**) were derived from the common precursor (*R*,*R*,*R*,*R*)-**42**, the configurations of **46**, **48**, and **50** remain secure.

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(24) The solution of $Ph_3P{=}CH_2$ was prepared on the requisite scale by the addition of KHMDS (0.5 M in PhMe, 1.0 equiv) to a stirred suspension of methyltriphenylphosponium iodide (1.0 M in THF, 1.0 equiv) at rt, and the resultant suspension was stirred at rt for 1 h.

(25) The solution of $Ph_3P{=}CHCH_2CH_3$ was prepared on the requisite scale by the addition of KHMDS (0.5 M in PhMe, 1.0 equiv) to a stirred suspension of propyltriphenylphosponium bromide (1.0 M in THF, 1.0 equiv) at rt, and the resultant suspension was stirred at rt for 1 h.

(26) The Bolmann band frequencies and intensities in the IR spectra of the tetraponerine alkaloids have previously been used to assign the configuration at the C(5)-position. The even numbered alkaloids (i.e., T2, T4, T6, and T8) typically have more intense Bohlmann bands at ∼2790 cm$^{-1}$, whereas the odd numbered alkaloids (i.e., T1, T3, T5, and T7) display weaker Bohlmann bands at ∼2805 cm$^{-1}$; for further discussion of this analysis, see: Garraffo, H. M.; Spande, T. F.; Jain, P.; Kaneko, T.; Jones, T. H.; Blum, M. S.; Ali, T. M. M.; Snelling, R. R.; Isbell, L. A.; Robertson, H. G.; Daly, J. W. *Rapid Commun. Mass Spectrom.* **2001**, *15*, 1409.

(27) For both (+)-tetraponerine 1 (**55**) and (+)-tetraponerine 5 (**56**), the resonance corresponding to *C*(10a) in their $^{13}$C NMR spectra (in $CDCl_3$) was obscured by the solvent peak.



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