A General Method for the Synthesis of Bastaranes and Isobastaranes: First Total Synthesis of Bastadins 5, 10, 12, 16, 20, and 21

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Abstract: A general strategy for the synthesis of twenty naturally occurring bastadins (all but bastadin 3) is presented. A key retrosynthetic disconnection of the two amide bonds, common in all target molecules, bisects the macrocyclic core into two diaryl ether fragments, an α,ω-diamine (western part) and an α,ω-dicarboxylic acid (eastern part). Efficient preparation of the synthetically challenging *o*-mono or dibromo-substituted diaryl ether linkages was achieved employing the diaryl iodonium salt method. Regarding the western part, variations of the aliphatic chain were more efficiently secured by the preparation of two different α,ω-aminonitrile moieties. Cobalt boride mediated reduction of the nitrile functionality established the required diamines and, at the same time, provided the necessary variation of the aromatic-ring bromination pattern. Regarding the eastern part, two different dicarboxyl precursors had to be prepared in order to accommodate bromination-pattern variations. Coupling and subsequent macrolactamization of different combinations of these key intermediates may lead at will to any member of this family of marine natural products. Four bastaranes (bastadins 5, 10, 12 and 16) and two isobastaranes (bastadins 20 and 21) were synthesized as a demonstration of the flexibility and efficiency of the approach presented.

Keywords: diaryl ethers · hypervalent compounds · natural products · oximino amides · total synthesis

Introduction

Bastadins are an ever-growing family of marine natural products isolated from sponges of the order Verongida.[1] Apart from open-chain bastadins 1 and 2 and biphenylyl bastadin 3, they are macrocyclic bis-diaryl ethers and, depending on the relative orientation of their diaryl ether segments, are further classified either as bastaranes or isobastaranes (Figure 1). They feature unique α-oximino amides, both of *E* configuration, and an unprecedented mixture of mono- and di-*o*-brominated diarylethers, biosynthetically derived through oxidative phenolic coupling of tyramine–tyrosine units in an apparently combinatorial fashion.[1h,2] The

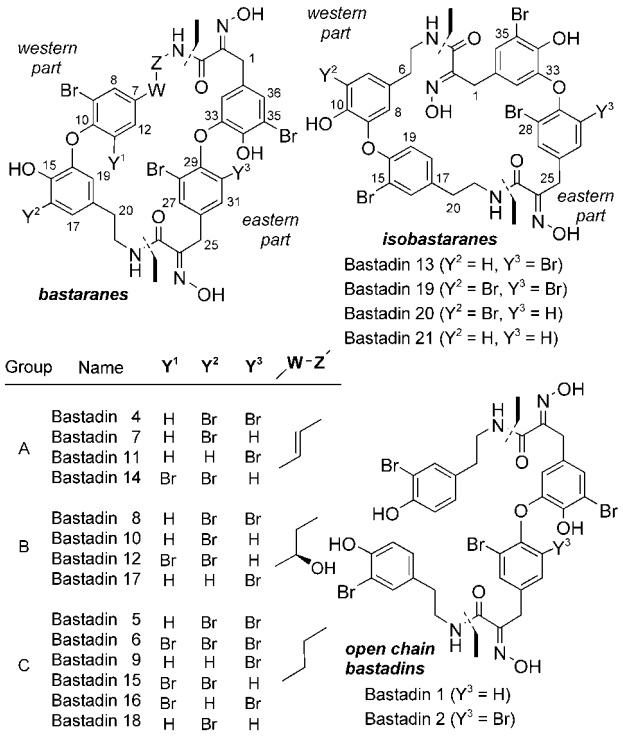

Figure 1. Naturally occurring bastadins (except bastadin 3).

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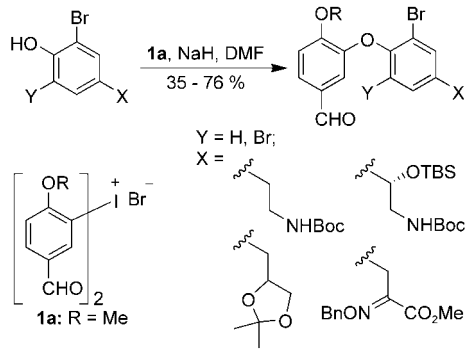
pluralism of their macrocyclic framework substitution pattern parallels a diverse and important biological profile, including anticancer[1d,f,k] and antimicrobial activity,[1b,k,3] inhibition of inosine-5′-phosphate dehydrogenase,[1h] inhibition of lipoxygenases,[4] and specific interaction with intracellular calcium channels.[1i,l,5]

Due to the this last property, they are considered useful chemical probes for related biological studies,[6] albeit only bastadins 5, 10 and 19 are commercially available in pure form. Although chemical synthesis could in principle alleviate this problem, the preparation of such diaryl ethers (i.e. *o*-heteroatom-substituted) remains a challenge, despite recent methodological advances.[7] Thus, even the copper(II)-promoted coupling of boronic acids with phenols, which has been haled as a general solution for the construction of diaryl ethers due to its versatility and mild conditions employed,[7b] is not applicable in the case of bastadins. To address this problem, ingenious biomimetic approaches, employing either a thallium trinitrate[8] or a chemoenzymatic-mediated phenolic oxidative dimerization,[9] have been successfully attempted. Nonetheless, the prerequisite of di-*o*-brominated precursors restricts their applicability to the preparation of open chain bastadins and the per-*o*-brominated bastadin 6. Furthermore, alternative methodologies have only been successful, thus far, in the preparation of non-natural bastarane intermediates and derivatives.[10]

As part of a project aiming to develop a general and flexible synthetic strategy towards bastadins, we have recently demonstrated the efficiency of a rarely employed method,[11] the coupling of phenols with an aryl iodonium salt (**1a**, Scheme 1), to yield either mono- or di-*o*-brominated diaryl ethers and its utility for the construction of bastarane derivatives.[12] In this manuscript we present in detail the evolution of our strategy and demonstrate its generality by the first total syntheses of group B and C bastaranes (bastadins 5, 10, 12, and 16), as well as isobastaranes (bastadins 20 and 21) from common, advanced synthetic intermediates.

Abstract in Greek:

Στο άρθρο αυτό παρουσιάζεται μία γενική συνθετική μέθοδος για όλες τις φυσικά απαντώμενες Βασταδίνες (Βασταδίνες 1-21) εκτός της Βασταδίνης 3. Μία καίρια ρετροσυνθετική αποσύνδεση των δύο αμιδικών δεσμών (κοινών σε όλα τα στοχευόμενα μόρια) τέμνει το μόριο σε δύο διαρυλο-αιθερικά τμήματα, μία α,ω-διαμίνη (δυτικό τμήμα) και ένα α,ω-δικαρβοξυλικό οξύ (ανατολικό τμήμα). Η συνθετική πρόκληση της δημιουργίας *o*-μονο- ή δι-βρωμοδιάρυλο αιθερικών δεσμών αντιμετωπίσθηκε με χρήση της μεθόδου των διαρυλοϊωδωνιακών αλάτων. Όσον αφορά το δυτικό τμήμα, για την επίτευξη των παραλλαγών του βαθμού οξείδωσης της αλειφατικής αλυσίδας ήταν περισσότερο αποτελεσματικό να παρασκευασθούν δύο διαφορετικά α,ω-αμινονιτρίλια. Αναγωγή τους με νατριοβορο-ϋδρίδιο παρουσία χλωριούχου κοβαλτίου οδήγησε στο σχηματισμό των αντίστοιχων διαμινών επιτρέποντας παράλληλα τις απαραίτητες παραλλαγές στο βαθμό βρωμίωσης του αρωματικού δακτυλίου. Για την επίτευξη παραλλαγών στο βαθμό βρωμίωσης του ανατολικού τμήματος χρειάστηκε να παρασκευασθούν δύο διαφορετικά δικαρβοξυλικά οξέα. Σύζευξη και στη συνέχεια μακρολακταμοποίηση διαφόρων συνδυασμών αυτών των βασικών ενδιαμέσων δύναται να οδηγήσει κατά βούληση σε οποιοδήποτε μέλος αυτής της οικογένειας θαλασσίων φυσικών προϊόντων. Τέσσερα βασταράνια (οι Βασταδίνες 5, 10, 12 και 16) και δύο ισοβασταράνια (οι Βασταδίνες 20 και 21) παρασκευάσθηκαν προς επίδειξη της ευελιξίας και της αποτελεσματικότητας της μεθόδου.

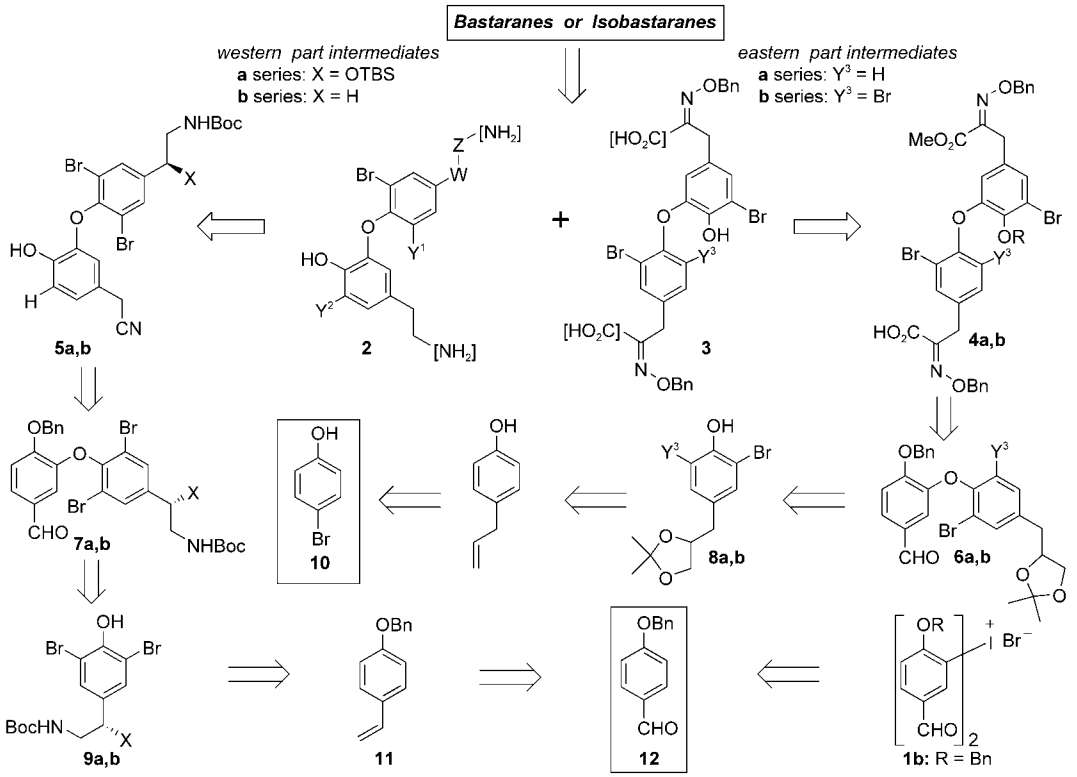


Scheme 1. Application of the diaryl iodonium salt method for the preparation of bastadin precursors.

Results and Discussion

Retrosynthetic analysis: A key disconnection at the two amide bonds reduces all macrocyclic bastadins into two suitably substituted precursors, namely α,ω-diamine **2** and α,ω-dicarboxylic acid **3** (Scheme 2). In order to ensure a topologically controlled coupling and subsequent macrolactamization between these entities, their terminal functionalities should be selectively differentiated. Therefore, diaryl ether **4**, possessing one primary carboxyl and one ester group at each end, respectively, was envisioned as the appropriate key intermediate for the eastern part of both bastaranes and isobastaranes. However, to guarantee that all variations at the Y^3-position will be accessible, two versions (**4a** and **4b**) of this advanced intermediate should be prepared.

On the other hand, diaryl ether **5a**, terminated at each end with a nitrile group and a protected amine, respectively, could serve as the common building block for the western part of all target molecules. Thus, regiospecific *o*-bromination[13] was anticipated to secure variations at the Y^2-position, while variations at the Y^1-position could be conven-



Scheme 2. General retrosynthetic analysis for bastaranes and isobastaranes.

iently achieved at this advanced stage concomitant with nitrile group reduction by cobalt boride.[12,14] In addition, regarding the W–Z region (Groups A, B or C in Figure 1), model studies have shown that the benzylic hydroxyl group could lead either to the respective aliphatic or olefinic derivative, providing thus a possible common entry to all variations of this part of the molecule.[12b,15] Nevertheless, use of the more easily accessible deoxy analogue **5b** (vide infra) for the preparation of isobastaranes and group C bastaranes might be preferable, since the efficiency of a parallel straightforward approach would counterbalance the benefit of a divergent common route.

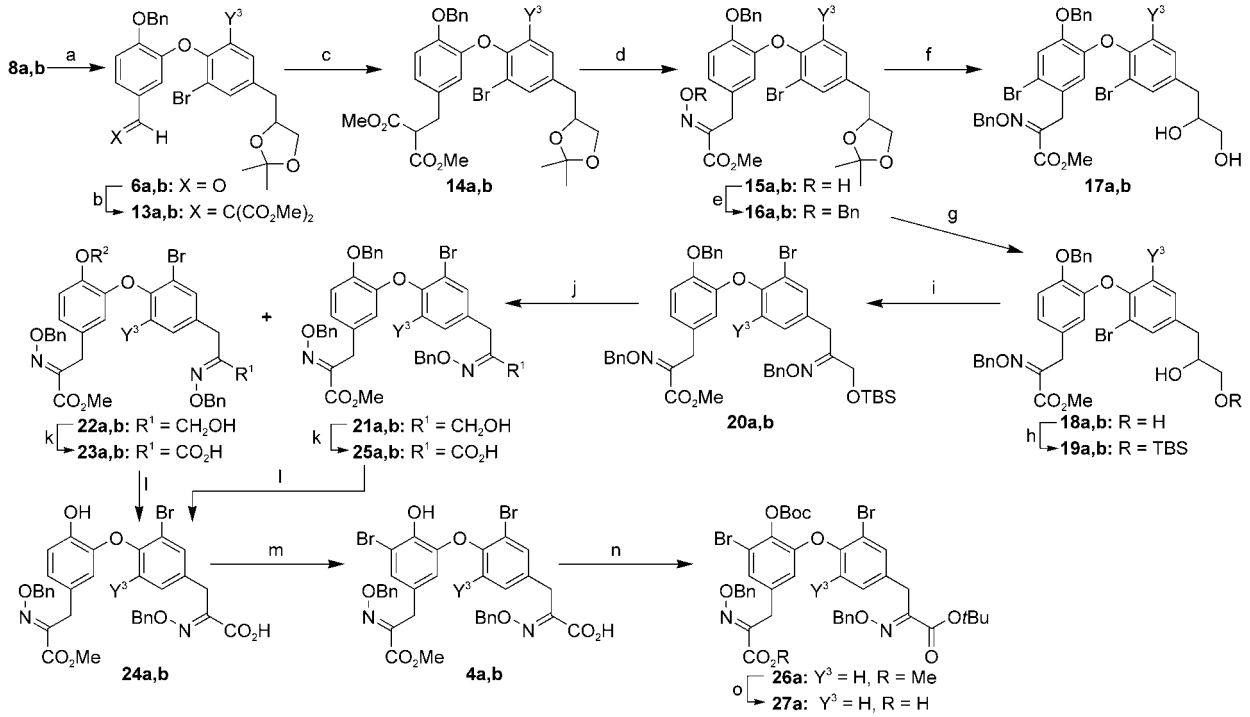
Both the α-oximino ester (in the case of **4a**,**b**) and the nitrile groups (in the case of **5a**,**b**) can be retrosynthetically reduced to a formyl one, revealing benzaldehydes **6a**,**b** and **7a**,**b** respectively, as key synthetic intermediates. These can be easily obtained by the coupling of an aryl iodonium salt with the appropriate phenols (**8a**,**b** or **9a**,**b** respectively). Further application of the *o*-specific phenolic bromination and olefin dihydroxylation (racemic, for **8a**,**b**, or asymmetric variant, for **9a**,**b**) transformations reveals the protected *p*-bromo- and *p*-vinyl-phenols (**10** and **11**) as the required starting materials.

With regard to the exact nature of the iodonium salt's phenol group protection, although, in preliminary studies, the more widely used methoxy derivative (**1a**, Scheme 1) allowed us entry to the bastaranic framework, efficient final deprotection was problematic. Consequently, the benzyloxy derivative (**1b**, Scheme 2) was opted for the total synthesis of bastadins as a compromise between salt's accessibility and ease of deprotection. It should be noted that even though this derivative has been employed in synthesis before,[11d] no detailed protocol for its preparation from *p*-benzyloxybenzaldehyde (**12**) was available and considerable experimentation was required to establish a reproducible one.[16]

Finally, the synthetic potential of esters **4a**,**b** for the preparation of open chain bastadins 1 and 2 is evident. Thus, the flexibility of the iodonium salt method allows for the conception of a convergent and common retrosynthetic scheme encompassing all naturally occurring bastadins except for bastadin 3.

Synthesis of eastern part precursors: The required mono- or di-*o*-brominated phenols **8a**,**b** were easily obtained from 4-bromophenol (**10**) in six steps and 78% overall yield.[12a] Treatment of either phenol with iodonium salt **1b** in the presence of potassium carbonate in DMF furnished in excellent yield the corresponding diaryl ethers **6a** or **6b** (Scheme 3). Transformation of the formyl group to the desired α-oximino ester (**16a** or **16b**) was accomplished by a four-step sequence amenable to large-scale work. Thus, Knoevenagel condensation with dimethyl malonate followed by sodium borohydride mediated olefin reduction[17] and subsequent treatment with butylisonitrite/sodium methoxide furnished oximes **15a** or **15b**, respectively.[18] To complete the sequence, the resulting oximes were converted to the corresponding *O*-benzyl derivatives. Gratifyingly, inspection of the ^{13}C NMR spectra revealed that both oxime **16a** and **16b** had the required *E* configuration.[19]

At this stage, regiospecific *o*-bromination of the benzyloxy-substituted aromatic ring of **16a** or **16b** was attempted



Scheme 3. Preparation of eastern part precursors. Y^3 = H (**a** series); Y^3 = Br (**b** series). Reagents and conditions: a) K_2CO_3, imidazole, **1b**, DMF, 80 °C, 96 % (**6a**), 98 % (**6b**); b) piperidine, dimethyl malonate, Ac_2O, THF, 80 °C, 99 % (**13a**), 97 % (**13b**); c) $NaBH_4$, MeOH:CH_3CN (1:1), 0 °C to RT, 86 % (**14a**), 83 % (**14b**); d) NaOMe, BuONO, MeOH, 0 °C, 88 % (**15a**), 87 % (**15b**); e) K_2CO_3, imidazole, BnBr, DMF, RT, 91 % (**16a**), 88 % (**16b**); f) NBS, CH_3CN, 90 °C, 52 % (**17a**), 56 % (**17b**); g) 1 N $HCl_{(aq.)}$, THF, RT, 99 %; h) TBSCl, imidazole, DMF, 0 °C to RT, 88 % (**19a**), 89 % (**19b**); i) KBr, TEMPO, 0.3 M $NaOCl_{(aq)}$, $NaHCO_3$, H_2O/CH_2Cl_2, 0 °C; $BnONH_2$·HCl, pyridine, EtOH, RT, 96 % (**20a**), 93 % (**20b**); j) 1.0 M TBAF, THF, RT, 24 % (**21a**) and 69 % (**22a**) or 11 % (**21b**) and 88 % (**22b**); k) KBr, TEMPO, 0.3 M $NaOCl_{(aq)}$, $NaHCO_3$, H_2O/CH_3CN, 0 °C, 96 % (**23a**), 98 % (**23b**), 97 % (**25a**), 98 % (**25b**); l) pentamethylbenzene, TFA, 0 °C, 94 % (**24a**), 96 % (**24b**); m) NBS, CH_3CN, 0 °C, 100 %; n) Boc_2O, DMAP, THF, 0 °C to RT, 81 %; o) 1 N NaOH, THF/MeOH/H_2O, 0 °C, 85 %.

by using *N*-bromosuccinimide (NBS) in acetonitrile.[20] The reaction required reflux temperature to proceed and was accompanied by loss of the acetonide protective group. More important, however, was the finding that bromination, although regiospecific, had occurred *meta*- rather than *ortho*- to the benzyloxy substituent to yield **17a** or **17b**, respectively. Phenol deprotection and subsequent bromination promised a possible solution to this unexpected obstacle.[13] However, since this protection was necessary for subsequent synthetic steps, investigation of this possibility was postponed.

Towards installing the remaining α-oximino acid functionality, the acetonide protective group of **16a** or **16b** was hydrolyzed to the corresponding free diol (**18a** or **18b**), of which the primary hydroxy group was selectively protected and the secondary one was subsequently oxidized to yield, upon treatment with *O*-benzylhydroxylamine, bis-oxime intermediates **20a** or **20b**, respectively. Although, inspection of their ^{13}C NMR spectra revealed that introduction of the second oxime was less stereoselective than that of the first one, separation of the *Z*/*E* isomers was not possible until subsequent TBAF-mediated (TBAF = tetrabutyl ammonium fluoride) silyl ether protective group cleavage. Disappointingly, the desired (*E*,*E*)-bis-oxime **21a** was obtained in 24 % yield whilst the *E*,*Z*-isomer **22a** was formed in 69 % from **20a**. Similarly, the (*E*,*E*)-bis-oxime **21b** was obtained in 11 % yield whilst the *E*,*Z*-isomer **22b** was formed in 88 % from **20b**. Since oximes are know to isomerize thermally, photochemically, or upon treatment with acid, we decided to overlook this issue at this point hoping that, if necessary, it will be possible to rectify oxime configuration at a latter stage of the synthesis.[19,21] Thus, **22a** or **22b** was oxidized to the corresponding carboxylic acid **23a** or **23b**.

Having served its purpose, it was now time to remove the phenol benzyl ether protective group in order to pave the way for the crucial *o*-specific bromination. The presence of two *O*-benzyl-protected oximes in the same molecule made this task far from trivial. Thus, hydrogenolysis or treatment with boron tribromide in thioanisole resulted in cleavage of all benzyl ethers. Gratifyingly, it was found that selective deprotection could be achieved in excellent yield with trifluoroacetic acid (TFA) in the presence of pentamethylbenzene. More important, under the reaction conditions complete isomerization of the oxime configuration occurred. Thus, inspection of the ^{13}C NMR spectra of **24a** and **24b** indicated that both products had now the desired *E*,*E* geometry and were identical in all respects with the phenols obtained in the same fashion from alcohols **21a** or **21b**. Regiospecific nuclear *o*-bromination with NBS in acetonitrile was now uneventful and proceeded in excellent yield at 0 °C to afford the eastern part precursors of bastaranes, acids **4a** and **4b**.

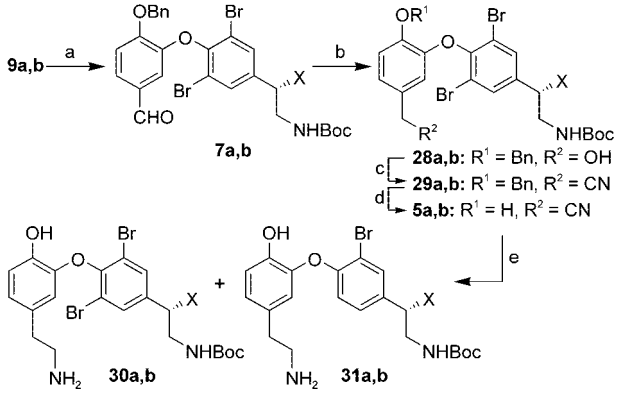
To be employed in the preparation of isobastaranes the acid and ester moieties of these building blocks had to be interchanged. To this end, acid **4a** was converted to the corre-

sponding *tert*-butyl ester **26a** by treatment with $(Boc)_2O$/DMAP (Boc = butoxycarbonyl, DMAP = 4-dimethylamino pyridine) in THF[22] with concomitant phenol protection. Subsequent selective saponification[23] afforded acid **27a**, a building block for the eastern part of isobastaranes bastadin 20 and 21.

Synthesis of western part precursors: Preparation of phenol **9a**, required for the construction of western part precursors of group B bastadins, was achieved in eight steps and 58% overall yield starting from *p*-benzyloxybenzaldehyde (**12**).[12b] It should be noted that the stereogenic center embedded in this building block and ultimately defining the chirality of the whole synthetic sequence was established by asymmetric dihydroxylation using the Sharpless protocol.[24] The enantioselectivity of this transformation was determined spectroscopically (^{1}H NMR spectroscopy; Mosher ester derivative) to be $\geq$97% *ee*.[12b]

On the other hand, phenol **9b**, required for the preparation of isobastaranes and group C bastaranes, was prepared very efficiently by bromination and subsequent protection of tyramine.[9]

Coupling of phenol **9a** or phenol **9b** with iodonium salt **1b** furnished in good yield the corresponding diaryl ethers **7a** or **7b** (Scheme 4). Sodium borohydride reduction of

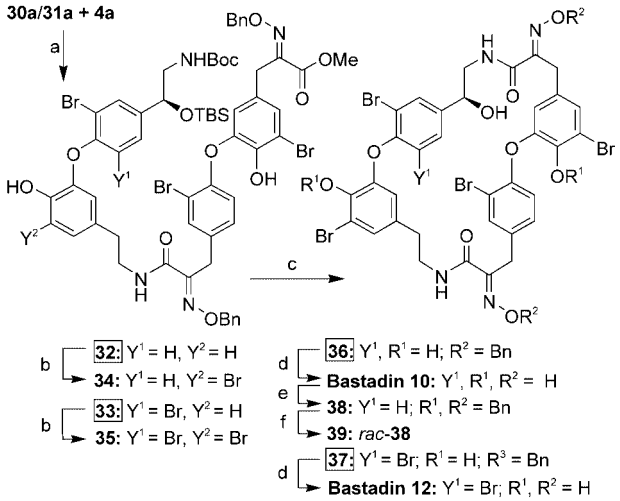


Scheme 4. Preparation of western part precursors. X = H (**a** series); X = OTBS (**b** series). Reagents and conditions: a) K_2CO_3, pyridine, **1b**, 90 °C, 82% (**7a**), 85% (**7b**); b) $NaBH_4$, MeOH:THF (1:1), 0 °C to RT, 96% (**28a**), 98% (**28b**); c) PPh_3, imidazole, I_2, THF, RT; KCN, DMF, 40 °C, 86% (**29a**), 84% (**29b**); d) H_2, 10% Pd/C, dioxane, RT, 95% (**5a**), 98% (**5b**); e) $CoCl_2 \cdot 6H_2O$, $NaBH_4$, MeOH, 0 °C, 80% (estimated yield for 1:1 mixture).

these aldehydes, conversion of the resulting alcohols (**28a** or **28b**) to the corresponding iodides and subsequent displacement by cyanide anion provided nitriles **29a** or **29b**. Then, the now redundant benzyl ether protection was hydrogenolyzed to yield phenols **5a** or **5b**, respectively. Sodium borohydride reduction in the presence of $CoCl_2$ completed the preparation of western-part building blocks securing at the same time diversity at the Y^1-position. Thus, dibromoamine **30a** was obtained as a 1:1 mixture with its monobromo counterpart **31a**. This mixture, or the corresponding mixture of amines **30b**/**31b**, was easily separated after coupling with the desired eastern part precursors (vide infra).

Apparently, coupling of these building blocks (compounds **4**, **27** and **30**, **31**) in a combinatorial fashion, should furnish after a few steps, all naturally occurring bastaranes and isobastaranes together with some unnatural (or not yet isolated) analogues. A few examples are given below.

Total synthesis of group B bastaranes: Coupling of the mixture of amine pair **30a**/**31a** with acid **4a** provided after chromatographic separation "tetramers" **32** and **33** (Scheme 5).

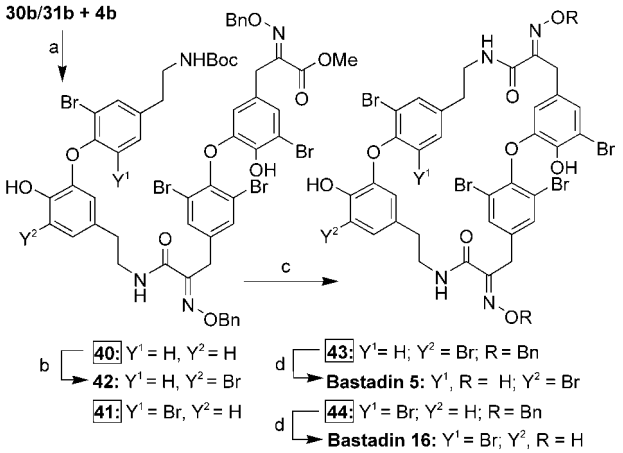


Scheme 5. Synthesis of naturally occurring group B bastaranes. Reagents and conditions: a) EDC, HOBt, iPr$_2$EtN, DMF/CH_2Cl_2, 0 °C to RT, 68% (**32**:**33** = 1:1); b) NBS, CH_3CN, 0 °C, 75% (**34**), 78% (**35**); c) LiOH, MeOH/THF/H_2O, RT; TFA/CH_2Cl_2, RT; PyBOP, iPr$_2$EtN, DMF/CH_2Cl_2, 0 °C to RT; TBAF, THF, RT, 52% (**36**), 61% (**37**); d) BBr_3, thioanisole, 0 °C to RT, 48% (for bastadin 10), 51% (for bastadin 12); e) BnBr, K_2CO_3, DMF, 83%; f) TEMPO, NaOCl, KBr, $NaHCO_3$, CH_3CN, 0 °C; $NaBH_4$, MeOH, 0 °C, 78%.

At this stage, the *o*-position of phenols **32** and **33** was very efficiently and specifically brominated. Products **34** and **35** were then subjected to saponification, TFA-mediated cleavage of the Boc group, and macrolactamization. Subsequent TBAF-mediated cleavage of the *tert*-butyl dimethyl silyl (TBS) group afforded protected bastadins 10 (compound **36**) and 12 (compound **37**) respectively, in high yields. After various attempts, the most reliable and reproducible deprotection protocol was found to be treatment with BBr_3 in the presence of thioanisole as cation scavenger,[25] resulting in the fully deprotected final products, identical in all respects (TLC, NMR) with the corresponding natural material. Moreover, in order to ensure that the sensitive benzylic chirality had not been compromised during the final, rather harsh deprotection step, synthetic bastadin 10 was converted to its tetrabenzyl derivative **38**. Oxidation of the benzylic alcohol moiety and subsequent restoration by sodium borohydride mediated reduction furnished the corresponding racemate **39**. HPLC chromatography of **38**, **39**, and the corresponding mixture on a chiral column (CHIRALPAK® AD-H, hexane:2-propanol = 60:40, 0.5 mL min^{-1}) revealed beyond any doubt the homochirality of the synthetically prepared bastadin.[26a]

Thus, a combination of three out of the seven key intermediates prepared gave, after seven chemical operations in a parallel fashion, bastadins 10 and 12 in 6% and 8% overall yields (based on acid **4a**), respectively.

Total synthesis of group C bastaranes: Similarly, coupling of amine pair **30b**/**31b** with acid **4b** provided after chromatographic separation "tetramers" **40** and **41** (Scheme 6). Re-



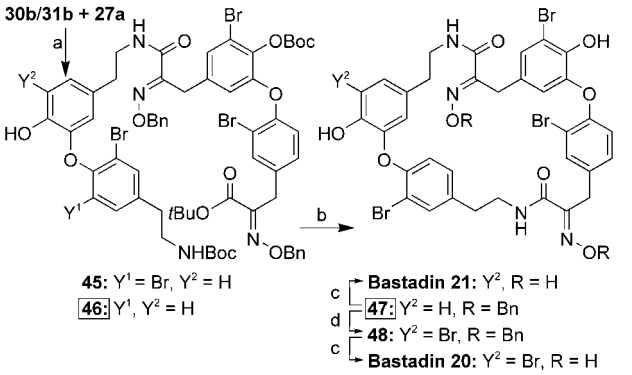
Scheme 6. Synthesis of naturally occurring group C bastaranes. Reagents and conditions: a) EDC, HOBt, *i*Pr_2EtN, DMF/CH_2Cl_2, 0°C to RT, 58% (**40**:**41** = 1:1); b) NBS, CH_3CN, 0°C, 75% (**42**); c) LiOH, MeOH/THF/H_2O, RT; TFA/CH_2Cl_2, RT; PyBOP, *i*Pr_2EtN, DMF/CH_2Cl_2, 0°C to RT, 58% (**43**), 66% (**44**); d) BBr_3, thioanisole, 0°C to RT, 43% (for bastadin 5), 41% (for bastadin 16).

giospecific bromination of **40** led to intermediate **42**. Deprotection of the carboxylic acid and amine moieties of **41** or **42** and subsequent macrolactamization furnished the dibenzyl derivative **43** of bastadin 5 or the corresponding derivative **44** of bastadin 16. Finally, protective-group removal was accomplished as above by treatment with BBr_3 in the presence of thioanisole to yield free bastadin 5 or 16, respectively in 5% overall yield (based on acid **4b**).[26b]

Total synthesis of isobastaranes: Coupling the same amine pair **30b**/**31b** with acid **27a** provided, after chromatographic separation, "tetramers" **45** and **46** (Scheme 7). The latter was treated with TFA to remove the Boc and *tert*-butyl ester protective groups and subsequent macrolactamization furnished the protected isobastarane **47**. Immediate deprotection, utilizing the above described protocol, afforded bastadin 21 within five chemical operations and in 11% total yield. On the other hand, regiospecific bromination of **47** followed by deprotection afforded bastadin 20 within six chemical operations and in 5% total yield.[26b]

Conclusion

We have shown the applicability of our strategy towards the total synthesis of bastadins. Practically, bastaranes of groups B and C as well as isobastaranes and open chain bas-



Scheme 7. Synthesis of naturally occurring isobastaranes. Reagents and conditions: a) EDC, HOBt, *i*Pr_2EtN, DMF/CH_2Cl_2, 0°C to RT, 76% (**45**:**46** = 1:1); b) TFA/CH_2Cl_2, pentamethylbenzene, RT; PyBOP, *i*Pr_2EtN, DMF/CH_2Cl_2, 0°C to RT, 55%; c) BBr_3, thioanisole, 0°C to RT, 55% (for bastadin 21), 46% (for bastadin 20); d) NBS, CH_3CN, 0°C, 72%.

tadins may be synthesized in a short, efficient, and highly convergent way, by using advanced common intermediates. Elaboration of the above encouraging results into a universal practical common route, including group A derivatives, remains to be investigated.

Experimental Section

General: All reactions were carried out under a dry argon atmosphere with anhydrous, freshly distilled solvents under anhydrous conditions unless otherwise noted. All reactions were magnetically stirred with Teflon stir bars, and temperatures were measured externally. Reactions requiring anhydrous conditions were carried out in oven-dried (120°C, 24 h) or flame-dried (vacuum < 0.5 Torr) glassware. Yields refer to chromatographically and spectroscopically (^{1}H NMR spectroscopy) homogeneous materials. All reagents were obtained from Aldrich and used without further purification. All reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica gel plates (60F-254). Merck silica gel (60, particle size 0.040–0.063 mm) was used for flash column chromatography. Infrared spectra (IR) were recorded, as neat films on potassium bromide plates, on Nicolet Magna FT-IR 550. Mass spectra were recorded on an IonSpec Ultima FTMS (MALDI) or an Agilent (ESI-TOF) instrument. Optical rotations were recorded with a Perkin–Elmer 241 polarimeter. Nuclear magnetic resonance (NMR) spectra were recorded on a Bruker AM-250 or a Bruker Avance DRX-500 instrument as noted individually. Chemical shifts are measured in parts per million (δ) relative to the deuterated solvent used in the experiment. Multiplicities are designated as singlet (s), doublet (d), triplet (t), or multiplet (m). Broad or obscured peaks are indicated as "br" or "obs" respectively.

General procedure for the preparation of 6a or 6b: Imidazole (13 mmol) and potassium carbonate (42 mmol) were added to a solution of phenol **8a** or **8b** (21 mmol) in DMF (140 mL). The mixture was stirred at ambient temperature for 1 h and, after addition of iodonium salt **1b** (31 mmol), was heated at 80°C for 6 h. The mixture was then poured into water (250 mL) and extracted with EtOAc (3×50 mL). The combined organic phases were washed with brine (50 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue thus obtained was purified by flash column chromatography (20% EtOAc in hexanes).

Data for 6a: Yield 96% as colorless oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 9.71 (s, 1H; C*H*O), 7.51 (dd, *J* = 8.6, 2.2 Hz, 1H; Ar*H*), 7.40 (d, *J* = 2.2 Hz, 1H; Ar*H*), 7.32 (d, *J* = 1.9 Hz, 1H; Ar*H*), 7.25–7.15 (m, 5H; Ar*H*), 7.02 (d, *J* = 8.6 Hz, 1H; Ar*H*), 6.99 (dd, *J* = 8.6, 1.9 Hz, 1H; Ar*H*), 6.69 (d, *J* = 8.6 Hz, 1H; Ar*H*), 5.13 (s, 2H; OCH_2Ph), 4.23–4.15 (m, 1H; $ArCH_2CHCH_2$), 3.90 (dd, *J* = 8.2, 6.0 Hz, 1H; $ArCH_2CHCHH$), 3.52 (dd,

J=8.2, 7.1 Hz, 1H; ArCH$_2$CHCHH), 2.83 (dd, J=13.8, 6.3 Hz, 1H; ArCHH), 2.66 (dd, J=13.8, 6.3 Hz, 1H; ArCHH), 1.33 (s, 3H; CH_3CCH$_3$), 1.26 ppm (s, 3H; CH$_3$CCH_3); ^{13}C NMR (62.5 MHz, CDCl$_3$): δ=190.2, 154.8, 152.2, 146.3, 135.7, 134.7, 134.4, 130.4, 129.4, 128.6, 128.2, 128.1, 126.9, 119.3, 118.9, 114.1, 113.8, 109.3, 76.2, 70.8, 68.8, 38.9, 27.0, 25.7 ppm; IR (KBr): $\tilde{\nu}$=3094, 3072, 3035, 2990, 2940, 2876, 2835, 2737, 1696, 1602, 1583, 1509, 1491, 1459, 1439 cm^{-1}; HR-MALDI-FTMS: m/z [M+Na]$^+$ calcd for $C_{26}H_{25}BrO_5$: 519.0777; found: 519.0792.

Data for 6b: Yield 98% as colorless oil; ^{1}H NMR (250 MHz, CDCl$_3$): δ=9.71 (s, 1H; CHO), 7.52–7.43 (m, 5H; ArH), 7.40–7.26 (m, 3H; ArH), 7.09 (d, J=8.3 Hz, 1H; ArH), 6.96 (d, J=1.7 Hz, 1H; ArH), 5.31 (s, 2H; OCH_2Ph), 4.37–4.27 (m, 1H; ArCH$_2$CHCH$_2$), 4.05 (dd, J=8.0, 6.0 Hz, 1H; ArCH$_2$CHCHH), 3.61 (dd, J=8.0, 7.1 Hz, 1H; ArCH$_2$CHCHH), 2.87 (dd, J=14.2, 6.9 Hz, 1H; ArCHH), 2.77 (dd, J=14.2, 5.4 Hz, 1H; ArCHH), 1.42 (s, 3H; CH_3CCH$_3$), 1.36 ppm (s, 3H; CH$_3$CCH_3); ^{13}C NMR (62.5 MHz, CDCl$_3$): δ=190.1, 152.9, 147.1, 146.5, 138.1, 135.8, 133.6, 129.8, 128.4, 127.9, 127.3, 127.0, 117.7, 113.7, 112.7, 109.2, 75.4, 70.7, 68.4, 38.5, 26.7, 25.4 ppm; IR (KBr): $\tilde{\nu}$=3062, 3037, 2991, 2934, 2879, 2854, 2738, 1692, 1600, 1551, 1514, 1454 cm^{-1}; HR-MALDI-FTMS: m/z [M+Na]$^+$ calcd for $C_{26}H_{24}Br_2O_5$: 596.9883; found: 596.9895.

General procedure for the preparation of 13a or 13b: A solution of aldehyde **6a** or **6b** (20 mmol), piperidine (40 mmol), dimethyl malonate (22 mmol), and acetic anhydride (22 mmol) in THF (130 mL) was stirred at 80°C for 24 h. The mixture was allowed to cool to ambient temperature and was then poured into a saturated aqueous solution of ammonium chloride (200 mL) and extracted with EtOAc (3×50 mL). The combined organic phases were washed with brine (50 mL), dried over Na$_2$SO$_4$, and concentrated under reduced pressure. The residue thus obtained was purified by flash column chromatography (20% EtOAc in hexanes) to yield product **13a** or **13b** and some unreacted starting aldehyde **6a** or **6b**.

Data for 13a: Yield 99% (70% conversion) as light yellow oil; ^{1}H NMR (250 MHz, CDCl$_3$): δ=7.57 (s, 1H; ArCH=C), 7.47 (d, J=1.9 Hz, 1H; ArH), 7.32–7.18 (m, 5H; ArH), 7.14 (dd, J=8.6, 2.2 Hz, 1H; ArH), 7.06 (dd, J=8.6, 1.9 Hz, 1H; ArH), 6.96 (d, J=8.6 Hz, 1H; ArH), 6.96 (d, J=2.2 Hz, 1H; ArH), 6.74 (d, J=8.6 Hz, 1H; ArH), 5.11 (s, 2H; OCH_2Ph), 4.30–4.20 (m, 1H; ArCH$_2$CHCH$_2$), 3.97 (dd, J=8.2, 6.0 Hz, 1H; ArCH$_2$CHCHH), 3.76 (s, 3H; COOCH_3), 3.67 (s, 3H; COOCH_3), 3.58 (dd, J=8.2, 7.1 Hz, 1H; ArCH$_2$CHCHH), 2.88 (dd, J=13.8, 6.3 Hz, 1H; ArCHHCHCH$_2$), 2.72 (dd, J=13.8, 6.3 Hz, 1H; ArCHHCHCH$_2$), 1.40 (s, 3H; CH_3CCH$_3$), 1.32 ppm (s, 3H; CH$_3$CCH_3); ^{13}C NMR (62.5 MHz, CDCl$_3$): δ=166.9, 164.4, 152.3, 151.6, 145.7, 141.5, 135.9, 134.4, 134.1, 129.2, 128.3, 127.8, 127.2, 126.8, 125.8, 123.5, 120.2, 118.7, 114.5, 113.5, 109.1, 76.1, 70.5, 68.6, 52.4, 38.8, 26.8, 25.5 ppm; IR (KBr): $\tilde{\nu}$=3092, 3066, 3034, 2986, 2951, 2877, 2824, 1760, 1739, 1629, 1602, 1576, 1512, 1489, 1455, 1435 cm^{-1}; HR-MALDI-FTMS: m/z [M+Na]$^+$ calcd for $C_{31}H_{31}BrO_8$: 633.1094; found: 633.1094.

Data for 13b: Yield 97% (88% conversion) as light yellow oil; ^{1}H NMR (250 MHz, CDCl$_3$): δ=7.58–7.46 (m, 5H; ArCH=C, ArH), 7.43–7.29 (m, 3H; ArH), 7.08 (dd, J=8.5, 2.0 Hz, 1H; ArH), 7.00 (d, J=8.5 Hz, 1H; ArH), 6.57 (d, J=2.0 Hz, 1H; ArH), 5.31 (s, 2H; OCH_2Ph), 4.39–4.29 (m, 1H; ArCH$_2$CHCH$_2$), 4.10 (dd, J=8.2, 6.0 Hz, 1H; ArCH$_2$CHCHH), 3.78 (s, 3H; COOCH_3), 3.65 (s, 3H; COOCH_3), 3.72–3.59 (obs m, 1H; ArCH$_2$CHCHH), 2.92 (dd, J=14.1, 7.0 Hz, 1H; ArCHHCHCH$_2$), 2.80 (dd, J=14.1, 5.5 Hz, 1H; ArCHHCHCH$_2$), 1.46 (s, 3H; CH_3CCH$_3$), 1.38 ppm (s, 3H; CH$_3$CCH_3); ^{13}C NMR (62.5 MHz, CDCl$_3$): δ=166.9, 164.5, 149.9, 147.3, 146.2, 141.7, 138.1, 136.2, 133.6, 128.5, 127.9, 127.1, 125.8, 125.5, 123.1, 117.9, 114.6, 114.4, 109.4, 75.7, 70.8, 68.6, 52.4, 38.7, 26.8, 25.5 ppm; IR (KBr): $\tilde{\nu}$=3092, 3069, 3037, 2990, 2953, 2879, 1731, 1629, 1604, 1576, 1550, 1515, 1457, 1439 cm^{-1}; HR-MALDI-FTMS: m/z [M+Na]$^+$ calcd for $C_{31}H_{30}Br_2O_8$: 711.0199; found: 711.0191.

General procedure for the preparation of 14a or 14b: A stirred solution of **13a** or **13b** (26 mmol) in a mixture of methanol (100 mL) and acetonitrile (100 mL) was treated at 0°C with sodium borohydride (28 mmol). The mixture was allowed to gradually warm up to ambient temperature over 4 h and during this period two more portions of sodium borohydride (10 mmol) were added in order to achieve complete consumption of the starting material. The reaction mixture was then poured into a saturated aqueous solution of ammonium chloride (200 mL) and extracted with EtOAc (3×50 mL). The combined organic phases were washed with brine (50 mL), dried over Na$_2$SO$_4$, and concentrated under reduced pressure. The residue thus obtained was purified by flash column chromatography (30% EtOAc in hexanes).

Data for 14a: Yield 86% as colorless oil; ^{1}H NMR (250 MHz, CDCl$_3$): δ=7.47 (d, J=1.9 Hz, 1H; ArH), 7.34–7.18 (m, 5H; ArH), 7.02 (dd, J=8.6, 1.9 Hz, 1H; ArH), 6.93 (s, 1H; ArH), 6.92 (s, 1H; ArH), 6.83 (s, 1H; ArH), 6.64 (d, J=8.6 Hz, 1H; ArH), 5.06 (s, 2H; OCH_2Ph), 4.30–4.19 (m, 1H; ArCH$_2$CHCH$_2$), 3.97 (dd, J=8.2, 6.0 Hz, 1H; ArCH$_2$CHCHH), 3.68 (s, 6H; COOCH_3), 3.64–3.55 (m, 2H; ArCH$_2$CHCHH, CH$_2$CH(COOMe)$_2$), 3.12 (d, J=7.8 Hz, 2H; CH_2CH(COOMe)$_2$), 2.92 (dd, J=14.1, 6.3 Hz, 1H; ArCHHCHCH$_2$), 2.72 (dd, J=14.1, 6.3 Hz, 1H; ArCHHCHCH$_2$), 1.42 (s, 3H; CH_3CCH$_3$), 1.35 ppm (s, 3H; CH$_3$CCH_3); ^{13}C NMR (62.5 MHz, CDCl$_3$): δ=168.8, 153.1, 148.7, 145.1, 136.6, 133.9, 133.3, 131.2, 128.9, 128.1, 127.5, 126.8, 125.2, 121.3, 117.2, 115.6, 112.5, 109.0, 76.2, 70.8, 68.6, 53.4, 52.3, 38.7, 33.7, 26.8, 25.5 ppm; IR (KBr): $\tilde{\nu}$=3071, 3042, 2989, 2952, 2874, 1756, 1740, 1610, 1583, 1514, 1489, 1455, 1437 cm^{-1}; HR-MALDI-FTMS: m/z [M+Na]$^+$ calcd for $C_{31}H_{33}BrO_8$: 635.1251; found: 635.1257.

Data for 14b: Yield 83% as colorless oil; ^{1}H NMR (250 MHz, CDCl$_3$): δ=7.55–7.45 (m, 4H; ArH), 7.42–7.27 (m, 3H; ArH), 6.94 (d, J=7.7 Hz, 1H; ArH), 6.79 (br d, J=8.2 Hz, 1H; ArH), 6.29 (br s, 1H; ArH), 5.24 (s, 2H; OCH_2Ph), 4.40–4.30 (m, 1H; ArCH$_2$CHCH$_2$), 4.08 (dd, J=7.5, 6.3 Hz, 1H; ArCH$_2$CHCHH), 3.65 (s, 6H; COOCH_3), 3.70–3.52 (m, 2H; ArCH$_2$CHCHH, CH$_2$CH(COOMe)$_2$), 3.06 (d, J=7.8 Hz, 2H; CH_2CH(COOMe)$_2$), 2.92 (dd, J=14.1, 6.8 Hz, 1H; ArCHHCHCH$_2$), 2.81 (dd, J=14.1, 5.4 Hz, 1H; ArCHHCHCH$_2$), 1.46 (s, 3H; CH_3CCH$_3$), 1.40 ppm (s, 3H; CH$_3$CCH_3); ^{13}C NMR (62.5 MHz, CDCl$_3$): δ=168.7, 147.6, 146.3, 146.1, 137.5, 136.9, 133.4, 130.6, 128.2, 127.5, 127.1, 122.7, 117.8, 115.7, 114.5, 109.2, 75.5, 71.2, 68.4, 53.4, 52.2, 38.4, 33.8, 26.7, 25.4 ppm; IR (KBr): $\tilde{\nu}$=3093, 3067, 3037, 2987, 2952, 2936, 2870, 1758, 1737, 1612, 1593, 1551, 1516, 1460, 1434 cm^{-1}; HR-MALDI-FTMS: m/z [M+Na]$^+$ calcd for $C_{31}H_{32}Br_2O_8$: 713.0356; found: 713.0365.

General procedure for the preparation of 15a or 15b: Sodium methoxide (47 mmol) and BuONO (26 mmol) were added to a stirred solution of **14a** or **14b** (24 mmol) in methanol (300 mL) at 0°C. The mixture was allowed to stand at 0°C for 24 h and then additional BuONO (13 mmol) was added. After being kept at 0°C for another 24 h, the reaction mixture was poured into a saturated aqueous solution of ammonium chloride (300 mL) and extracted with EtOAc (3×100 mL). The combined organic phases were washed with brine (50 mL), dried over Na$_2$SO$_4$, and concentrated under reduced pressure. The residue thus obtained was purified by flash column chromatography (30% EtOAc in hexanes).

Data for 15a: Yield 88% as colorless foam; ^{1}H NMR (250 MHz, CDCl$_3$): δ=10.70–10.00 (br s, 1H; NOH), 7.38 (d, J=1.9 Hz, 1H; ArH), 7.24–7.07 (m, 5H; ArH), 7.00–6.87 (m, 3H; ArH), 6.82 (d, J=8.2 Hz, 1H; ArH), 6.58 (d, J=8.6 Hz, 1H; ArH), 4.94 (s, 2H; OCH_2Ph), 4.32–4.21 (m, 1H; ArCH$_2$CHCH$_2$), 3.87 (dd, J=8.2, 6.0 Hz, 1H; ArCH$_2$CHCHH), 3.79 (s, 2H; ArCH_2C=NOH), 3.69 (s, 3H; COOCH_3), 3.53 (dd, J=8.2, 6.7 Hz, 1H; ArCH$_2$CHCHH), 2.80 (dd, J=13.8, 6.3 Hz, 1H; ArCHHCHCH$_2$), 2.64 (dd, J=13.8, 6.3 Hz, 1H; ArCHHCHCH$_2$), 1.35 (s, 3H; CH_3CCH$_3$), 1.27 ppm (s, 3H; CH$_3$CCH_3); ^{13}C NMR (62.5 MHz, CDCl$_3$): δ=163.7, 153.2, 150.5, 148.5, 144.9, 136.7, 133.9, 133.0, 129.3, 129.0, 128.2, 127.5, 126.8, 125.6, 122.0, 117.2, 115.4, 112.5, 109.2, 76.2, 70.8, 68.4, 52.5, 38.6, 29.5, 26.7, 25.4 ppm; HR-MALDI-FTMS: m/z [M+Na]$^+$ calcd for $C_{29}H_{30}BrNO_7$: 606.1098; found: 606.1095, .

Data for 15b: Yield 87% as colorless foam; ^{1}H NMR (250 MHz, CDCl$_3$): δ=10.60–9.45 (br s, 1H; NOH), 7.56–7.45 (m, 4H; ArH), 7.43–7.25 (m, 3H; ArH), 6.89 (br s, 2H; ArH), 6.46 (s, 1H; ArH), 5.23 (s, 2H; OCH_2Ph), 4.46–4.36 (m, 1H; ArCH$_2$CHCH$_2$), 4.07 (dd, J=8.2, 6.4 Hz, 1H; ArCH$_2$CHCHH), 3.77 (s, 2H; ArCH_2C=NOH), 3.75 (s, 3H; COOCH_3), 3.65 (dd, J=8.2, 6.5 Hz, 1H; ArCH$_2$CHCHH), 2.89 (dd, J=14.2, 5.0 Hz, 1H; ArCHHCHCH$_2$), 2.80 (dd, J=14.2, 6.3 Hz, 1H; ArCHHCHCH$_2$), 1.46 (s, 3H; CH_3CCH$_3$), 1.38 ppm (s, 3H; CH$_3$CCH_3); ^{13}C NMR (62.5 MHz, CDCl$_3$): δ=163.6, 150.7, 148.0, 146.2, 137.1, 136.8, 133.8, 130.8, 129.0, 128.6, 128.3, 127.6, 127.2, 123.1, 118.0, 115.5, 115.3, 109.5, 75.4, 71.3, 67.8, 52.4, 38.2, 29.6, 26.4, 25.0 ppm; HR-MALDI-FTMS: m/z [M+Na]$^+$ calcd for $C_{29}H_{29}Br_2NO_7$: 684.0203; found: 684.0229.

General procedure for the preparation of 16a or 16b: Oxime **15a** or **15b** (25 mmol) was dissolved in DMF (70 mL), the solution was cooled at

0 °C and then potassium carbonate (38 mmol) and imidazole (10 mmol) were added. The mixture was stirred for 30 min and then benzyl bromide (27 mmol) was added. The reaction mixture was allowed to gradually warm up to ambient temperature and after 12 h it was poured into water (150 mL) and extracted with EtOAc (3×30 mL). The combined organic phases were washed with brine (30 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue thus obtained was purified by flash column chromatography (15% EtOAc in hexanes).

Data for 16a: Yield 91% as light yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.43 (d, J=1.9 Hz, 1H; Ar*H*), 7.33–7.14 (m, 10H; Ar*H*), 6.98–6.90 (m, 3H; Ar*H*), 6.85 (d, J=8.2, Hz, 1H; Ar*H*), 6.55 (d, J=8.2 Hz, 1H; Ar*H*), 5.25 (s, 2H; OCH_2Ph), 5.00 (s, 2H; OCH_2Ph), 4.31–4.20 (m, 1H; ArCH$_2$C*H*CH$_2$), 3.91 (dd, J=8.2, 6.0 Hz, 1H; ArCH$_2$CHC*H*H), 3.82 (s, 2H; ArCH_2CNOBn), 3.79 (s, 3H; COOCH_3), 3.56 (dd, J=8.2, 7.1 Hz, 1H; ArCH$_2$CHCH*H*), 2.87 (dd, J=13.8, 6.3 Hz, 1H; ArC*H*HCHCH$_2$), 2.67 (dd, J=13.8, 6.3 Hz, 1H; ArCH*H*CHCH$_2$), 1.38 (s, 3H; CH_3CCH$_3$), 1.31 ppm (s, 3H; CH$_3$CCH_3); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=163.7, 153.4, 150.6, 148.7, 144.6, 136.7, 136.1, 133.8, 133.0, 129.3, 128.9, 128.4, 128.2, 127.6, 126.9, 125.8, 122.4, 116.8, 115.4, 112.3, 109.1, 77.8, 76.3, 70.8, 68.7, 52.7, 38.7, 30.5, 26.9, 25.6 ppm; IR (KBr): $\tilde{\nu}$=3093, 3066, 3035, 2989, 2952, 2935, 2877, 1726, 1607, 1582, 1509, 1488, 1453, 1430 cm^{-1}; HR-MALDI-FTMS: m/z $[M+Na]^+$ calcd for $C_{36}H_{36}BrNO_7$: 696.1567; found: 696.1557.

Data for 16b: Yield 88% as light yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.53–7.19 (m, 12H; Ar*H*), 6.88 (d, J=8.3 Hz, 1H; Ar*H*), 6.80 (dd, J=8.3, 1.6 Hz, 1H; Ar*H*), 6.43 (d, J=1.6 Hz, 1H; Ar*H*), 5.24 (s, 2H; OCH_2Ph), 5.23 (s, 2H; OCH_2Ph), 4.34–4.24 (m, 1H; ArCH$_2$C*H*CH$_2$), 4.03 (dd, J=8.0, 6.0 Hz, 1H; ArCH$_2$CHC*H*H), 3.78 (s, 5H; ArCH_2CNOBn, COOCH_3), 3.61 (dd, J=8.0, 7.3 Hz, 1H; ArCH$_2$CHCH*H*), 2.88 (dd, J=14.1, 6.8 Hz, 1H; ArC*H*HCHCH$_2$), 2.74 (dd, J=14.1, 5.6 Hz, 1H; ArCH*H*CHCH$_2$), 1.44 (s, 3H; CH_3CCH$_3$), 1.36 ppm (s, 3H; CH$_3$CCH_3); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=163.6, 150.7, 147.9, 146.3, 146.1, 137.3, 137.1, 136.3, 133.4, 128.8, 128.3, 128.0, 127.9, 127.7, 127.2, 123.1, 118.0, 115.7, 115.3, 109.4, 77.5, 75.7, 71.4, 68.5, 52.6, 38.6, 30.6, 26.8, 25.5 ppm; HR-MALDI-FTMS: m/z $[M+Na]^+$ calcd for $C_{36}H_{35}Br_2NO_7$: 774.0672; found: 774.0655.

General procedure for the preparation of 17a or 17b: A stirred solution of **16a** or **16b** (2.5 mmol) and NBS (3 mmol) in acetonitrile (30 mL) was heated at reflux for 4 h. The reaction mixture was allowed to cool to ambient temperature and was then poured into a saturated aqueous solution of sodium bicarbonate (30 mL) containing 5% w/v potassium iodide. The mixture was extracted with EtOAc (3×30 mL), and the combined organic phases were washed with saturated aqueous solution of Na_2SO_3 (30 mL) and brine (30 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue thus obtained was purified by flash column chromatography (30% EtOAc in hexanes + 3% methanol).

Data for 17a: Yield 52% as yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ= 7.47 (d, J=1.9 Hz, 1H; Ar*H*), 7.34–7.15 (m, 11H; Ar*H*), 6.98 (dd, J=8.4, 1.9 Hz, 1H; Ar*H*), 6.70 (s, 1H; Ar*H*), 6.59 (d, J=8.4 Hz, 1H; Ar*H*), 5.25 (s, 2H; OCH_2Ph), 5.03 (s, 2H; OCH_2Ph), 3.96 (s, 2H; ArCH_2CNOBn), 3.96–3.63 (m, 2H; ArCH$_2$C*H*CH$_2$, ArCH$_2$CHC*H*H), 3.81 (s, 3H; COOCH_3), 3.50–3.43 (m, 1H; ArCH$_2$CHC*H*H), 2.75–2.66 ppm (m, 4H; ArCH_2CHCH$_2$, CHO*H*, CH$_2$O*H*); HR-MALDI-FTMS: m/z $[M+Na]^+$ calcd for $C_{33}H_{31}Br_2NO_7$: 734.0359; found: 734.0367.

Data for 17b: Yield 56% as yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ= 7.52–7.18 (m, 13H; Ar*H*), 6.14 (s, 1H; Ar*H*), 5.20 (s, 2H; OCH_2Ph), 5.18 (s, 2H; OCH_2Ph), 3.88 (brs, 3H; ArCH_2CNOBn, ArCH$_2$C*H*CH$_2$), 3.75 (s, 3H; COOCH_3), 3.63 (dd, J=11.0, 3.3 Hz, 1H; ArCH$_2$CHC*H*H), 3.46 (dd, J=11.0, 7.0 Hz, 1H; ArCH$_2$CHCH*H*), 3.25 (brs, 1H; O*H*), 2.97 (brs, 1H; O*H*), 2.77–2.61 ppm (m, 2H; ArCH_2CHCH$_2$); HR-MALDI-FTMS: m/z $[M+Na]^+$ calcd for $C_{33}H_{30}Br_3NO_7$: 811.9464; found: 811.9493,.

General procedure for the preparation of 18a or 18b: An aqueous solution of HCl (1 N, 100 mL) was added to a solution of **16a** or **16b** (24 mmol) in THF (100 mL), and the mixture was stirred at ambient temperature overnight. Approximately half of the solvent was evaporated under reduced pressure and the remaining mixture was extracted with EtOAc (3×30 mL). The combined organic phases were washed with brine (30 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue thus obtained was purified by flash column chromatography (30% EtOAc in hexanes + 3% methanol).

Data for 18a: Yield 99% as light yellow foam; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.48 (d, J=2.0 Hz, 1H; Ar*H*), 7.34–7.20 (m, 10H; Ar*H*), 7.00–6.94 (m, 3H; Ar*H*), 6.89 (d, J=8.3 Hz, 1H; Ar*H*), 6.62 (d, J=8.3 Hz, 1H; Ar*H*), 5.29 (s, 2H; OCH_2Ph), 5.05 (s, 2H; OCH_2Ph), 3.92–3.84 (m, 1H; ArCH$_2$C*H*CH$_2$), 3.86 (s, 2H; ArCH_2CNOBn), 3.83 (s, 3H; COOCH_3), 3.65 (dd, J=11.1, 3.3 Hz, 1H; ArCH$_2$CHC*H*H), 3.47 (dd, J=11.1, 6.9 Hz, 1H; ArCH$_2$CHC*H*H), 2.77–2.63 (m, 2H; ArCH_2CHCH$_2$), 2.20 ppm (brs, 2H; 2×O*H*); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=163.8, 153.4, 150.6, 148.7, 144.8, 136.8, 136.1, 134.0, 133.3, 129.4, 129.1, 128.5, 128.3, 127.7, 126.9, 125.8, 122.2, 117.1, 115.6, 112.6, 77.8, 72.8, 71.0, 65.8, 52.8, 38.5, 30.5 ppm; IR (KBr): $\tilde{\nu}$=3416, 3092, 3068, 3040, 2950, 2980, 1729, 1607, 1573, 1497, 1487, 1455, 1440 cm^{-1}; HR-ESI: m/z $[M+Na]^+$ calcd for $C_{33}H_{32}BrNO_7$: 656.1260; found: 656.1254.

Data for 18b: Yield 99% as light yellow foam; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.61–7.43 (m, 4H; Ar*H*), 7.39–7.22 (m, 7H; Ar*H*), 6.88 (d, J=8.3 Hz, 1H; Ar*H*), 6.79 (dd, J=8.3, 1.8 Hz, 1H; Ar*H*), 6.66 (s, 1H; Ar*H*), 6.35 (d, J=1.8 Hz, 1H; Ar*H*), 5.22 (s, 4H; 2×OCH_2Ph), 3.93–3.80 (m, 1H; ArCH$_2$C*H*CH$_2$), 3.75 (s, 5H; ArCH_2CNOBn, COOCH_3), 3.63 (dd, J=11.0, 3.2 Hz, 1H; ArCH$_2$CHC*H*H), 3.46 (dd, J=11.0, 6.9 Hz, 1H; ArCH$_2$CHCH*H*), 2.78 (brs, 2H; 2×O*H*), 2.75–2.60 ppm (m, 2H; ArCH_2CHCH$_2$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=164.2, 163.8, 150.7, 149.5, 147.8, 146.3, 138.0, 137.1, 136.2, 133.6, 128.7, 128.4, 128.2, 128.1, 127.9, 127.7, 127.3, 123.2, 118.1, 116.1, 115.9, 115.0, 77.5, 72.4, 71.5, 65.7, 52.7, 38.3, 30.5 ppm; HR-ESI: m/z $[M+H]^+$ calcd for $C_{33}H_{31}Br_2NO_7$: 714.0525; found: 714.0521.

General procedure for the preparation of 19a or 19b: A stirred solution of diol **18a** or **18b** (25 mmol) and imidazole (40 mmol) in DMF (100 mL) was cooled at 0 °C and then TBSCl (30 mmol) was added in small portions. The mixture was stirred at this temperature for 3 h and was then allowed to gradually warm up to ambient temperature. After 8 h the reaction mixture was poured into a saturated aqueous solution of ammonium chloride (100 mL) and extracted with EtOAc (3×30 mL). The combined organic phases were washed with water (50 mL) and brine (50 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue thus obtained was purified by flash column chromatography (20% EtOAc in hexanes).

Data for 19a: Yield 88% as colorless oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.46 (d, J=2.0 Hz, 1H; Ar*H*), 7.33–7.16 (m, 10H; Ar*H*), 6.97 (dd, J=8.4, 2.0 Hz, 1H; Ar*H*), 6.92 (s, 2H; Ar*H*), 6.86 (d, J=8.2 Hz, 1H; Ar*H*), 6.59 (d, J=8.4 Hz, 1H; Ar*H*), 5.26 (s, 2H; OCH_2Ph), 5.02 (s, 2H; OCH_2Ph), 3.86–3.73 (m, 1H; ArCH$_2$C*H*CH$_2$), 3.83 (s, 2H; ArCH_2CNOBn), 3.80 (s, 3H; COOCH_3), 3.57 (dd, J=9.9, 3.8 Hz, 1H; ArCH$_2$CHC*H*H), 3.43 (dd, J=9.9, 6.4 Hz, 1H; ArCH$_2$CHCH*H*), 2.68 (d, J=6.5 Hz, 2H; ArCH_2CHCH$_2$), 2.33 (d, J=4.5 Hz, 1H; O*H*), 0.89 (s, 9H; *tBu*Si), 0.05 (s, 3H; CH_3Si), 0.04 ppm (s, 3H; CH_3Si); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=164.3, 163.8, 153.2, 150.7, 148.7, 144.9, 136.8, 136.2, 134.0, 133.9, 129.4, 129.1, 128.5, 128.3, 128.2, 127.7, 127.0, 125.7, 122.3, 117.0, 115.6, 112.5, 77.9, 72.5, 71.0, 66.0, 52.8, 38.3, 30.6, 25.8, 3.7, 3.7 ppm; IR (KBr): $\tilde{\nu}$=3558, 3089, 3068, 3032, 2954, 2929, 2883, 2857, 1730, 1609, 1572, 1498, 1485, 1456, 1441 cm^{-1}; HR-ESI: m/z $[M+H]^+$ calcd for $C_{39}H_{46}BrNO_7Si$: 748.2300; found: 748.2297.

Data for 19b: Yield 89% as colorless oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ=7.48–7.38 (m, 4H; Ar*H*), 7.35–7.16 (m, 8H; Ar*H*), 6.82 (d, J=8.3 Hz, 1H; Ar*H*), 6.74 (dd, J=8.3, 1.7 Hz, 1H; Ar*H*), 6.38 (d, J=1.7 Hz, 1H; Ar*H*), 5.17 (s, 2H; OCH_2Ph), 5.16 (s, 2H; OCH_2Ph), 3.85–3.71 (m, 1H; ArCH$_2$C*H*CH$_2$), 3.71 (s, 2H; ArCH_2CNOBn), 3.69 (s, 3H; COOCH_3), 3.56 (dd, J=9.9, 4.0 Hz, 1H; ArCH$_2$CHC*H*H), 3.43 (dd, J=9.9, 6.3 Hz, 1H; ArCH$_2$CHCH*H*), 2.71–2.57 (m, 2H; ArCH_2CHCH$_2$), 2.42 (brd, J=2.3 Hz, 1H; O*H*), 0.89 (s, 9H; *tBu*Si), 0.05 ppm (s, 6H; CH_3Si); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ=163.5, 150.6, 147.6, 146.3, 146.2, 138.2, 137.1, 136.3, 133.5, 128.8, 128.3, 128.1, 127.9, 127.8, 127.6, 127.2, 123.0, 117.9, 115.7, 115.2, 77.4, 72.0, 71.4, 66.0, 52.5, 38.1, 30.5, 25.7, 18.1, 3.4, 3.4 ppm; HR-ESI-TOF: m/z $[M+H]^+$ calcd for $C_{39}H_{45}Br_2NO_7Si$: 826.1405; found: 826.1410.

General procedure for the preparation of 20a or 20b: Alcohol **19a** or **19b** (7.2 mmol) was dissolved in dichloromethane (80 mL). A solution of KBr in water (4.3 mL, 0.5 M; 2.2 mmol) and a solution of TEMPO in dichloromethane (8 mL, 9 mM; 72 μmol) were added to this mixture. An

aqueous solution of NaOCl (37 mL, 0.3 M; 11 mmol) containing $NaHCO_3$ (1.1 g, 13 mmol) was added in small portions (over 1 h) to this vigorously stirred mixture at 0 °C. The reaction was allowed to proceed for an additional hour and was then quenched by the addition of 2-propanol (1 mL). EtOAc (150 mL) was added to the mixture and it was washed successively with water (50 mL) and brine (50 mL). The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The residue thus obtained was dissolved in ethanol (25 mL) and treated at ambient temperature with *O*-benzyl hydroxylamine hydrochloride (1.2 g, 7.4 mmol) and pyridine (0.6 mL, 7.4 mmol). The mixture was poured into aqueous HCl (0.01 N, 30 mL) and extracted with EtOAc (3×30 mL). The combined organic phases were washed with water (2×30 mL) and brine (30 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue thus obtained was purified by flash column chromatography (20% EtOAc in hexanes).

Data for 20a: Yield 96% (ca. 3:1 mixture of isomers) as light yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.50 (d, J = 2.0 Hz, 1H; Ar*H*), 7.48 (d, J = 2.0 Hz, 3H; Ar*H*), 7.38–7.16 (m, 60H; Ar*H*), 7.00–6.91 (m, 12H; Ar*H*), 6.86 (d, J = 8.2 Hz, 3H; Ar*H*), 6.56 (d, J = 8.4 Hz, 3H; Ar*H*), 6.54 (2 d, J = 8.4 Hz, 1H; Ar*H*), 5.26 (s, 8H; OCH_2Ph), 6.56 (s, 2H; OCH_2Ph), 6.54 (s, 6H; OCH_2Ph), 5.03 (2 s, 6H; OCH_2Ph), 5.02 (s, 2H; OCH_2Ph), 4.42 (s, 6H; CH_2OTBS), 4.06(s, 2H; CH_2OTBS), 3.83 (s, 6H; ArCH_2CNOBn), 3.80 (s, 9H; COOCH_3), 3.70 (s, 2H; ArCH_2CNOBn), 3.54 (2 s, 6H; ArCH_2CNOBn), 0.87 (s, 9H; *tBu*Si), 0.85 (s, 27H; *tBu*Si), 0.00 (s, 6H; CH_3Si), −0.05 ppm (s, 18H; CH_3Si); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 163.8, 160.8, 158.0, 153.2, 150.7, 148.8, 145.0, 137.9, 136.8, 136.8, 136.1, 134.0, 133.8, 133.1, 129.4, 129.1, 128.7, 128.5, 128.3, 128.3, 128.3, 128.1, 127.9, 127.7, 127.6, 127.0, 126.9, 125.7, 125.6, 122.3, 122.2, 116.9, 116.9, 115.6, 115.6, 112.3, 77.9, 75.9, 75.8, 71.0, 71.0, 62.9, 57.9, 52.8, 35.1, 30.6, 30.3, 25.8, 18.2, 4.0, 3.7 ppm; HR-ESI: m/z $[M+H]^+$ calcd for $C_{46}H_{51}BrN_2O_7Si$: 851.2722; found: 851.2721.

Data for 20b: Yield 93% (ca. 8:1 mixture of isomers) as light yellow oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.54–7.44 (m, 36H; Ar*H*), 7.43–7.21 (m, 117H; Ar*H*), 6.87 (br d, J = 8.3 Hz, 9H; Ar*H*), 6.79 (br dd, J = 8.3, 2.0 Hz, 9H; Ar*H*), 6.41 (br d, J = 2.0 Hz, 9H; Ar*H*), 5.24 (br s, 36H; OCH_2Ph), 5.13 (s, 2H; OCH_2Ph), 5.12 (s, 16H; OCH_2Ph), 4.51 (s, 16H; CH_2OTBS), 4.15 (s, 2H; CH_2OTBS), 3.76 (s, 27H; COOCH_3), 3.75 (s, 16H; ArCH_2-CNOBn), 3.72 (s, 2H; ArCH_2CNOBn), 3.58 (s, 18H; ArCH_2CNOBn), 0.92 (s, 9H; *tBu*Si), 0.90 (s, 72H; *tBu*Si), 0.07 (s, 6H; CH_3Si), 0.02 ppm (s, 48H; CH_3Si); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 164.1, 160.5, 157.4, 151.2, 148.2, 146.9, 146.7, 138.3, 137.8, 137.7, 136.8, 134.0, 133.7, 129.3, 128.9, 128.7, 128.7, 128.6, 128.5, 128.4, 128.4, 128.3, 128.3, 128.3, 128.2, 127.7, 123.5, 123.5, 118.4, 116.3, 115.8, 78.0, 78.0, 75.6, 71.9, 63.7, 58.7, 53.1, 35.6, 31.1, 31.0, 26.3, 18.6, 4.3, 4.1 ppm; IR (KBr): $\tilde{\nu}$ = 3092, 3064, 3031, 2953, 2930, 2884, 2854, 1731, 1607, 1548, 1500, 1456 cm^{-1}; HR-ESI: m/z $[M+H]^+$ calcd for $C_{46}H_{50}Br_2N_2O_7Si$: 929.1827; found: 929.1834.

General procedure for the preparation of alcohols 21a, 21b, 22a, and 22b: A solution of silyl ether **20a** or **20b** (7.0 mmol) in THF (30 mL) was treated for 30 min at ambient temperature with 1.0 M solution of TBAF in THF (7 mL). The reaction mixture was then poured into a saturated aqueous solution of ammonium chloride (50 mL) and extracted with EtOAc (3×30 mL). The combined organic phases were washed with water (20 mL) and brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue thus obtained was purified by flash column chromatography (30% EtOAc in hexanes) to yield, in order of elution, **22a** and **21a** or **22b** and **21b**, respectively.

Data for 21a: Yield 24% as colorless foam; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.50 (d, J = 2.0 Hz, 1H; Ar*H*), 7.43–7.18 (m, 15H; Ar*H*), 7.04–6.95 (m, 3H; Ar*H*), 6.91 (d, J = 8.1 Hz, 1H; Ar*H*), 6.59 (d, J = 8.3 Hz, 1H; Ar*H*), 5.31 (s, 2H; OCH_2Ph), 5.17 (s, 2H; OCH_2Ph), 5.04 (s, 2H; OCH_2Ph), 4.10 (br s, 2H; CH_2OH), 3.89 (s, 2H; ArCH_2CNOBn), 3.82 (s, 3H; COOCH_3), 3.66 (s, 2H; ArCH_2CNOBn), 2.53 ppm (br s, 1H; O*H*); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 163.7, 159.8, 156.8, 153.5, 150.5, 148.7, 144.6, 137.3, 136.6, 136.1, 133.7, 131.1, 129.3, 129.2, 128.7, 128.3, 128.2, 127.9, 127.8, 127.6, 126.8, 125.8, 122.3, 116.9, 116.0, 115.5, 112.4, 128.4, 128.1, 77.7, 76.1, 70.9, 62.4, 52.6, 31.2, 30.5 ppm; IR (KBr): $\tilde{\nu}$ = 3505, 3094, 3069, 3035, 2955, 2926, 2871, 1728, 1609, 1490, 1460 cm^{-1}.

Data for 21b: Yield 11% as colorless foam; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.53–7.44 (m, 4H; Ar*H*), 7.43–7.23 (m, 13H; Ar*H*), 6.90 (d, J = 8.3 Hz, 1H; Ar*H*), 6.83 (dd, J = 8.3, 1.9 Hz, 1H; Ar*H*), 6.42 (d, J = 1.9 Hz, 1H; Ar*H*), 5.25 (s, 2H; OCH_2Ph), 5.24 (s, 2H; OCH_2Ph), 5.17 (s, 2H; OCH_2Ph), 4.15 (s, 2H; CH_2OH), 3.78 (s, 2H; ArCH_2CNOBn), 3.75 (s, 3H; COOCH_3), 3.66 (s, 2H; ArCH_2CNOBn), 2.45 ppm (br s, 1H; O*H*); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 163.6, 156.1, 150.7, 148.0, 146.3, 146.2, 137.1, 136.3, 135.6, 133.3, 128.8, 128.4, 128.3, 128.2, 128.0, 128.0, 127.9, 127.9, 127.7, 127.2, 123.2, 118.1, 115.8, 115.2, 77.5, 76.3, 71.4, 62.6, 52.6, 31.1, 30.5 ppm; IR (KBr): $\tilde{\nu}$ = 3500, 3096, 3069, 3035, 2955, 2931, 2876, 1733, 1609, 1555, 1505, 1456, 1439 cm^{-1}.

Data for 22a: Yield 69% as colorless foam; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.47 (d, J = 2.0 Hz, 1H; Ar*H*), 7.37–7.17 (m, 15H; Ar*H*), 7.00–6.92 (m, 3H; Ar*H*), 6.88 (d, J = 8.3 Hz, 1H; Ar*H*), 6.58 (d, J = 8.3 Hz, 1H; Ar*H*), 5.27 (s, 2H; OCH_2Ph), 5.12 (s, 2H; OCH_2Ph), 5.02 (s, 2H; OCH_2Ph), 4.29 (br s, 2H; CH_2OH), 3.84 (s, 2H; ArCH_2CNOBn), 3.80 (s, 3H; COOCH_3), 3.53 ppm (s, 2H; ArCH_2CNOBn); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 163.8,159.8, 153.6, 150.6, 148.7, 144.8, 137.5, 136.8, 136.1, 133.6, 132.1, 129.4, 128.7, 128.4, 128.2, 128.0, 127.9, 127.7, 126.9, 125.8, 122.3, 117.1, 115.6, 112.6, 109.5, 128.4, 128.3, 77.8, 76.1, 71.0, 58.5, 52.7, 36.5, 30.5 ppm; IR (KBr): $\tilde{\nu}$ = 3535, 3091, 3072, 3032, 2957, 2928, 2878, 1726, 1616, 1492, 1460 cm^{-1}; HR-ESI: m/z $[M+H]^+$ calcd for $C_{40}H_{37}BrN_2O_7$: 737.1857; found: 737.1854.

Data for 22b: Yield 88% as colorless foam; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.51–7.46 (m, 4H; Ar*H*), 7.40–7.25 (m, 13H; Ar*H*), 6.88 (d, J = 8.3 Hz, 1H; Ar*H*), 6.80 (dd, J = 8.3, 1.9 Hz, 1H; Ar*H*), 6.33 (d, J = 1.9 Hz, 1H; Ar*H*), 5.23 (s, 4H; 2×OCH_2Ph), 5.14 (s, 2H; OCH_2Ph), 4.43 (s, 2H; CH_2OH), 3.76 (s, 2H; ArCH_2CNOBn), 3.74 (s, 3H; COOCH_3), 3.59 ppm (s, 2H; ArCH_2CNOBn); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.7, 159.5, 150.6, 147.9, 146.3, 146.3, 137.4, 137.1, 136.8, 136.2, 133.1, 128.7, 128.4, 128.1, 128.0, 127.9, 127.7, 128.4, 127.3, 123.2, 118.2, 115.9, 115.0, 77.5, 76.1, 71.5, 58.3, 52.7, 36.0, 30.5 ppm; IR (KBr): $\tilde{\nu}$ = 3521, 3095, 3071, 3036, 2957, 2927, 2876, 1731, 1612, 1553, 1506, 1457, 1439 cm^{-1}; HR-ESI-TOF: m/z $[M+H]^+$ calcd for $C_{40}H_{36}Br_2N_2O_7$: 815.0962; found: 815.0961.

General procedure for the preparation of acids 23a, 23b, 25a, and 25b: One of the above alcohols (4.6 mmol) was dissolved in acetonitrile (140 mL) and a solution of KBr in water (2.8 mL, 0.5 M; 1.4 mmol) and a solution of TEMPO in acetonitrile (2.9 mL, 16 mM; 46 μmol) were added. To this stirred mixture was added in small portions (over 1 h) and at 0 °C an aqueous solution of NaOCl (39 mL, 0.3 M; 11.5 mmol) containing $NaHCO_3$ (1.2 g, 13 mmol). The reaction was allowed to proceed for two additional hours and was then quenched by addition of 2-propanol (2 mL). EtOAc (150 mL) was added to the mixture and it was washed successively with water (50 mL) and brine (50 mL). The combined organic phases were dried over Na_2SO_4 and concentrated under reduced pressure. The residue thus obtained was purified by flash column chromatography (30% EtOAc in hexanes + 2% AcOH) to yield the corresponding carboxylic acid.

Data for 23a: Yield 96% as colorless foam; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.49 (d, J = 1.9 Hz, 1H; Ar*H*), 7.41–7.18 (m, 15H; Ar*H*), 7.05–6.88 (m, 4H; Ar*H*), 6.59 (d, J = 8.3 Hz, 1H; Ar*H*), 5.28 (s, 4H; 2×OCH_2Ph), 5.04 (s, 2H; OCH_2Ph), 3.86 (s, 2H; ArCH_2CNOBn), 3.82 (s, 3H; COOCH_3), 3.72 ppm (s, 2H; ArCH_2CNOBn); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 163.8, 153.8, 150.6, 149.7, 148.7, 144.8, 136.7, 136.1, 133.9, 130.6, 129.3, 129.2, 128.8, 128.7, 128.6, 128.4, 128.3, 127.6, 127.0, 125.9, 122.2, 117.0, 115.6, 112.5, 78.5, 77.9, 71.0, 52.8, 36.3, 30.5 ppm; IR (KBr): $\tilde{\nu}$ = 3267, 3094, 3069, 3040, 2951, 2881, 1733, 1609, 1495, 1455 cm^{-1}; HR-ESI-TOF: m/z $[M+H]^+$ calcd for $C_{40}H_{35}BrN_2O_8$: 751.1649; found: 751.1644.

Data for 23b: Yield 98% as colorless foam; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.56–7.45 (m, 4H; Ar*H*), 7.43–7.27 (m, 13H; Ar*H*), 6.94–6.90 (m, 1H; Ar*H*), 6.86–6.83 (m, 1H; Ar*H*), 6.38–6.34 (m, 1H; Ar*H*), 5.28 (s, 2H; OCH_2Ph), 5.27 (s, 2H; OCH_2Ph), 5.26 (s, 2H; OCH_2Ph), 3.80 (br s, 2H; ArCH_2CNOBn), 3.78 (s, 3H; COOCH_3), 3.72 ppm (s, 2H; ArCH_2-CNOBn); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.7, 161.4, 150.6, 149.3, 148.3, 146.3, 146.2, 137.1, 136.2, 135.8, 135.6, 134.9, 133.4, 128.7, 128.6, 128.4, 128.1, 128.0, 127.7, 127.3, 123.2, 118.2, 115.8, 114.8, 77.9, 77.5, 71.4, 52.8, 36.2, 30.5 ppm; HR-ESI-TOF: m/z $[M+H]^+$ calcd for $C_{40}H_{34}Br_2N_2O_8$: 829.0755; found: 829.0749.

Data for 25a: Yield 97% as colorless foam; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.54 (br s, 1H; Ar*H*), 7.43–6.88 (m, 19H; Ar*H*), 6.50 (br d, J = 6.9 Hz, 1H; Ar*H*), 5.32 (br s, 2H; OCH_2Ph), 5.26 (br s, 2H; OCH_2Ph), 5.01 (br s, 2H; OCH_2Ph), 3.86 (AB_q, J = 16.9 Hz, $\Delta\nu$ = 18.2 Hz, 2H; ArCH_2-

CNOBn), 3.81 ppm (brs, 5H; ArCH_2CNOBn, COOCH_3); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 163.6, 150.5, 148.6, 144.7, 153.1, 136.6, 136.1, 135.7, 133.9, 129.2, 128.4, 128.3, 128.3, 128.2, 128.1, 128.1, 127.5, 126.8, 125.5, 122.2, 116.8, 115.5, 112.2, 77.7, 70.8, 52.6, 30.4, 29.6 ppm; IR (KBr): $\tilde{\nu}$ = 3347, 3069, 2920, 2852, 1714, 1674, 1615, 1515, 1495, 1460 cm^{-1}.

Data for 25b: Yield 98% as colorless foam; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.55–7.17 (m, 17H; Ar*H*), 6.89 (brd, *J* = 7.9 Hz, 1H; Ar*H*), 6.81 (brd, *J* = 7.7 Hz, 1H; Ar*H*), 6.42 (brs, 1H; Ar*H*), 5.23 (s, 2H; OCH_2Ph), 5.21 (s, 4H; 2×OCH_2Ph), 3.74 ppm (brs, 7H; 2×ArCH_2CNOBn, COOCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.2, 150.3, 147.5, 146.0, 145.9, 136.8, 135.9, 133.3, 128.5, 128.3, 128.0, 127.9, 127.7, 127.6, 127.3, 126.9, 122.7, 117.6, 115.5, 115.0, 77.2, 71.1, 52.3, 30.2, 29.3 ppm.

General procedure for the preparation of 24a or 24b: TFA (8 mL) was added to a mixture of benzyl ether (0.9 mmol) and pentamethyl benzene (2.7 g, 18 mmol) at 0°C. The mixture was stirred at this temperature for 30 min and was then allowed to warm up to ambient temperature. After 2 h the mixture was evaporated under reduced pressure and the residue was purified by flash column chromatography (30% EtOAc in hexanes + 3% AcOH) to yield the corresponding free phenol.

Data for 24a: Yield 94% as white amorphous solid; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.53 (d, *J* = 1.9 Hz, 1H; Ar*H*), 7.42–7.20 (m, 10H; Ar*H*), 7.10 (dd, *J* = 8.4, 1.9 Hz, 1H; Ar*H*), 6.92 (brs, 1H; Ar*H*), 6.73 (brs, 1H; Ar*H*), 6.72 (d, *J* = 8.2 Hz, 1H; Ar*H*), 5.32 (brs, 2H; OCH_2Ph), 5.24 (brs, 2H; OCH_2Ph), 3.86 (brs, 2H; ArCH_2CNOBn), 3.80 (s, 2H; ArCH_2-CNOBn), 3.78 ppm (s, 3H; COOCH_3); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 163.7, 163.1, 152.1, 150.7, 145.7, 142.7, 136.1, 135.5, 134.4, 132.1, 129.6, 128.7, 128.4, 128.3, 128.2, 128.1, 125.7, 128.2, 119.2, 118.7, 116.3, 113.6, 78.5, 77.8, 52.7, 30.6, 29.4 ppm; HR-ESI-TOF: *m*/*z* [*M*+H]$^+$ calcd for $C_{33}H_{29}BrN_2O_8$: 661.1180; found: 661.1177.

Data for 24b: Yield 96% as white amorphous solid; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.48 (brs, 2H; Ar*H*), 7.43–7.21 (m, 10H; Ar*H*), 6.92 (d, *J* = 8.2 Hz, 1H; Ar*H*), 6.83 (brd, *J* = 8.2 Hz, 1H; Ar*H*), 6.33 (brs, 1H; Ar*H*), 5.31 (brs, 2H; OCH_2Ph), 5.22 (brs, 2H; OCH_2Ph), 3.86 (brs, 2H; ArCH_2-CNOBn), 3.74 ppm (brs, 5H; ArCH_2CNOBn, COOCH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.7, 150.9, 147.7, 144.1, 143.2, 136.3, 135.4, 135.3, 133.7, 128.9, 128.5, 128.5, 128.3, 128.2, 128.0, 127.6, 124.2, 118.2, 115.9, 114.4, 78.6, 77.6, 52.7, 30.7, 29.5 ppm; HR-ESI-TOF: *m*/*z* [*M*+H]$^+$ calcd for $C_{33}H_{28}Br_2N_2O_8$: 739.0285; found: 739.0283.

General procedure for the preparation of 4a or 4b: A stirred solution of the phenol (1.1 mmol) in acetonitrile (30 mL) was treated at 0°C with *N*-bromosuccinimide (195 mg, 1.1 mmol). After 1 h the reaction was quenched by addition of an aqueous solution of potassium iodide (2 mL, 10% w/v) followed by addition of Na_2SO_3·7H_2O in small portions until complete disappearance of the red color of the mixture. Water (30 mL) was added and the mixture was extracted with EtOAc (3×20 mL). The combined organic extracts were washed with brine (10 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was further purified by flash column chromatography (30% EtOAc in hexanes + 3% AcOH).

Data for 4a: Yield 100% as light yellow foam; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.41 (brs, 1H; Ar*H*), 7.33–7.05 (m, 11H; Ar*H*), 6.94 (brd, *J* = 8.4 Hz, 1H; Ar*H*), 6.57 (brd, *J* = 1.4 Hz, 1H; Ar*H*), 6.39 (brd, *J* = 8.4 Hz, 1H; Ar*H*), 5.21 (s, 2H; OCH_2Ph), 5.03 (brs, 2H; OCH_2Ph), 3.69 (brs, 5H; ArCH_2CNOBn, COOCH_3), 3.65 ppm (brs, 2H; ArCH_2-CNOBn); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 163.6, 151.4, 150.0, 143.6, 143.5, 135.9, 134.2, 133.9, 129.4, 128.7, 128.5, 128.3, 128.0, 128.3, 118.9, 118.6, 113.4, 110.2, 78.0, 76.5, 52.8, 30.2, 29.4 ppm; HR-ESI-TOF: *m*/*z* [*M*+Na]$^+$ calcd for $C_{33}H_{28}Br_2N_2O_8$: 763.0090; found: 763.0076.

Data for 4b: Yield 100% as light yellow foam; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.38 (brs, 2H; Ar*H*), 7.30–7.08 (m, 10H; Ar*H*), 6.97 (brs, 1H; Ar*H*), 6.16 (brs, 1H; Ar*H*), 5.11 (brs, 2H; OCH_2Ph), 5.03 (brs, 2H; OCH_2Ph), 3.70 (brs, 2H; ArCH_2CNOBn), 3.58 (brs, 3H; COOCH_3), 3.55 ppm (brs, 2H; ArCH_2CNOBn); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 166.6, 163.4, 150.0, 146.8, 143.7, 141.7, 137.1, 136.0, 135.6, 133.8, 128.9, 128.6, 128.5, 128.2, 128.1, 128.0, 127.1, 117.6, 113.7, 109.5, 77.8, 77.0, 52.7, 31.0, 30.2 ppm; HR-ESI-TOF: *m*/*z* [*M*+H]$^+$ calcd for $C_{33}H_{27}Br_3N_2O_8$: 816.9390; found: 816.9388.

Preparation of 26a: DMAP (24 mg, 0.2 mmol) and Boc_2O (320 mg, 1.5 mmol) were added to a solution of acid **4a** (300 mg, 0.41 mmol) in THF (5 mL) cooled to 0°C. The mixture was stirred at this temperature for 12 h and then poured into water (10 mL) and extracted with EtOAc (2×5 mL). The combined organic phases were washed with brine (10 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue thus obtained was purified by flash column chromatography (10% EtOAc in hexanes) to yield diester **26a** (298 mg, 81%) as colorless oil. ^{1}H NMR (250 MHz, $CDCl_3$): δ = 7.46 (d, *J* = 2.1 Hz, 1H; Ar*H*), 7.36–7.18 (m, 11H; Ar*H*), 7.02 (dd, *J* = 8.4, 2.1 Hz, 1H; Ar*H*), 6.69 (d, *J* = 8.4 Hz, 1H; Ar*H*), 6.68 (d, *J* = 1.9 Hz, 1H; Ar*H*), 5.26 (s, 2H; OCH_2Ph), 5.22 (s, 2H; OCH_2Ph), 3.78 (s, 2H; ArCH_2C=N), 3.77 (s, 5H; ArCH_2C= N, COOCH_3), 1.47 (s, 9H; OC(CH_3)$_3$), 1.46 ppm (s, 9H; OC(CH_3)$_3$); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 164.3, 163.4, 162.0, 151.6, 151.1, 150.1, 149.5, 149.3, 138.5, 136.3, 135.5, 134.3, 133.5, 129.4, 128.6, 128.5, 128.4, 128.3, 128.2, 119.5, 119.2, 117.8, 113.9, 84.2, 82.8, 78.1, 77.8, 52.9, 30.7, 30.4, 27.9, 27.5 ppm; HR-ESI-TOF: *m*/*z* [*M*−H]$^-$ calcd for $C_{42}H_{44}Br_2N_2O_{10}$: 893.1290; found: 893.1279.

Preparation of acid 27a: A solution of the above diester (97 mg, 0.1 mmol) in a mixture of THF (5 mL) and MeOH (3 mL) was treated at 0°C with a solution of NaOH in H_2O (1N, 0.3 mL). The progress of the reaction was monitored by TLC and upon completion it was quenched by addition of acetic acid (0.5 mL). The mixture was poured into water (10 mL) and extracted with EtOAc (4×10 mL). The combined organic phases were washed with brine (10 mL), dried over Na_2SO_4, and concentrated under reduced pressure. Further purification by flash column chromatography (30% EtOAc in hexanes + 3% acetic acid) afforded acid **27a** (75 mg, 85%) as colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.58 (d, *J* = 1.9 Hz, 1H; Ar*H*), 7.46–7.37 (m, 8H; Ar*H*), 7.34–7.30 (m, 3H; Ar*H*), 7.15 (dd, *J* = 8.4, 1.9 Hz, 1H; Ar*H*), 6.82 (d, *J* = 8.4 Hz, 1H; Ar*H*), 6.81 (s, 1H; Ar*H*), 5.38 (s, 2H; OCH_2Ph), 5.31 (s, 2H; OCH_2Ph), 3.90 (s, 2H; ArCH_2C=N), 3.86 (s, 2H; ArCH_2C=N), 1.58 ppm (s, 18H; 2× OC(CH_3)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): δ = 163.5, 162.0, 151.5, 151.1, 150.0, 149.4, 148.9, 138.6, 136.2, 135.4, 134.9, 134.2, 133.5, 129.4, 128.6, 128.5, 128.5, 128.3, 128.2, 128.1, 119.6, 119.1, 117.8, 113.9, 84.2, 82.9, 78.4, 77.8, 30.4, 29.8, 27.9, 27.5 ppm; HR-ESI-TOF: *m*/*z* [*M*+Na]$^+$ calcd for $C_{41}H_{42}Br_2N_2O_{10}$: 903.1098; found: 903.1122.

General procedure for the preparation of 7a or 7b: Potassium carbonate (48 mmol) was added to a solution of phenol **9a** or **9b** (8.0 mmol) in pyridine (30 mL). The mixture was stirred at ambient temperature for 1 h and, after addition of iodonium salt **1b** (10 mmol), was heated at 90°C for 4 h. The mixture was then poured into water (100 mL) and extracted with EtOAc (3×30 mL). The combined organic phases were washed in sequence with saturated aqueous $CuSO_4$ solution (4×30 mL) and brine (30 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue thus obtained was purified by flash column chromatography (15% EtOAc in hexanes).

Data for 7a: Yield 82% as colorless foam; $[\alpha]_D^{20}$ = +7.0 (*c* = 1.0 in CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): δ = 9.70 (s, 1H; C*H*O), 7.59 (brs, 2H; Ar*H*), 7.47 (dd, *J* = 8.2, 1.9 Hz, 1H; Ar*H*), 7.40–7.25 (m, 5H; Ar*H*), 7.08 (d, *J* = 8.2 Hz, 1H; Ar*H*), 6.92 (d, *J* = 1.9 Hz, 1H; Ar*H*), 5.32 (s, 2H; CH_2Ph), 4.92–4.74 (m, 2H; ArC*H*OTBS, N*H*Boc), 3.39 (m, 1H; C*H*HNHBoc), 3.07 (m, 1H; CH*H*NHBoc), 1.43 (s, 9H; *tBu*OCO), 0.90 (s, 9H; *tBu*Si), 0.07 (s, 3H; CH_3Si), −0.03 ppm (s, 3H; CH_3Si); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 190.3, 155.7, 153.0, 147.8, 146.6, 142.8, 135.9, 130.5, 129.9, 128.6, 128.1, 127.2, 127.1, 118.0, 113.9, 113.1, 79.5, 72.1, 70.9, 48.9, 28.3, 25.7, 18.1, 3.2, 3.0 ppm; IR (KBr): $\tilde{\nu}$ = 3454, 3364, 3067, 3034, 2957, 2932, 2857, 2734, 1716, 1696, 1602, 1580, 1510, 1454, 1434 cm^{-1}; HR-MALDI-FTMS: *m*/z [*M*+Na]$^+$ calcd for $C_{33}H_{41}Br_2NO_6Si$: 756.0962; found: 756.0966.

Data for 7b: Yield 85% as colorless oil; ^{1}H NMR (250 MHz, $CDCl_3$): δ = 9.74 (s, 1H; C*H*O), 7.51–7.32 (m, 8H; Ar*H*), 7.10 (d, *J* = 8.3 Hz, 1H; Ar*H*), 6.95 (d, *J* = 1.9 Hz, 1H; Ar*H*), 5.36 (s, 2H; CH_2Ph), 4.66 (brm, 1H; N*H*Boc), 3.43–3.55 (m, 2H; CH_2NHBoc), 2.80 (t, *J* = 7.0 Hz, 2H; ArCH_2CH$_2$), 1.46 ppm (s, 9H; *tBu*OCO); ^{13}C NMR (62.5 MHz, $CDCl_3$): δ = 190.1, 155.6, 152.8, 146.9, 146.4, 139.4, 136.7, 135.7, 133.1, 129.8, 129.7, 128.3, 127.8, 127.1, 126.9, 117.7, 116.8, 113.7, 112.7, 78.9, 70.7, 41.0, 34.8, 28.1 ppm; IR (KBr): $\tilde{\nu}$ = 3436, 3355, 3070, 3035, 2980, 2934, 2859, 2736, 1694, 1601, 1579, 1511, 1458, 1436 cm^{-1}; HR-ESI: *m*/*z* [*M*+Na]$^+$ calcd for $C_{27}H_{27}Br_2NO_5$: 626.0154; found: 626.0155.

General procedure for the preparation of 28a or 28b: Sodium borohydride (1.6 mmol) was added in small portions to a stirred solution of aldehyde **7a** or **7b** (1.0 mmol) in a mixture of MeOH (5 mL) and THF

(5 mL) at 0 °C. After 30 min the reaction mixture was allowed to reach ambient temperature and saturated aqueous NH_4Cl solution (10 mL) was carefully added. The mixture was extracted with EtOAc (3×20 mL). The combined organic phases were washed in sequence with water (30 mL) and brine (30 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue thus obtained was purified by flash column chromatography (30% EtOAc in hexanes).

Data for 28a: Yield 96% as amorphous white solid; $[\alpha]_D^{20}=+10.5$ ($c=0.9$ in CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta=7.58$ (brs, 2H; Ar*H*), 7.53–7.27 (m, 5H; Ar*H*), 6.98 (d, $J=8.6$ Hz, 1H; Ar*H*), 6.92 (dd, $J=8.6$, 1.9 Hz, 1H; Ar*H*), 6.41 (d, $J=1.9$ Hz, 1H; Ar*H*), 5.28 (s, 2H; CH_2Ph), 4.90–4.74 (m, 2H; ArC*H*OTBS, N*H*Boc), 4.49 (s, 2H; ArCH_2OH), 3.40 (m, 1H; C*H*HNHBoc), 3.08 (m, 1H; CH*H*NHBoc), 1.45 (s, 9H; *tBu*OCO), 0.92 (s, 9H; *tBu*Si), 0.08 (s, 3H; CH_3Si), −0.03 ppm (s, 3H; CH_3Si); ^{13}C NMR (62.5 MHz, $CDCl_3$): $\delta=155.8$, 148.4, 147.2, 146.6, 142.4, 137.2, 134.3, 130.5, 128.5, 127.8, 127.3, 121.4, 118.3, 115.9, 113.0, 79.6, 72.3, 71.5, 64.8, 49.0, 28.4, 25.8, 18.2, 3.3, 3.1 ppm; IR (KBr): $\tilde{\nu}=$ 3443, 3065, 3033, 2957, 2932, 2858, 1702, 1616, 1595, 1553, 1512, 1459, 1426 cm^{-1}; HR-MALDI-FTMS: *m*/z $[M+Na]^+$ calcd for $C_{33}H_{43}Br_2NO_6Si$: 758.1118; found: 758.1104.

Data for 28b: Yield 98% as colorless foam; ^{1}H NMR (250 MHz, $CDCl_3$): $\delta=7.48$ (brs, 1H; Ar*H*), 7.46 (brs, 1H; Ar*H*), 7.35–7.25 (m, 5H; Ar*H*), 6.93 (d, $J=8.3$ Hz, 1H; Ar*H*), 6.86 (dd, $J=8.3$, 1.6 Hz, 1H; Ar*H*), 6.45 (d, $J=1.6$ Hz, 1H; Ar*H*), 5.20 (s, 2H; CH_2Ph), 5.01 (brt, $J=4.1$ Hz, 1H; N*H*Boc), 4.36 (s, 2H; ArCH_2OH), 3.26–3.18 (brm, 2H; CH_2NHBoc), 3.15 (brs, 1H; O*H*), 2.65 (t, $J=6.6$ Hz, 2H; ArCH_2CH$_2$), 1.42 ppm (s, 9H; *tBu*OCO); ^{13}C NMR (62.5 MHz, $CDCl_3$): $\delta=155.7$, 147.3, 146.5, 146.2, 138.8, 136.8, 134.3, 132.9, 128.1, 128.0, 127.5, 127.1, 120.9, 117.9, 115.4, 112.6, 79.0, 71.1, 63.8, 41.0, 34.7, 28.1 ppm; IR (KBr): $\tilde{\nu}=$3422, 3550, 3066, 3037, 2978, 2933, 2868, 1692, 1616, 1598, 1549, 1512, 1455, 1426 cm^{-1}; HR-MALDI-FTMS: *m*/z $[M+Na]^+$ calcd for $C_{27}H_{29}Br_2NO_5$: 628.0305; found: 628.0202.

General procedure for the preparation of 29a or 29b: PPh_3 (210 mg, 0.8 mmol), imidazole (82 mg, 1.2 mmol) and iodine (203 mg, 0.8 mmol) were added to a stirred solution of alcohol **28a** or **28b** (0.41 mmol) in THF (10 mL) at ambient temperature. After 30 min the solvent was removed under reduced pressure and DMF (2 mL) and KCN (52 mg, 0.8 mmol) were added. The mixture was stirred at 40 °C for 30 min and then was poured into saturated aqueous NH_4Cl solution (10 mL) and extracted with EtOAc (3×10 mL). The combined organic phases were washed in sequence with water (20 mL) and brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue thus obtained was purified by flash column chromatography (20% EtOAc in hexanes).

Data for 29a: Yield 86% as amorphous white solid; $[\alpha]_D^{20}=+8.7$ ($c=1.3$ in CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta=7.53$ (s, 2H; Ar*H*), 7.42–7.17 (m, 5H; Ar*H*), 6.89 (d, $J=8.2$ Hz, 1H; Ar*H*), 6.82 (dd, $J=8.2$, 1.9 Hz, 1H; Ar*H*), 6.21 (d, $J=1.9$ Hz, 1H; Ar*H*), 5.16 (s, 2H; CH_2Ph), 4.81 (t, $J=5.6$ Hz, 1H; N*H*Boc), 4.70 (dd, $J=7.1$, 3.7 Hz, 1H; ArC*H*OTBS), 3.40 (s, 2H; ArCH_2CN), 3.30 (m, 1H; C*H*HNHBoc), 3.00 (m, 1H; CH*H*NHBoc), 1.38 (s, 9H; *tBu*OCO), 0.85 (s, 9H; *tBu*Si), 0.02 (s, 3H; CH_3Si), −0.10 ppm (s, 3H; CH_3Si); ^{13}C NMR (62.5 MHz, $CDCl_3$): $\delta=$ 155.8, 148.0, 147.4, 146.6, 142.6, 136.7, 130.5, 128.5, 127.9, 127.3, 122.7, 122.2, 118.1, 117.6, 116.1, 113.8, 79.6, 72.3, 71.4, 48.9, 28.4, 25.7, 22.9, 18.1, 3.3, 3.0 ppm; IR (KBr): $\tilde{\nu}=$3446, 3078, 3069, 3037, 2959, 2929, 2858, 2253, 1713, 1599, 1516, 1457, 1432 cm^{-1}; HR-MALDI-FTMS: *m*/z $[M+Na]^+$ calcd for $C_{34}H_{42}Br_2N_2O_5Si$: 767.1122; found: 767.1152.

Data for 29b: Yield 84% as colorless foam; ^{1}H NMR (250 MHz, $CDCl_3$): $\delta=7.46$–7.23 (m, 7H; Ar*H*), 6.95 (d, $J=8.3$ Hz, 1H; Ar*H*), 6.88 (dd, $J=$ 8.3, 1.6 Hz, 1H; Ar*H*), 6.28 (d, $J=1.6$ Hz, 1H; Ar*H*), 5.22 (s, 2H; CH_2Ph), 4.67 (brs, 1H; N*H*Boc), 3.51 (s, 2H; ArCH_2CN), 3.37–3.29 (m, 2H; CH_2NHBoc), 2.75 (t, $J=6.9$ Hz, 2H; ArCH_2CH$_2$), 1.42 ppm (s, 9H; *tBu*OCO); ^{13}C NMR (62.5 MHz, $CDCl_3$): $\delta=155.7$, 147.3, 146.6, 139.2, 136.7, 133.2, 128.4, 128.2, 127.8, 127.3, 122.7, 122.1, 118.0, 116.0, 113.8, 79.5, 71.3, 41.3, 35.1, 28.3, 22.8 ppm; IR (KBr): $\tilde{\nu}=$3430, 3365, 3065, 3040, 2976, 2931, 2869, 2252, 1706, 1614, 1596, 1552, 1516, 1454, 1431 cm^{-1}; HR-ESI: *m*/*z* $[M+H]^+$ calcd for $C_{28}H_{28}Br_2N_2O_4$: 615.0494; found: 615.0490.

General procedure for the preparation of 5a or 5b: Pd/C (10%, 120 mg) was added to a degassed solution of benzyl ether **29a** or **29b** (0.32 mmol) in dioxane (20 mL); the mixture was stirred under an atmosphere of hydrogen for 12 h at ambient temperature. Upon reaction completion, the mixture was filtered through a Celite bed to remove catalyst and the filtrate was concentrated under reduced pressure to yield the corresponding free phenol.

Data for 5a: Yield 95% as colorless foam; $[\alpha]_D^{20}=+8.5$ ($c=1.0$ in CH_2Cl_2); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta=7.61$ (s, 2H; Ar*H*), 7.05 (d, $J=$ 8.2 Hz, 1H; Ar*H*), 6.96 (dd, $J=8.2$, 1.9 Hz, 1H; Ar*H*), 6.28 (d, $J=1.9$ Hz, 1H; Ar*H*), 5.94 (brs, 1H; ArO*H*), 4.90–4.74 (m, 2H; ArC*H*OTBS, N*H*Boc), 3.55 (s, 2H; ArCH_2CN), 3.40 (m, 1H; C*H*HNHBoc), 3.10 (m, 1H; CH*H*NHBoc), 1.45 (s, 9H; *tBu*OCO), 0.93 (s, 9H; *tBu*Si), 0.09 (s, 3H; CH_3Si), −0.02 ppm (s, 3H; CH_3Si); ^{13}C NMR (62.5 MHz, $CDCl_3$): $\delta=157.8$, 147.7, 145.4, 143.7, 143.4, 130.7, 123.3, 121.7, 118.1, 116.6, 113.2, 79.7, 72.3, 49.0, 29.7, 28.4, 25.8, 23.0, 18.2, 3.4, 3.1 ppm; IR (KBr): $\tilde{\nu}=$ 3368, 2957, 2932, 2856, 2256, 1705, 1604, 1518, 1455 cm^{-1}; HR-MALDI-FTMS: *m*/z $[M+Na]^+$ calcd for $C_{27}H_{36}Br_2N_2O_5Si$: 677.0652; found: 677.0658.

Data for 5b: Yield 98% as colorless foam; ^{1}H NMR (250 MHz, $CDCl_3$): $\delta=7.46$ (s, 2H; Ar*H*), 7.04 (d, $J=8.2$ Hz, 1H; Ar*H*), 6.95 (dd, $J=8.2$, 1.9 Hz, 1H; Ar*H*), 6.30 (d, $J=1.9$ Hz, 1H; Ar*H*), 5.93 (brs, 1H; ArO*H*), 4.67 (brs, 1H; N*H*Boc), 3.56 (s, 2H; ArCH_2CN), 3.43–3.35 (m, 2H; CH_2NHBoc), 2.81 (t, $J=7.0$ Hz, 2H; ArCH_2CH$_2$), 1.45 ppm (s, 9H; *tBu*OCO); ^{13}C NMR (62.5 MHz, $CDCl_3$): $\delta=147.0$, 145.3, 139.9, 133.4, 128.3, 123.2, 121.6, 118.1, 116.5, 113.1, 41.4, 35.3, 28.3, 23.0; IR (KBr): $\tilde{\nu}=$ 3361, 2979, 2932, 2856, 2255, 1695, 1606, 1516, 1456, 1441 cm^{-1}; HR-MALDI-FTMS: *m*/z $[M+Na]^+$ calcd for $C_{21}H_{22}Br_2N_2O_4$: 546.9838; found: 546.9848.

General procedure for the reduction of nitriles 5a,b: A vigorously stirred solution of nitrile **5a** or **5b** (0.21 mmol) in MeOH (6 mL) was cooled in an ice bath and $CoCl_2\cdot 6H_2O$ (catalytic amount, 5 mg) was added. $NaBH_4$ (20 mg, 0.53 mmol) was carefully added in small portions to this light pink mixture in such a rate as to maintain the black precipitate of boride that appeared following each addition. Upon completion of the reaction, a saturated aqueous solution of NH_4Cl (15 mL) was added, and the mixture was stirred for an additional 15 min. The mixture was extracted with EtOAc (4×10 mL) and the combined organic phases were washed with brine (10 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The mixture of amines **30a/31a** or **30b/31b** thus obtained as light brown oil was used without further purification for coupling with the appropriate acid.

General procedure for the coupling of acids 4a or 4b or 27a with amine mixtures 30a/31a or 30b/31b: *N*,*N*-diisopropylethylamine (25 μL, 0.14 mmol), 1-hydroxybenzotriazole (20 mg, 0.15 mmol) and 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (30 mg, 0.16 mmol) were added to a stirred solution of acid (0.13 mmol) and the crude mixture of amines (0.2 mmol) in a mixture of dichloromethane (10 mL) and DMF (0.5 mL) at 0 °C. The mixture was stirred overnight and allowed to gradually warm up to ambient temperature. Water (10 mL) was added and the mixture was extracted with EtOAc (3×10 mL). The combined organic extracts were washed with brine (2×5 mL), dried over Na_2SO_4, and concentrated under reduced pressure; the residue was purified by flash column chromatography (20% EtOAc in hexanes).

Data for 32: Yield 34% as colorless oil; $[\alpha]_D^{20}=+2.5$ ($c=0.95$ in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=7.62$ (s, 1H; Ar*H*), 7.54 (s, 1H; Ar*H*), 7.39–7.24 (m, 9H; Ar*H*), 7.21 (d, $J=7.5$ Hz, 1H; Ar*H*), 7.16 (s, 1H; Ar*H*), 7.12 (d, $J=8.4$ Hz, 1H; Ar*H*), 6.94 (d, $J=8.2$, 1H; Ar*H*), 6.86 (d, $J=8.4$ Hz, 1H; Ar*H*), 6.82 (d, $J=8.2$ Hz, 1H; Ar*H*), 6.70 (d, $J=8.4$ Hz, 1H; Ar*H*), 6.69–6.64 (m, 2H; Ar*H*, N*H*CO), 5.96 (brs, 1H; ArO*H*), 5.61 (brs, 1H; ArO*H*), 5.24 (s, 2H; OCH_2Ph), 5.18 (s, 2H; OCH_2Ph), 4.83 (brm, 1H; N*H*Boc), 4.76 (brm, 1H; ArC*H*OTBS), 3.86 (s, 2H; ArCH_2C≡N), 3.80 (s, 3H; COOCH_3), 3.75 (s, 2H; ArCH_2C≡N), 3.47–3.35 (m, 3H; C*H*HNHBoc, CH$_2$CH_2NHCO), 3.07–3.00 (m, 1H; CH*H*NHBoc), 2.69 (t, $J=6.9$ Hz, 2H; CH_2CH$_2$NHCO), 1.44 (s, 9H; OC(CH_3)$_3$), 0.91 (s, 9H; SiC(CH_3)$_3$), 0.07 (s, 3H; CH_3Si), −0.05 ppm (s, 3H; CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=163.5$, 162.0, 155.7, 152.5, 151.6, 151.4, 150.0, 145.8, 143.6, 143.4, 143.0, 139.5, 136.3, 135.9, 134.4, 133.4, 131.2, 130.9, 129.6, 128.6, 128.5, 128.5, 128.3, 128.3, 128.2, 128.1, 126.1, 125.2, 118.9, 118.5, 118.3, 116.5, 113.5, 113.4, 109.8, 79.4, 77.9, 77.4, 72.6, 52.7, 48.9, 40.5, 34.7, 30.2, 28.8, 28.3, 25.7, −4.7, −5.0 ppm; IR (KBr): $\tilde{\nu}=$3650, 3100, 3036, 2960, 2861, 1729, 1679, 1617, 1518, 1060,

1006 cm^{-1}; HR-ESI-TOF: m/z $[M+Na]^+$ calcd for $C_{60}H_{67}Br_3N_4O_{12}Si$: 1323.1967; found: 1323.1956.

Data for 33: Yield 34% as colorless oil; $[\alpha]_D^{20}=+3.7$ ($c=0.51$ in CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$): $\delta=7.61$ (brs, 2H; Ar*H*), 7.55 (s, 1H; Ar*H*), 7.41–7.26 (m, 9H; Ar*H*), 7.18 (s, 1H; Ar*H*), 7.13 (d, $J=8.4$ Hz, 1H; Ar*H*), 6.96 (d, $J=8.1$ Hz, 1H; Ar*H*), 6.76 (d, $J=8.1$, 1H; Ar*H*), 6.72 (d, $J=8.4$ Hz, 1H; Ar*H*), 6.69 (s, 1H; Ar*H*), 6.66 (brt, $J=6.0$ Hz, 1H; N*H*CO), 6.22 (s, 1H; Ar*H*), 5.97 (brs, 1H; ArO*H*), 5.74 (brs, 1H; ArO*H*), 5.26 (s, 2H; OCH_2Ph), 5.18 (s, 2H; OCH_2Ph), 4.91 (brm, 1H; N*H*Boc), 4.81 (brm, 1H; ArC*H*OTBS), 3.87 (s, 2H; ArCH_2C=N), 3.81 (s, 3H; COOCH_3), 3.76 (s, 2H; ArCH_2C=N), 3.45–3.39 (m, 3H; C*H*HNHBoc, CH_2CH_2NHCO), 3.14–3.05 (m, 1H; CH*H*NHBoc), 2.64 (t, $J=6.9$ Hz, 2H; CH_2CH_2NHCO), 1.46 (s, 9H; OC(CH_3)$_3$), 0.94 (s, 9H; SiC(CH_3)$_3$), 0.11 (s, 3H; CH_3Si), 0.00 ppm (s, 3H; CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=163.5$, 162.0, 155.7, 151.5, 151.3, 150.0, 147.9, 144.0, 143.6, 143.4, 143.3, 142.8, 136.3, 135.9, 134.4, 133.5, 130.4, 129.6, 128.6, 128.5, 128.4, 128.2, 128.1, 123.6, 119.0, 118.5, 118.1, 116.0, 113.6, 109.8, 77.9, 77.4, 72.1, 52.7, 48.8, 40.5, 34.7, 30.2, 28.8, 28.3, 25.7, −4.7, −4.9 ppm; IR (KBr): $\tilde{\nu}=3650$, 3100, 3066, 3032, 2955, 2932, 2860, 1717, 1674, 1604, 1525, 1452, 1366, 1129, 1106 cm^{-1}; HR-ESI-TOF: m/z $[M+Na]^+$ calcd for $C_{60}H_{66}Br_4N_4O_{12}Si$: 1401.1072; found: 1401.1077.

Data for 40: Yield 28% as colorless oil; ^1H NMR (500 MHz, $CDCl_3$): $\delta=$ 7.50 (s, 2H; Ar*H*), 7.46 (s, 1H; Ar*H*), 7.43–7.23 (m, 10H; Ar*H*), 7.08 (s, 1H; Ar*H*), 7.06 (d, $J=8.2$ Hz, 1H; Ar*H*), 6.98 (d, $J=8.2$ Hz, 1H; Ar*H*), 6.86 (d, $J=8.2$ Hz, 1H; Ar*H*), 6.82 (dd, $J=8.2$, 1.5 Hz, 1H; Ar*H*), 6.69 (t, $J=5.9$ Hz, 1H; N*H*CO), 6.61 (d, $J=1.3$ Hz, 1H; Ar*H*), 6.31 (d, $J=$ 1.3 Hz, 1H; Ar*H*), 6.09 (brs, 1H; ArO*H*), 5.70 (brs, 1H; ArO*H*), 5.22 (s, 2H; OCH_2Ph), 5.18 (s, 2H; OCH_2Ph), 4.61 (brs, 1H; N*H*Boc), 3.85 (s, 2H; ArCH_2C=N), 3.76 (s, 3H; COOCH_3), 3.69 (s, 2H; ArCH_2C=N), 3.47–3.43 (m, 2H; CH_2NHCO), 3.39–3.31 (m, 2H; CH_2NHCO), 2.76 (brt, $J=6.6$ Hz, 2H; ArCH_2CH$_2$), 2.69 (t, $J=7.0$ Hz, 2H; ArCH_2CH$_2$), 1.45 ppm (s, 9H; OC(CH_3)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=163.5$, 161.9, 155.8, 151.5, 150.9, 150.2, 147.1, 145.6, 143.7, 143.5, 141.7, 136.8, 136.1, 134.0, 133.9, 133.3, 131.0, 129.1, 128.8, 128.6, 128.4, 128.3, 128.2, 127.2, 125.0, 119.6, 118.0, 117.8, 116.4, 114.0, 109.4, 77.9, 77.8, 52.8, 41.7, 40.7, 35.3, 34.9, 30.4, 28.9, 28.4 ppm; HR-ESI-TOF: m/z $[M+Na]^+$ calcd for $C_{54}H_{52}Br_4N_4O_{11}$: 1271.0258; found: 1271.0211.

Data for 41: Yield 29% as colorless oil; ^1H NMR (500 MHz, $CDCl_3$): $\delta=$ 7.50 (s, 2H; Ar*H*), 7.43 (s, 1H; Ar*H*), 7.40–7.25 (m, 11H; Ar*H*), 7.08 (s, 1H; Ar*H*), 6.98 (d, $J=8.1$ Hz, 1H; Ar*H*), 6.78 (d, $J=8.1$ Hz, 1H; Ar*H*), 6.68 (t, $J=5.6$ Hz, 1H; N*H*CO), 6.31 (s, 1H; Ar*H*), 6.22 (s, 1H; Ar*H*), 5.83 (brs, 1H; ArO*H*), 5.22 (s, 2H; OCH_2Ph), 5.18 (s, 2H; OCH_2Ph), 4.74 (brs, 1H; N*H*Boc), 3.85 (s, 2H; ArCH_2C=N), 3.76 (s, 3H; COOCH_3), 3.69 (s, 2H; ArCH_2C=N), 3.43–3.34 (m, 4H; 2×CH_2NHCO), 2.84–2.73 (m, 2H; ArCH_2CH$_2$), 2.65 (t, $J=6.8$ Hz, 2H; ArCH_2CH$_2$), 1.45 ppm (s, 9H; OC(CH_3)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=163.5$, 161.9, 155.8, 150.8, 150.2, 147.3, 147.1, 144.1, 143.7, 143.6, 141.7, 139.7, 136.8, 136.1, 133.9, 133.6, 133.3, 130.5, 128.7, 128.5, 128.3, 128.3, 128.2, 127.1, 123.7, 118.2, 117.8, 116.1, 113.9, 113.7, 109.4, 77.8, 77.7, 52.8, 41.4, 40.7, 35.2, 34.8, 30.4, 28.9, 28.4 ppm; HR-ESI-TOF: m/z $[M+Na]^+$ calcd for $C_{54}H_{51}Br_5N_4O_{11}$: 1348.9363; found: 1348.9386.

Data for 46: Yield 38% as colorless foam; ^1H NMR (500 MHz, $CDCl_3$): $\delta=7.48$ (d, $J=1.8$ Hz, 1H; Ar*H*), 7.44 (s, 1H; Ar*H*), 7.38–7.23 (m, 8H; Ar*H*), 7.19–7.18 (m, 2H; Ar*H*), 7.04–7.03 (m, 2H; Ar*H*), 6.95 (d, $J=$ 8.2 Hz, 1H; Ar*H*), 6.84–6.79 (m, 3H; Ar*H*), 6.73–6.67 (m, 3H; N*H*CO, Ar*H*), 6.62 (d, $J=1.8$ Hz, 1H; Ar*H*), 6.06 (brs, 1H; ArO*H*), 5.29 (s, 2H; OCH_2Ph), 5.08 (s, 2H; OCH_2Ph), 4.70 (brs, 1H; N*H*Boc), 3.80 (brs, 4H; 2×ArCH_2C=N), 3.46–3.30 (m, 4H; 2×CH_2NHCO), 2.78–2.64 (m, 4H; 2×ArCH_2CH$_2$), 1.49 (s, 9H; OC(CH_3)$_3$), 1.49 (s, 9H; OC(CH_3)$_3$), 1.44 ppm (s, 9H; OC(CH_3)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=161.9$, 161.8, 155.7, 151.7, 151.1, 151.0, 150.0, 148.9, 145.7, 143.3, 138.4, 136.2, 135.9, 134.1, 133.8, 133.2, 130.9, 130.0, 129.2, 129.0, 128.4, 128.2, 128.0, 125.0, 119.7, 119.2, 119.1, 118.3, 117.8, 117.6, 116.4, 113.8, 113.5, 84.1, 82.7, 77.7, 77.3, 41.5, 40.6, 35.1, 34.7, 30.3, 29.1, 28.3, 27.9, 27.4 ppm; HR-ESI-TOF: m/z $[M+Na]^+$ calcd for $C_{62}H_{67}Br_3N_4O_{13}$: 1335.2147; found: 1335.2083,.

General procedure for the regiospecific *o*-brominations: A stirred solution of the phenol (15 μmol) in acetonitrile (2 mL) was treated at 0°C with *N*-bromosuccinimide (2.7 mg, 15 μmol). After 2 h the reaction was quenched by addition of an aqueous solution of potassium iodide (0.5 mL, 10% w/v). To the resulting mixture was added in small portions $Na_2SO_3\cdot 7H_2O$ until complete disappearance of its red color. Water (10 mL) was added and the mixture was extracted with EtOAc (3× 10 mL). The combined organic extracts were washed with brine (10 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The residue was further purified by flash column chromatography.

Data for 34: Yield 75% as colorless oil; $[\alpha]_D^{20}=+4.2$ ($c=4.6$ in CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$): $\delta=7.64$ (brs, 1H; Ar*H*), 7.56 (d, $J=1.6$ Hz, 1H; Ar*H*), 7.40–7.23 (m, 11H; Ar*H*), 7.18 (d, $J=1.4$ Hz, 1H; Ar*H*), 7.14–7.11 (m, 2H; Ar*H*), 6.86 (d, $J=8.4$ Hz, 1H; Ar*H*), 6.73 (t, $J=$ 5.1 Hz, 1H; CH_2N*H*CO), 6.72 (d, $J=8.2$ Hz, 1H; Ar*H*), 6.69 (d, $J=$ 1.5 Hz, 1H; Ar*H*), 6.60 (s, 1H; Ar*H*), 6.22 (brs, 2H; 2×ArO*H*), 5.25 (s, 2H; OCH_2Ph), 5.21 (s, 2H; OCH_2Ph), 4.89 (brm, 1H; N*H*Boc), 4.79 (brm, 1H; ArC*H*OTBS), 3.87 (s, 2H; ArCH_2C=N), 3.79 (s, 3H; COOCH_3), 3.76 (s, 2H; ArCH_2C=N), 3.45–3.37 (m, 3H; C*H*HNHBoc, CH_2CH_2NHCO), 3.09–2.99 (m, 1H; CH*H*NHBoc), 2.66 (t, $J=6.9$ Hz, 2H; CH_2CH_2NHCO), 1.45 (s, 9H; OC(CH_3)$_3$), 0.93 (s, 9H; SiC(CH_3)$_3$), 0.09 (s, 3H; CH_3Si), −0.03 ppm (s, 3H; CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=163.5$, 162.1, 155.7, 152.0, 151.5, 151.3, 150.0, 143.9, 143.6, 143.3, 143.2, 140.1, 136.3, 135.9, 134.4, 133.5, 131.7, 131.3, 129.6, 128.7, 128.6, 128.5, 128.3, 128.2, 128.1, 128.0, 126.2, 119.0, 118.5, 117.8, 113.7, 113.6, 110.0, 109.7, 79.4, 77.9, 77.5, 72.6, 52.7, 49.0, 40.3, 34.6, 30.2, 28.8, 28.3, 25.7, −4.7, −5.0 ppm; HR-ESI-TOF m/z $[M+Na]^+$ calcd for $C_{60}H_{66}Br_4N_4O_{12}Si$: 1401.1072; found: 1401.1075.

Data for 35: Yield 78% as colorless oil; $[\alpha]_D^{20}=+2.9$ ($c=7.3$ in CH_2Cl_2); ^1H NMR (500 MHz, $CDCl_3$): $\delta=7.60$ (brs, 2H; Ar*H*), 7.55 (s, 1H; Ar*H*), 7.39–7.25 (m, 9H; Ar*H*), 7.17 (s, 1H; Ar*H*), 7.13 (d, $J=8.4$ Hz, 1H; Ar*H*), 7.05 (s, 1H; Ar*H*), 6.72 (d, $J=8.4$, 1H; Ar*H*), 6.72 (d, $J=8.4$ Hz, 1H; Ar*H*), 6.98 (brm, 2H; Ar*H*, CH_2N*H*CO), 6.17 (s, 1H; Ar*H*), 6.09 (brs, 1H; ArO*H*), 5.98 (brs, 1H; ArO*H*), 5.25 (s, 2H; OCH_2Ph), 5.19 (s, 2H; OCH_2Ph), 4.91 (brm, 1H; N*H*Boc), 4.81 (brm, 1H; ArC*H*OTBS), 3.86 (s, 2H; ArCH_2C=N), 3.80 (s, 3H; COOCH_3), 3.75 (s, 2H; ArCH_2C=N), 3.47–3.34 (m, 3H; C*H*HNHBoc, CH_2CH_2NHCO), 3.13–3.05 (m, 1H; CH*H*NHBoc), 2.62 (t, $J=6.9$ Hz, 2H; CH_2CH_2NHCO), 1.45 (s, 9H; OC(CH_3)$_3$), 0.93 (s, 9H; SiC(CH_3)$_3$), 0.10 (s, 3H; CH_3Si), −0.01 ppm (s, 3H; CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=163.6$, 162.1, 155.8, 151.5, 151.3, 150.1, 147.5, 143.9, 143.6, 143.3, 141.6, 136.3, 135.9, 134.5, 133.6, 131.4, 130.6, 129.7, 128.8, 128.6, 128.5, 128.4, 128.3, 128.3, 128.2, 126.8, 119.1, 118.5, 117.9, 113.7, 113.0, 109.7, 109.5, 79.6, 78.0, 77.6, 72.2, 52.8, 48.9, 40.3, 34.7, 30.3, 28.9, 28.4, 25.7, −4.7, −4.9 ppm; HR-ESI-TOF: m/z $[M+Na]^+$ calcd for $C_{60}H_{65}Br_5N_4O_{12}Si$: 1479.0177; found: 1479.0233.

Data for 42: Yield 75% as colorless oil; ^1H NMR (500 MHz, $CDCl_3$): $\delta=$ 7.51 (s, 2H; Ar*H*), 7.46 (s, 1H; Ar*H*), 7.43–7.25 (m, 10H; Ar*H*), 7.11 (s, 1H; Ar*H*), 7.08 (s, 2H; Ar*H*), 6.87 (d, $J=8.3$ Hz, 1H; Ar*H*), 6.71 (t, $J=$ 5.9 Hz, 1H; N*H*CO), 6.55 (s, 1H; Ar*H*), 6.31 (s, 1H; Ar*H*), 6.04 (brs, 1H; ArO*H*), 5.22 (s, 2H; OCH_2Ph), 5.21 (s, 2H; OCH_2Ph), 4.62 (brs, 1H; N*H*Boc), 3.85 (s, 2H; ArCH_2C=N), 3.76 (s, 3H; COOCH_3), 3.69 (s, 2H; ArCH_2C=N), 3.45–3.32 (m, 4H; 2×CH_2NHCO), 2.77 (brt, $J=$ 7.7 Hz, 2H; ArCH_2CH$_2$), 2.68 (t, $J=7.0$ Hz, 2H; ArCH_2CH$_2$), 1.44 ppm (s, 9H; OC(CH_3)$_3$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=163.5$, 162.0, 155.8, 151.2, 150.8, 150.2, 147.1, 144.3, 143.7, 143.1, 141.7, 136.7, 136.1, 136.1, 134.1, 133.9, 133.4, 131.7, 130.9, 129.2, 128.8, 128.6, 128.4, 128.3, 128.2, 127.8, 127.2, 120.0, 117.9, 117.2, 114.0, 109.9, 109.4, 77.9, 52.8, 41.7, 40.5, 35.3, 34.7, 30.4, 28.9, 28.4 ppm; HR-ESI-TOF: m/z $[M+Na]^+$ calcd for $C_{54}H_{51}Br_5N_4O_{11}$: 1348.9363; found: 1348.9346.

Data for 48: Yield 72% colorless oil; ^1H NMR (500 MHz, $CDCl_3$): $\delta=$ 7.51 (brs, 1H; Ar*H*), 7.43 (brs, 1H; Ar*H*), 7.38–7.28 (m, 9H; Ar*H*), 7.22–7.20 (m, 2H; Ar*H*), 7.06–7.02 (m, 3H; Ar*H*), 6.86 (d, $J=8.4$ Hz, 1H; Ar*H*), 6.70 (brt, $J=6$ Hz, 1H; N*H*CO), 6.69 (d, $J=8.3$ Hz, 1H; Ar*H*), 6.65 (brt, $J=6$ Hz, 1H; N*H*CO), 6.57 (brs, 1H; ArH), 6.49 (brs, 1H; Ar*H*), 6.01 (brs, 1H; ArO*H*), 5.89 (brs, 1H; ArO*H*), 5.18 (s, 2H; OCH_2Ph), 5.14 (s, 2H; OCH_2Ph), 3.85 (s, 2H; ArCH_2C=N), 3.67 (s, 2H; ArCH_2C=N), 3.60–3.56 (m, 2H; CH_2NHCO), 3.38–3.34 (m, 2H; CH_2NHCO), 2.78–2.76 (m, 2H; ArCH_2CH$_2$), 2.64–2.60 ppm (m, 2H; ArCH_2CH$_2$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=162.3$, 152.0, 151.5, 151.2, 151.1, 144.5, 143.6, 143.0, 142.7, 137.0, 136.4, 134.6, 134.1, 133.5, 131.6, 130.3, 129.5, 129.4, 129.2, 128.7, 128.6, 128.3, 128.0, 127.5, 121.0, 119.2, 118.8, 118.0, 116.4, 114.7, 113.7, 109.5, 109.4, 77.4, 40.6, 40.3, 34.9, 34.7, 28.9, 28.9 ppm; HR-ESI-TOF: m/z $[M+H]^+$ calcd for $C_{48}H_{40}Br_4N_4O_8$: 1116.9652; found: 1116.9623.

General procedure for the preparation of α,ω-amino acids: In the case of bastaranes, a solution of the protected α,ω-amino acid (30 μmol) in a mixture of THF (3 mL) and methanol (3 mL) was treated at 0 °C with an aqueous solution of LiOH (3 N, 0.2 mL) for 5 h. The residue obtained after standard aqueous workup of the reaction was dissolved in dichloromethane (3 mL) and treated at 0 °C with TFA (1.5 mL). Evaporation of the reaction mixture under reduced pressure provided the free α,ω-amino acid that was used in the next step without further purification.

In the case of isobastaranes, a solution of the protected α,ω-amino acid (56 μmol) and pentamethylbenzene (125 mg, 0.8 mmol) in dichloromethane (3 mL) was treated at 0 °C with TFA (3 mL). The reaction mixture was allowed to gradually warm up to ambient temperature and, after 2 h, the solvent and excess TFA was removed under reduced pressure to provide the corresponding free α,ω-amino acid that was used in the next step without further purification.

General procedure for the macrolactamizations: *N*,*N*-diisopropylethylamine (60 μL, 0.34 mmol), and benzotriazol-1-yloxytripyrrolidinophosphonium hexafluorophosphate (138 mg, 0.41 mmol) were added to a stirred solution of the α,ω-amino acid (56 μmol) in a mixture of dichloromethane (100 mL) and DMF (10 mL) at 0 °C. The temperature of the reaction was maintained at 0 °C for 1 h and then the mixture was allowed to gradually warm up to ambient temperature. After 24 h the reaction mixture was poured into saturated aqueous solution of ammonium chloride (100 mL) and extracted with EtOAc (5×30 mL). The combined organic extracts were washed sequentially with water (2×20 mL) and brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure.

In the case of group B bastaranes, removal of the Boc protection was accompanied by partial loss of the TBS protective group. As a consequence, the residue obtained after macrolactamization contained a mixture of free and TBS-protected products that, for convenience, was not separated at this stage. The crude mixture was treated with 1.0 M solution of TBAF in THF to afford after standard aqueous workup and flash column chromatography (40% EtOAc in hexanes) the desired product.

Data for 36: Yield 52% (from **34**) as colorless oil; $[\alpha]_D^{20}=+6.8$ ($c=0.44$ in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=7.65$ (d, $J=1.8$ Hz, 1H; Ar*H*), 7.56 (d, $J=1.9$ Hz, 1H; Ar*H*), 7.43–7.26 (m, 9H; Ar*H*), 7.24 (d, $J=1.8$ Hz, 1H; Ar*H*), 7.17–7.13 (m, 3H; Ar*H*), 7.01 (d, $J=1.6$ Hz, 1H; Ar*H*), 6.98 (d, $J=8.4$ Hz, 1H; Ar*H*), 6.96 (brt, $J=6.3$ Hz, 1H; N*H*CO), 6.75 (d, $J=1.7$ Hz, 1H; Ar*H*), 6.69 (d, $J=8.4$ Hz, 1H; Ar*H*), 6.60 (brt, $J=5.8$ Hz, 1H; N*H*CO), 6.47 (d, $J=1.6$ Hz, 1H; Ar*H*), 5.20 (s, 2H; OCH_2Ph), 5.03 (AB_q, $J=11.6$ Hz, $\Delta\nu=15.8$ Hz, 2H; OCH_2Ph), 4.84 (dd, $J=6.5$, 3.7 Hz, 1H; C*H*OH), 3.79 (s, 2H; ArCH_2C=N), 3.77 (AB_q, $J=13$ Hz, $\Delta\nu=27$ Hz, 2H; ArCH_2C=N), 3.73–3.68 (m, 1H; C*H*HNHCO), 3.42–3.26 (m, 3H; CH_2NHCO, CH*H*NHCO), 2.62–2.52 ppm (m, 2H; ArCH_2CH$_2$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=163.3$, 162.2, 151.7, 151.5, 151.4, 151.4, 144.7, 143.5, 143.4, 142.7, 139.9, 136.3, 136.0, 134.6, 133.4, 131.3, 131.2, 129.8, 129.1, 128.7, 128.6, 128.4, 128.3, 128.2, 127.4, 126.5, 121.2, 118.7, 118.6, 115.7, 115.2, 113.5, 109.7, 109.6, 77.5, 77.5, 72.4, 47.0, 40.1, 34.6, 29.1, 28.7 ppm; IR (KBr): $\tilde{\nu}=3406$, 3092, 3065, 3034, 2926, 2873, 2855, 1671, 1611, 1527, 1502, 1455 cm^{-1}; HR-ESI-TOF: m/z $[M+Na]^+$ calcd for $C_{48}H_{40}Br_4N_4O_9$: 1154.9421; found: 1154.9447.

Data for 37: Yield 61% (from **35**) as colorless oil; $[\alpha]_D^{20}=+1.5$ ($c=1.8$ in CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=7.64$ (brs, 2H; Ar*H*), 7.58 (d, $J=1.9$ Hz, 1H; Ar*H*), 7.43–7.37 (m, 4H; Ar*H*), 7.35–7.31 (m, 3H; Ar*H*), 7.28 (s, 1H; Ar*H*), 7.25 (d, $J=1.9$ Hz, 1H; Ar*H*), 7.21–7.17 (m, 3H; Ar*H*), 7.08 (brt, $J=6.0$ Hz, 1H; N*H*CO), 7.01 (d, $J=1.6$ Hz, 1H; Ar*H*), 6.72 (d, $J=8.4$ Hz, 1H; Ar*H*), 6.68 (d, $J=1.7$ Hz, 1H; Ar*H*), 6.60 (brt, $J=6.0$ Hz, 1H; N*H*CO), 6.22 (d, $J=1.6$ Hz, 1H; Ar*H*), 5.21 (s, 2H; OCH_2Ph), 5.05 (AB_q, $J=12$ Hz, $\Delta\nu=21$ Hz, 2H; OCH_2Ph), 4.89 (dd, $J=7.1$, 3.1 Hz, 1H; C*H*OH), 3.80 (AB_q, $J=13$ Hz, $\Delta\nu=30$ Hz, 2H; ArCH_2C=N), 3.80–3.75 (m, 3H; ArCH_2C=N, CH*H*NHCO), 3.42–3.22 (m, 3H; C*H*HNHCO, CH_2NHCO), 2.67–2.53 ppm (m, 2H; CH_2CH$_2$NHCO); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=163.9$, 162.2, 151.4, 151.3, 147.6, 144.0, 143.8, 143.1, 142.2, 141.5, 136.3, 135.9, 134.6, 133.7, 130.8, 130.6, 130.0, 128.9, 128.9, 128.7, 128.6, 128.4, 128.3, 128.2, 126.8, 119.0, 118.2, 117.9, 112.2, 109.4, 77.7, 77.5, 72.4, 47.3, 39.5, 34.3, 29.2, 28.6 ppm; IR (KBr): $\tilde{\nu}=3408$, 3071, 3036, 2931, 2880, 1671, 1613, 1526, 1502, 1456 cm^{-1}; HR-ESI-TOF m/z $[M+H]^+$ calcd for $C_{48}H_{39}Br_5N_4O_9$: 1210.8706; found: 1210.8738.

In the case of group C bastaranes and isobastaranes, flash column chromatographic purification (30% EtOAc in hexanes) of the residue obtained after macrolactamization afforded the desired product.

Data for 43: Yield 58% as colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=$ 7.53 (s, 2H; Ar*H*), 7.48 (s, 1H; Ar*H*), 7.42–7.27 (m, 9H; Ar*H*), 7.17 (s, 1H; Ar*H*), 7.13 (dd, $J=8.0$, 1.1 Hz, 1H; Ar*H*), 7.09–7.07 (m, 1H; Ar*H*), 7.02 (s, 1H; Ar*H*), 7.00 (d, $J=8.2$ Hz, 1H; Ar*H*), 6.71 (t, $J=6.3$ Hz, 1H; N*H*CO), 6.59 (s, 1H; Ar*H*), 6.54 (t, $J=6.0$ Hz, 1H; N*H*CO), 6.34 (s, 1H; Ar*H*), 5.98 (brs, 1H; ArO*H*), 5.94 (brs, 1H; ArO*H*), 5.18 (s, 2H; OCH_2Ph), 4.80 (s, 2H; OCH_2Ph), 3.79 (s, 2H; ArCH_2C=N), 3.72 (s, 2H; ArCH_2C=N), 3.51–3.47 (m, 2H; CH_2NHCO), 3.33–3.29 (m, 2H; CH_2NHCO), 2.75 (t, $J=6.7$ Hz, 2H; ArCH_2CH$_2$), 2.54 ppm (t, $J=7.4$ Hz, 2H; ArCH_2CH$_2$); ^{13}C NMR (125 MHz, $CDCl_3$): $\delta=162.1$, 162.0, 152.0, 151.0, 150.7, 147.0, 143.9, 142.7, 141.5, 137.4, 136.7, 136.3, 136.1, 134.3, 133.9, 133.6, 131.4, 129.6, 128.8, 128.6, 128.6, 128.4, 128.3, 128.2, 127.9, 127.4, 121.2, 117.9, 115.8, 115.1, 113.3, 113.1, 109.1, 77.7, 77.1, 40.4, 40.0, 35.0, 34.5, 29.3, 28.9 ppm; HR-ESI-TOF: m/z $[M-H]^-$ calcd for $C_{48}H_{39}Br_5N_4O_8$: 1192.8612; found: 1192.8566,.

Data for 44: Yield 66% as colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): $\delta=$ 7.55 (s, 2H; Ar*H*), 7.47 (s, 2H; Ar*H*), 7.42–7.24 (m, 8H; Ar*H*), 7.18 (d, $J=1.6$ Hz, 1H; Ar*H*), 7.13–7.11 (m, 2H; Ar*H*), 6.98 (d, $J=8.2$ Hz, 1H; Ar*H*), 6.81 (t, $J=6.4$ Hz, 1H; N*H*CO), 6.75 (dd, $J=8.2$, 1.7 Hz, 1H; Ar*H*), 6.50 (t, $J=5.9$ Hz, 1H; N*H*CO), 6.39 (d, $J=1.7$ Hz, 1H; Ar*H*), 6.31 (d, $J=1.7$ Hz, 1H; Ar*H*), 5.98 (brs, 1H; ArO*H*), 5.72 (brs, 1H; ArO*H*), 5.18 (s, 2H; OCH_2Ph), 4.88 (s, 2H; OCH_2Ph), 3.80 (s, 2H;

Table 1. NMR data for bastadin 5 (500 MHz, [D$_6$]acetone).

Position	^{13}C δ	^{1}H δ	HMBC
1	28.4	3.67 (s, 2H)	H-36, H-38
2	152.5		N^{2}OH, H-1
3	163.3		H-1
4		7.73 (brt, 1H)	
5	41.3	3.52–3.41 (m, 2H)	H-6
6	34.8	2.84–2.74 (obs m, 2H)	H-5, H-8, H-12
7	138.0		H-5, H-6, H-11
8	134.5	7.54 (d, $J=1.9$ Hz, 1H)	H-6, H-12
9	114.5		H-8, H-11
10	152.3		H-8, H-11, H-12
11	121.2	7.00 (d, $J=8.3$ Hz, 1H)	
12	130.6	7.22 (dd, $J=8.3$, 1.9 Hz, 1H)	H-6, H-8
14	144.6		H-19
15	144.4		H-17
16	110.4		H-17, 15-OH
17	128.7	7.14 (d, $J=1.8$ Hz, 1H)	H-19, H-20
18	132.5		H-20, H-21
19	117.7	6.64 (d, $J=1.8$ Hz, 1H)	H-17, H-20
20	35.0	2.84–2.74 (obs m, 2H)	H-17, H-19, H-21
21	40.4	3.52–3.41 (m, 2H)	H-20
22		7.32 (brt, 1H)	
23	164.5		H-25
24	151.9		H-25, N^{24}OH
25	29.7	3.85 (s, 2H)	H-27, H-31
26	138.8		H-25
27	134.5	7.63 (s, 1H)	H-25, H-31
28	118.2		H-27
29	147.6		H-27, H-31
30	118.2		H-31
31	134.5	7.63 (s, 1H)	H-25, H-27
33	145.6		H-38
34	142.9		H-36, H-38
35	109.8		H-36, 34-OH
36	128.0	7.18 (d, $J=1.8$ Hz, 1H)	H-1, H-38
37	129.8		H-1, H-38
38	114.3	6.41 (d, $J=1.8$ Hz, 1H)	H-1, H-36
N^{2}OH		10.47 (s, 1H)	
N^{24}OH		11.32 (s, 1H)	
15-OH		8.74 (s, 1H)	
34-OH		8.70 (s, 1H)	

Table 2. NMR data for bastadin 20 (500 MHz, [D$_6$]DMSO).

Position	^{13}C δ	^{1}H δ	COSY	HMBC
1	27.7	3.45 (s, 2H)	H-36	H-36, H-38
2	151.2			N^{2}OH, H-1
3	162.8			H-1, H-5
4		7.86 (t, J=6 Hz, 1H)	H-5	
5	40.0	3.19–3.15 (m, 2H)	H-4, H-6	H-6
6	33.5	2.5 (obs m)	H-5	H-5, H-12, H-8
7	131.7			H-5, H-6
8	127.2	7.09 (d, J=2 Hz, 1H)	H-12	H-6, H-12
9	110.4			H-8, 10-OH
10	144.8			H-12
11	143.3			H-12
12	117.1	6.35 (d, J=2 Hz, 1H)	H-8	H-6, H-8
14	150.8			H-16,H-18,H-19
15	113.2			H-16, H-19
16	133.4	7.51 (d, J=2 Hz, 1H)	H-18	H-18, H-20
17	137.3			H-20
18	129.5	7.10 (dd, J=8, 2 Hz, 1H)	H-16,H-19	H-16, H-20
19	120.4	6.83 (d, J=8.4 Hz, 1H)	H-18	
20	33.8	2.71–2.68 (m, 2H)	H-21	H-16
21	39.8	3.40–3.36 (m, 2H)	H-20,H-22	H-20
22		8.08 (t, J=6 Hz, 1H)	H-21	
23	163.3			H-21, H-25
24	151.7			N^{24}OH, H-25
25	28.4	3.70 (s, 2H)	H-27	H-27, H-31
26	137.1			H-30
27	134.3	7.44 (d, J=2 Hz, 1H)	H-25,H-31	H-25
28	113.2			H-27, H-30
29	150.8			H-27,H-30,H-31
30	120.4	6.80 (d, J=8.3 Hz, 1H)	H-31	
31	129.5	7.08 (dd, J=8, 2 Hz, 1H)	H-27,H-30	H-25, H-27
33	144.8			H-38
34	143.3			H-36, H-38
35	110.4			H-36, 34-OH
36	127.2	7.01 (d, J=2 Hz, 1H)	H-1, H-38	H-1, H-38
37	128.9			H-1
38	116.9	6.29 (d, J=2 Hz, 1H)	H-36	H-1, H-36
N^{2}OH		11.70 (s, 1H)		
N^{24}OH		11.82 (s, 1H)		
10-OH		9.84 (brs, 1H)		
34-OH		9.78 (brs, 1H)		

General procedure for the deprotection of bastadins: A stirred solution of the dibenzyl ether derivative of bastadin (5 μmol) in thioanisole (2 mL) was cooled in an ice bath and a solution of BBr_3 in dichloromethane (1 M, 400 μL) was added. The ice bath was removed and the reaction was allowed to proceed at ambient temperature for 1 h. Aqueous HCl (0.5 M, 10 mL) was carefully added at 0 °C and, after stirring at ambient temperature for 45 min, the mixture was extracted with EtOAc (4×10 mL). The combined organic phases were washed sequentially with water (2×10 mL) and brine (10 mL), dried over Na_2SO_4, and then concentrated under reduced pressure. Residual thioanisole was removed under vacuum, and the oil thus obtained was purified by thin-layer chromatography (3% MeOH in dichloromethane) to afford free bastadin.

Bastadin 10: Yield 48% as amorphous white solid; $[\alpha]_D^{20}=-4.4$ (c=0.16 in MeOH); ^{1}H NMR (500 MHz, [D$_6$]DMSO): δ=11.13 (s, 1H; NO*H*), 10.88 (s, 1H; NO*H*), 8.74 (brs, 2H; 2× ArO*H*), 7.69 (d, J=1.8 Hz, 1H; Ar*H*), 7.59 (d, J=1.8 Hz, 1H; Ar*H*), 7.54 (brt, J=5.9 Hz, 1H; N*H*CO), 7.38 (brdd, J=6.4, 5.7 Hz, 1H; N*H*CO), 7.31 (dd, J=8.4, 1.8 Hz, 1H; Ar*H*), 7.27 (d, J=1.7 Hz, 1H; Ar*H*), 7.22 (dd, J=8.4, 1.9 Hz, 1H; Ar*H*), 7.15 (d, J=1.7 Hz, 1H; Ar*H*), 6.99 (d, J=8.4 Hz, 1H; Ar*H*), 6.82 (d, J=8.4 Hz, 1H; Ar*H*), 6.69 (d, J=1.8 Hz, 1H; Ar*H*), 6.63 (d, J=1.8 Hz, 1H; Ar*H*), 4.91 (brs, 1H; CHO*H*), 4.84 (brm, 1H; C*H*OH), 3.81 (AB_q, J=13.4 Hz, $\Delta\nu$=28.8 Hz, 2H; ArCH_2C=N), 3.74 (s, 2H; ArCH_2C=N), 3.55–3.50 (m, 1H; CH*H*NHCO), 3.49–3.41 (m, 2H; CH_2NHCO), 3.37–3.32 (m, 1H; C*H*HNHCO), 2.71 ppm (t, J=7.0 Hz, 2H; ArCH_2CH$_2$); ^{13}C NMR (125 MHz, [D$_6$]acetone): δ=165.1, 165.0, 154.2, 153.7, 153.6, 153.1, 146.7, 145.7, 145.5, 142.7, 136.8, 135.9, 133.9, 132.7, 131.6, 131.3, 130.2, 130.1, 130.0, 128.9, 121.8, 121.8, 119.7, 119.4, 115.5, 115.4, 111.7, 111.5, 73.0, 49.0, 41.7, 36.2, 29.4 ppm; HR-MALDI-FTMS: m/z $[M+Na]^+$ calcd for $C_{34}H_{28}Br_4N_4O_9$: 974.8482; found: 974.8487.

Bastadin 12: Yield 51% as amorphous white solid; $[\alpha]_D^{20}=-14$ (c=0.17 in MeOH); ^{1}H NMR (500 MHz, [D$_6$]acetone): δ=11.15 (s, 1H; NO*H*), 10.88 (s, 1H; NO*H*), 8.74 (brs, 1H; ArO*H*), 8.71 (brs, 1H; ArO*H*), 7.72 (brs, 2H; Ar*H*), 7.59 (d, J=2.1 Hz, 1H; Ar*H*), 7.54 (dd, J=6.1, 4.4 Hz, 1H; CH$_2$N*H*CO), 7.50 (brt, J=5.8 Hz, 1H; CH$_2$N*H*CO), 7.28 (dd, J=4.4, 2.1 Hz, 1H; Ar*H*), 7.27 (dd, J=4.0, 1.9 Hz, 1H; Ar*H*), 7.07 (d, J=1.9 Hz, 1H; Ar*H*), 6.85 (d, J=8.4 Hz, 1H; Ar*H*), 6.66 (d, J=1.9 Hz, 1H; Ar*H*), 6.37 (d, J=1.9 Hz, 1H; Ar*H*), 5.11 (brd, J=4.4 Hz, 1H; CHO*H*), 4.91–4.88 (m, 1H; C*H*OH), 3.88 (AB_q, J=13.3 Hz, $\Delta\nu$=19.3 Hz, 2H; ArCH_2C=N), 3.75 (s, 2H; ArCH_2C=N), 3.57–3.52 (m, 1H; C*H*HNHCO), 3.44–3.30 (m, 3H; C*H*HNHCO, CH_2NHCO), 2.70 ppm (t, J=2.7 Hz, 2H; ArCH_2CH$_2$); ^{13}C NMR (125 MHz, [D$_6$]acetone): δ=165.3, 165.1, 153.7, 153.6, 153.2, 149.1, 147.0, 146.7, 145.9, 145.5, 144.0, 136.9, 136.0, 133.1, 132.7, 131.8, 131.4, 130.2, 128.5, 122.0, 119.5, 115.6, 114.2, 111.6, 111.5, 72.7, 49.0, 41.2, 35.8, 29.3 ppm; HR-MALDI-FTMS: m/z $[M+Na]^+$ calcd for $C_{34}H_{27}Br_5N_4O_9$: 1052.7587; found: 1052.7615.

Bastadin 5: Yield 43% as amorphous white solid; for NMR data see Table 1; HR-ESI-TOF: m/z $[M-H]^-$ calcd for $C_{34}H_{27}Br_5N_4O_8$: 1012.7673; found: 1012.7654.

ArCH_2C=N), 3.74 (s, 2H; ArCH_2C=N), 3.53–3.49 (m, 2H; CH_2NHCO), 3.36–3.32 (m, 2H; CH_2NHCO), 2.79 (t, J=7.0 Hz, 2H; ArCH_2CH$_2$), 2.60 ppm (t, J=7.5 Hz, 2H; ArCH_2CH$_2$); ^{13}C NMR (125 MHz, CDCl$_3$): δ=162.3, 162.0, 151.9, 150.8, 147.4, 147.0, 144.0, 143.5, 141.5, 139.5, 136.8, 136.2, 134.0, 133.6, 130.1, 128.8, 128.6, 128.4, 128.3, 128.3, 128.2, 127.9, 123.7, 118.3, 117.8, 115.9, 113.1, 113.0, 109.0, 77.7, 77.4, 40.5, 39.7, 34.8, 34.4, 29.4, 28.8 ppm; HR-ESI-TOF: m/z $[M+H]^+$ calcd for $C_{48}H_{39}Br_5N_4O_8$: 1194.8757; found: 1194.8757.

Data for 47: Yield 55% (from **46**) as colorless glass; ^{1}H NMR (500 MHz, CDCl$_3$): δ=7.48 (d, J=2.0 Hz, 1H; Ar*H*), 7.41 (d, J=1.9 Hz, 1H; Ar*H*), 7.38–7.24 (m, 9H; Ar*H*), 7.20–7.16 (m, 2H; Ar*H*), 7.02–6.96 (m, 2H; Ar*H*), 6.92 (d, J=8.2 Hz, 1H; Ar*H*), 6.82 (d, J=8.3 Hz, 1H; Ar*H*), 6.77 (dd, J=8.2, 1.8 Hz, 1H; Ar*H*), 6.69 (brt, J=6 Hz, 1H; N*H*CO), 6.67–6.61 (m, 2H; N*H*CO, ArH), 6.57 (d, J=1.8 Hz, 1H; Ar*H*), 6.54 (d, J=1.8 Hz, 1H; Ar*H*), 5.15 (s, 2H; OCH_2Ph), 5.13 (brs, 1H; ArO*H*), 5.11 (s, 2H; OCH_2Ph), 5.10 (brs, 1H; ArO*H*), 3.83 (s, 2H; ArCH_2C=N), 3.66 (s, 2H; ArCH_2C=N), 3.57–3.54 (m, 2H; CH_2NHCO), 3.37–3.33 (m, 2H; CH_2NHCO), 2.76–2.71 (m, 2H; ArCH_2CH$_2$), 2.64–2.60 ppm (m, 2H; ArCH_2CH$_2$); ^{13}C NMR (125 MHz, CDCl$_3$): δ=162.3, 162.2, 152.0, 151.7, 151.6, 151.3, 145.4, 143.7, 143.6, 143.0, 136.4, 134.7, 134.0, 133.5, 130.9, 130.2, 129.5, 129.3, 129.2, 128.8, 128.6, 128.3, 128.1, 128.0, 124.7, 120.4, 119.1, 118.5, 118.2, 117.4, 116.2, 114.5, 113.7, 109.5, 77.4, 77.3, 40.9, 40.3, 34.9, 34.7, 29.0, 28.9 ppm; HR-ESI-TOF: m/z $[M+Na]^+$ calcd for $C_{48}H_{41}Br_3N_4O_8$: 1061.0367; found: 1061.0375.

Table 3. NMR data for bastadin 21 (500 MHz, [D$_6$]DMSO).

Position	^{13}C δ	^{1}H δ	HMBC
1	27.9	3.48 (s, 2H)	H-36, H-38
2	151.6		H-1, N^{2}OH
3	162.8		H-1, H-4, H-5
4		7.87 (t, J=6 Hz, 1H)	
5	39.9	3.22–3.18 (m, 2H)	H-6
6	33.9	2.5 (obs m)	H-5, H-8
7	131.0		H-5, H-6, H-11
8	119.8	6.52 (d, J=2 Hz, 1H)	H-6, H-12
9	142.2		H-8, H-11, 10-OH
10	147.3		H-8, H-12, 10-OH
11	116.4	6.83 (d, J=8 Hz, 1H)	10-OH
12	125.0	6.78 (dd, J=8, 2 Hz, 1H)	H-6, H-8
14	152.5		H-16, H-18, H-19
15	111.2		H-16, H-19
16	132.7	7.48 (d, J=2 Hz, 1H)	H-18, H-20
17	135.3		H-19, H-20, H-21
18	129.3	7.01 (dd, J=8, 2 Hz, 1H)	H-16, H-20
19	117.6	6.58 (d, J=8 Hz, 1H)	
20	33.1	2.70–2.68 (m, 2H)	H-16,
21	39.1	3.41–3.37 (m, 2H)	H-20
22		8.02 (t, J=6 Hz, 1H)	
23	163.6		H-21, H-22, H-25
24	152.5		H-25, N^{24}OH
25	28.8	3.67 (s, 2H)	H-27, H-31
26	134.4		H-25, H-28
27	129.4	7.05 (dd, J=8, 2 Hz, 1H)	H-25, H-31
28	120.0	6.81 (d, J=8 Hz, 1H)	
29	150.8		H-27, H-28, H-31
30	112.9		H-28, H-31
31	132.9	7.43 (d, J=2 Hz, 1H)	H-27
33	144.7		H-38, 34-OH
34	143.0		H-36, H-38
35	110.4		H-36, 34-OH
36	126.7	7.04 (d, J=2 Hz, 1H)	H-1, H-38
37	128.4		H-1
38	116.9	6.34 (d, J=2 Hz, 1H)	H-1, H-36
N^{2}OH		11.69 (s, 1H)	
N^{24}OH		11.79 (s, 1H)	
10-OH		9.34 (br s, 1H)	
34-OH		9.83 (br s, 1H)	

Bastadin 16: Yield 41% as amorphous white solid; ^{1}H NMR (500 MHz, [D$_6$]acetone): δ=11.33 (s, 1H; N^{24}O*H*), 10.42 (s, 1H; N^{2}O*H*), 8.71 (s, 1H; ArO*H*), 8.00 (s, 1H; ArO*H*), 7.70 (t, J=5.8 Hz, 1H; 4-N*H*CO), 7.62 (s, 2H; H-27, H-31), 7.57 (s, 2H; H-8, H-12), 7.41 (t, J=5.9 Hz, 1H; 22-N*H*CO), 7.18 (d, J=1.7 Hz, 1H; H-36), 6.90 (d, J=8.1 Hz, 1H; H-16), 6.76 (dd, J=8.1, 1.8 Hz, 1H; H-17), 6.38 (d, J=1.7 Hz, 1H; H-38), 6.33 (d, J=1.8 Hz, 1H; H-19), 3.92 (s, 2H; H-25), 3.68 (s, 2H; H-1), 3.51–3.47 (m, 2H; H-21), 3.41–3.37 (m, 2H; H-5), 2.88 (t, J=7.1 Hz, H-6), 2.73 ppm (t, J=7.1 Hz, H-20); ^{13}C NMR (125 MHz, [D$_6$]acetone): δ= 165.7, 164.7, 153.7, 153.2, 149.0, 148.7, 147.0, 146.6, 146.2, 144.0, 142.0, 140.1, 135.6, 135.5, 131.9, 131.2, 129.2, 125.3, 119.6, 119.4, 118.3, 115.4, 114.7, 111.0, 42.0, 41.6, 36.1, 35.7, 29.3 ppm; HR-ESI-TOF: m/z[M+Na]$^+$ calcd for $C_{34}H_{27}Br_5N_4O_8$: 1036.7638; found: 1036.7643.

Bastadin 20: Yield 46% as amorphous white solid; for NMR data see Table 2; HR-ESI-TOF: m/z [M+Na]$^+$ calcd for $C_{34}H_{28}Br_4N_4O_8$: 958.8533; found: 958.8519.

Bastadin 21: Yield 55% as amorphous white solid; for NMR data see Table 3; HR-MALDI-FTMS: m/z [M+Na]$^+$ calcd for $C_{34}H_{29}Br_3N_4O_8$: 880.9428; found: 880.9422.

Data for 38: Yield 83% as colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$): δ= 7.69 (d, J=2.0 Hz, 1H; Ar*H*), 7.59 (d, J=1.8 Hz, 1H; Ar*H*), 7.56 (d, J= 6.7 Hz, 2H; Ar*H*), 7.49 (d, J=6.7 Hz, 2H; Ar*H*), 7.43–7.25 (m, 16H; Ar*H*), 7.21–7.19 (m, 2H; Ar*H*), 7.14 (dd, J=8.4, 2.0 Hz, 1H; Ar*H*), 7.11 (d, J=1.9 Hz, 1H; Ar*H*), 6.98 (br t, J=6.4 Hz, 1H; N*H*CO), 6.93 (d, J= 8.3 Hz, 1H; Ar*H*), 6.83 (d, J=1.9 Hz, 1H; Ar*H*), 6.64 (br t, J=6.1 Hz, 1H; N*H*CO), 6.59 (d, J=8.4 Hz, 1H; Ar*H*), 6.55 (d, J=1.8 Hz, 1H; Ar*H*), 5.21 (s, 2H; OC*H*$_2$Ph), 5.19 (br s, 2H; OC*H*$_2$Ph), 5.10 (br s, 2H; OC*H*$_2$Ph), 5.09 (br s, 2H; OC*H*$_2$Ph), 4.83 (dd, J=6.7, 3.4 Hz, 1H; C*H*OH), 3.84 (AB$_q$, J=13 Hz, $\Delta\nu$=22 Hz, 2H; ArC*H*$_2$C=N), 3.81 (s, 2H; ArC*H*$_2$C=N), 3.74–3.69 (m, 1H; C*H*HNHCO), 3.41–3.22 (m, 3H; C*H*$_2$NHCO, CH*H*NHCO), 2.75 (br s, 1H; CHO*H*), 2.65–2.58 ppm (m, 2H; ArC*H*$_2$CH$_2$).

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[25] Hydrogenolysis of the benzyl ethers under previously described conditions (see reference [8b]) for related substrates was, in our hands, complicated by competing reduction of the aryl bromides.

[26] a) Copies of the chromatograms are available as Supporting Information; b) natural material was unavailable for direct comparison. The structure of synthetic product was verified by ^{1}H NMR, HSQC, and HMBC spectra that are available as Supporting Information.

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