Regiocontrolled Synthesis of the Antitumor Antibiotic AT2433-A1

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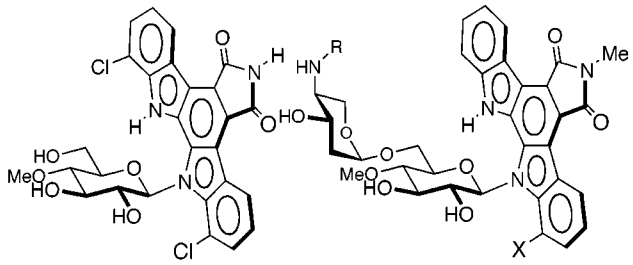
The indolo[2,3-*a*]carbazole glycosides are potent antitumor antibiotics currently undergoing clinical trials for the treatment of numerous types of cancer. AT2433-A1 is the most complex member of this family of compounds possessing a unique disaccharide with a sensitive aminodeoxysugar and an unsymmetric aglycon. The synthesis of this natural product requires a method for glycosylation that sets the stereochemistry of the anomeric center and the regiochemistry of the aglycon. These goals were accomplished by carrying out the Mannich cyclization of a bis-3,4-(3-indolyl)succinimide to give a key class of indoline intermediates that could be glycosylated stereoselectively with complex carbohydrates without hydroxyl protection or activation. The regiochemistry of the Mannich cyclization was precisely controlled by choosing between kinetic or thermodynamic conditions. This strategy culminated in the first synthesis of the antitumor antibiotic AT2433-A1.

I. Introduction

Interest in the indolo[2,3-*a*]carbazole glycosides comes from their potent antineoplastic properties. There are two classes of indolocarbazole glycosides, differing both in structure and in mechanism of action. The staurosporine class is characterized by two bonds between the glycoside and indolocarbazole heterocycle. These fused structures exhibit potent inhibition of protein kinases.[1] In contrast, the rebeccamycin[2] class of indolocarbazole glycosides have a single glycosidic linkage and have shown remarkable activity in the poisoning of DNA topoisomerase I.[3,4] The only clinically used antitumor drugs that selectively target topoisomerase I are irinotecan and topotecan, derivatives of camptothecin. Both camptothecin and the indolocarbazole glycosides have been shown to stabilize the intermediate DNA-topoisomerase I complex, leading to cell death.[5] Currently, rebeccamycin derivatives are in phase II clinical trials for the treatment of a wide range of malignancies including refractory pediatric neuroblastoma, advanced renal cell carcinoma, metastatic or locally recurrent colorectal cancer, and stage IIIB or IV breast cancer.

The excellent antitumor activity of indolocarbazole glycosides has led to a significant synthetic effort in this area, especially in the past 5 years.[6,7] The greatest challenge in the synthesis of the indolocarbazole glycosides is the formation of the *N*-glycosidic bond. There are three challenges associated with glycosylation. First, the nucleophilicity of the indole nitrogen is attenuated by aromaticity. Second, glycosylation must occur stereoselectively. Finally, in cases where the aglycon is unsymmetrical, as in AT2433-A1 and AT2433-A2, the glycosylation reaction must differentiate between the two indole nitrogens.



rebeccamycin

AT2433:

A1 R=Me X=Cl
A2 R=H X=Cl
B1 R=Me X=H
B2 R=H X=H

Unlike other indolocarbazole natural products, AT2433-A1, AT2433-A2, AT2433-B1, and AT2433-B2 possess a unique disaccharide with a sensitive 2-deoxy aminosugar.[8,9] The complexity of these targets requires an efficient method for regioselective glycosylation in the presence of diverse functionality. While rebeccamycin has chlorine atoms at the 1 and 11 positions of the aromatic sector, AT2433 A1 and A2 have chlorine atoms only at the 1 position. Thus, the disaccharide must be joined to the more hindered, less nucleophilic nitrogen atom.

A number of chemical approaches are available for the glycosylation of indoles and indolocarbazoles,[4,10−20] but

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all of these approaches require full protection of the carbohydrate hydroxyl groups and the imide nitrogen. In cases where the indolocarbazole aglycon is unsymmetrical, one of the indole nitrogens must also be protected.

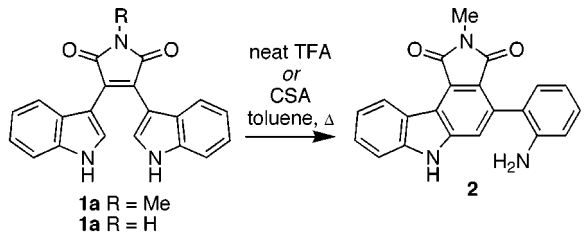
Mannich dimerization of indoles[21] is an important strategy for the synthesis of indolo[2,3-*a*]carbazole glycosides because the dimers can be glycosylated stereoselectively using unprotected, unactivated carbohydrates.[22−27] This method is even more efficient when the Mannich dimerization occurs intramolecularly as part of a cyclization reaction. When one indole is deactivated by a chlorine substituent, the regiochemistry can be controlled by carrying out the cyclization under kinetic or thermodynamic conditions as recently demonstrated in the synthesis of the antifungal compound tjipanazole F1.[28,29] The application of this strategy to AT2433-A1 and AT2433-A2 is complicated by the overall complexity of the target. Despite initial uncertainties about the generality of this strategy it has led to the first synthesis of AT2433-A1.

II. Mannich Studies

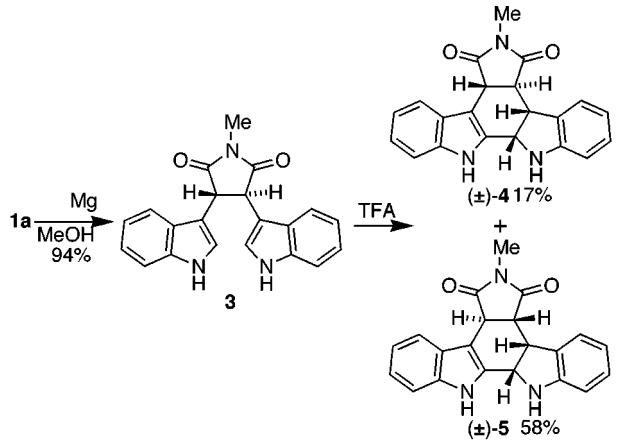
Indolines, such as **4** and **5**, are readily prepared by Mannich cyclization of bis-3,4-(3-indolyl)succinimides.[21] The indoline nitrogen undergoes facile glycosylation without requiring hydroxyl protection or anomeric activation to give good yields of glycosylated products. The *N*-glycosides obtained by this method possess the β anomeric stereochemistry found in the indolocarbazole glycoside natural products. Aromatization of the indolylindoline-*N*-glycosides can be easily effected with mild oxidizing agents such as DDQ[30] or, in some cases, light.[31]

N-Methylarcyriarubin A (**1a**) is readily available through literature procedures.[32,33] Attempted Mannich

Scheme 1



Scheme 2



cyclization of **1a** is accompanied by an undesired opening of the indoline ring to give carbazole **2**, unless the indoline intermediate is oxidized in situ.[34] This same rearrangement was observed by Steglich during attempted cyclization of **1a** with CSA in refluxing toluene (Scheme 1).[32]

Aromatization of the bisindolylmaleimide being too facile, cyclization of the *dl*-succinimide **3** was investigated. This compound was readily prepared as a 24:1 mixture (^{1}H NMR) of *dl*/*meso* isomers by conjugate reduction with magnesium in refluxing methanol. Mannich cyclization of the *dl*-succinimide was sluggish relative to intermolecular Mannich dimerization of 3-substituted indoles, provided two hexacyclic products, (±)-**4** and (±)-**5**, after 24 h in neat TFA (Scheme 2).

The relative stereochemistry of the two products was assigned on the basis of double pulsed field gradient spin−echo-NOEs (DPFGSE-NOEs). Irradiation of H4b in diastereomer **4** produced moderate enhancements to the signals from protons H7a and H12b, but not H4c, suggesting an anti-anti-cis stereochemistry. In contrast, irradiation of H4b in diastereomer **5** led to moderate enhancements of the signals from protons H4c and H12b, but not H7a, suggesting an anti-cis-cis stereochemistry.

These compounds were unstable in solution, rapidly undergoing oxidation in EtOAc/hexane mixtures, making their purification difficult. The instability and difficulty in working with mixtures of products led us to further investigate this cyclization of the meso succinimide, **6a** (Figure 1).

The corresponding *cis*-bisindolylsuccinimide **6b** cyclizes efficiently in neat trifluoroacetic acid (TFA) in less than 1 h. In contrast to the cyclization of the anti-bisindolyl-

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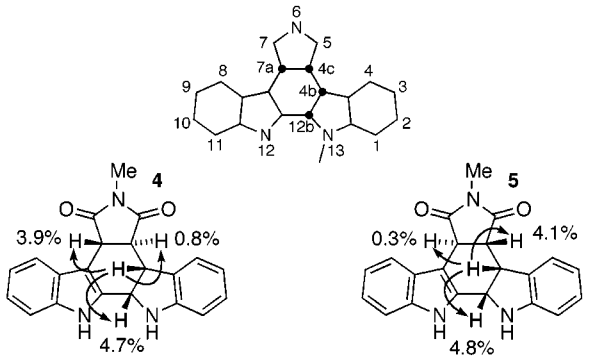
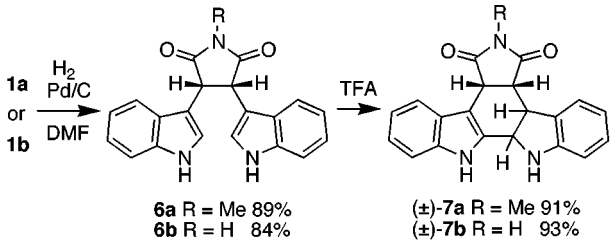


Figure 1. DPFGSE-NOEs (t_{mix}= 1 s) establish the stereochemistry of the indolylindolines (±)-**4** and (±)-**5**.

Scheme 3



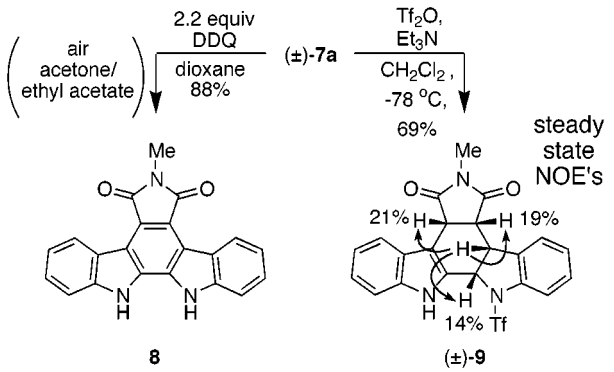
succinimide, the product of this reaction is a single racemic diastereomer. This cyclization works the same for free imide **1b**[35] as well, the methyl group not being required. Cyclization product (±)-**7a** also undergoes oxidation in solution, but more slowly than the trans isomers. During attempts to recrystallize from acetone/EtOAc, the fully aromatic indolocarbazole **8** crystallizes from solution as it is formed. The same product is formed by oxidation with 2 equiv of DDQ in dioxane. Indolocarbazole **8** is identical to material prepared by Gribble using a twin Fisher indole cyclization. Indoline (±)-**7a** may be conveniently precipitated from methanol at room temperature without oxidation (Scheme 3).

The relative stereochemistry of cyclization product (±)-**7a** was assigned on the basis of steady-state NOEs. Initial attempts were hampered by overlapping signals in the ^{1}H NMR spectrum, but conversion to the triflamide **9** spread the NMR signals over a larger range, making protons easier to irradiate selectively. Irradiation of H4b produced sizable enhancements to the signals from protons H7a, H12b, and H4c, suggesting a cis-syn-cis stereochemistry (Scheme 4).

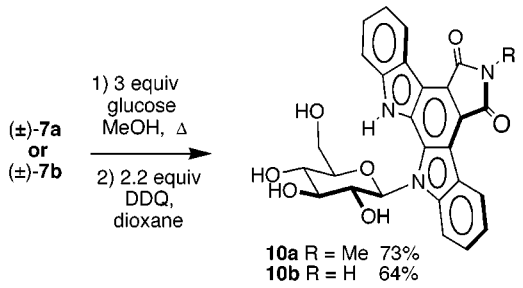
III. Carbohydrate Capture by Indolines

The glycosylation of indolines was first studied by Praeobrazhenskaya.[25] Later, this method of synthesizing glycosylated indoles was extended and optimized for the 2,2′-biindole system.[27] Gratifyingly, treatment of (±)-**7a** under these optimized conditions (three equiv of D-glucose in refluxing methanol) led to the formation of *N*-glycosylated products in good yield. Because the indoline is racemic and the sugar is a single enantiomer, two diastereomeric products are formed. Convergent oxidation of the two diastereomers with DDQ gives a single product, a fully functionalized indolocarbazole β-glycoside. Importantly, these reactions also proceed in good yield without protection of the imide nitrogen. This particular synthetic route stands out because all other methods of glycosylation require imide protection (Scheme 5).

Scheme 4



Scheme 5



Melnik has shown that glycosylation of indolines proceeds smoothly with the disaccharide lactose.[36,37] To explore the potential of this coupling strategy for the synthesis of AT2433, aglycon **7a** was condensed with a series of mono-, di-, and trisaccharides. Good glycosylation yields were realized for all sugars tested. While most of these indolocarbazole glycosides have disappointing solubility, the *N*-melibioside **13** was somewhat soluble in water (Table 1).

IV. Synthesis of AT2433-B1

With a viable route toward indolocarbazole glycosides bearing complex carbohydrates, a synthesis of AT2433-B1 was undertaken. The disaccharide of AT2433-B1 consists of a glucose and an aminosugar subunit, 2,4-dideoxy-4-amino-L-xylose. Derivatives of this aminosugar are present in the enediyne antitumor antibiotics calicheamicin and esperamicin.[26,38,39] Several known routes exist to 2,4-dideoxy-4-amino-xylosides,[40−44] but the method of Roush[45] was adopted for this synthesis based upon our

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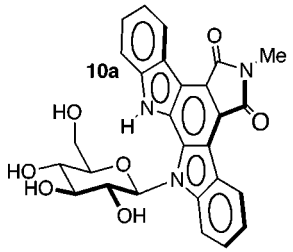
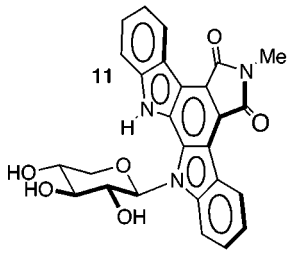
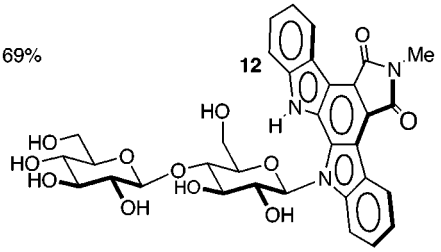
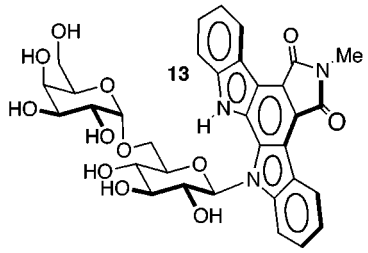
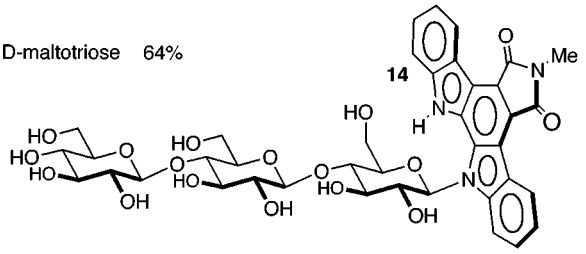
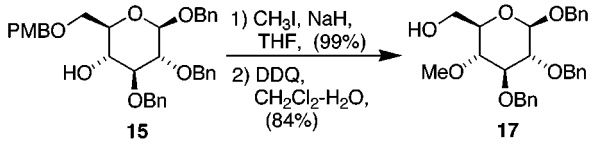
Table 1. Glycosylation/Oxidation of (±)-7a (Scheme 5)

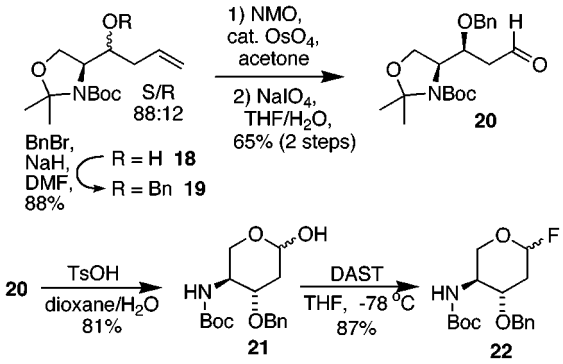
Entry	Sugar	Yield[a]	Product
1	D-Glucose	73%	 **10a**
2	D-Xylose	63%	 **11**
3	D-maltose	69%	 **12**
4	D-melibiose[b]	47%	 **13**
5	D-maltotriose	64%	 **14**

previous experience.[46] While 4-*O*-methylglucose has been previously prepared,[47] a strategy was needed for differential protection of the hydroxyl groups at the 6 position, 4 position, and positions 1−3. A suitable intermediate was prepared using the method of Samuelsson involving reductive opening of a 4,6-*p*-methoxybenzylidene acetal to give glucoside **15**.[48] Methylation of the secondary alcohol using methyl iodide and sodium hydride provided the 4′-*O*-methyl derivative, **16**. Selective removal of the 6′ PMB protecting group under oxidative conditions led to glucoside **17**, ready for glycosylation at the free 6′-OH (Scheme 6).

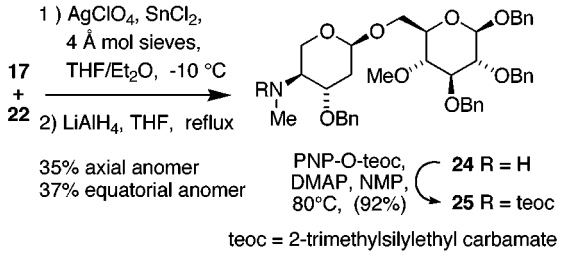
Scheme 6



Scheme 7



Scheme 8



Following the procedure of Roush and Hunt, homoallyl alcohol **18** was prepared from *R*-Garner's aldehyde using an allyl dioxaborolane derived from *R*,*R*-diisopropyl tartrate.[45] Homoallyl alcohol **18** was formed as an 88:12 mixture of diastereomers differing in stereochemistry at the alcohol stereocenter. The mixture of diastereomers was then benzylated, and the latent aldehyde was revealed by dihydroxylation of the double bond with catalytic osmium tetroxide followed by cleavage of the diol with sodium metaperiodate. At the aldehyde stage the undesired diastereomer was separated chromatographically. Selective removal of the acetonide[49] led to the lactol **21**, which was then converted to the glycosyl fluoride by the action of DAST (Scheme 7).

Coupling of the primary alcohol **17** with glycosyl fluoride **22** was performed under Mukaiyama−Nicolaou[40,50] conditions (Scheme 8). Within 15 min, the equatorial and axial glycosides are formed in a 2:1 ratio, consistent with recent results of Deslongshamps[51] and Woerpel.[52] However, within 1 h, equilibration equalizes

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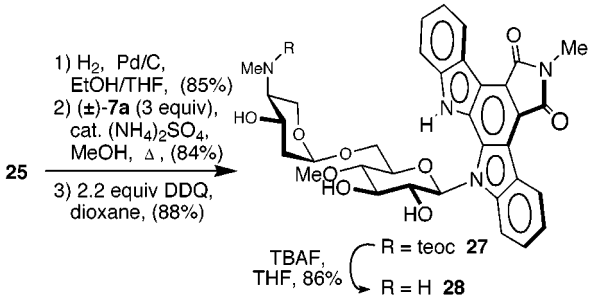
Scheme 9



the ratio of α and *β* anomers and a yield of 80% is obtained. Unfortunately, attempts improve the ratio of axial glycoside to equatorial glycoside by equilibrating under long reaction times led to decomposition.

The equatorial and axial anomers were inseparable until the *N*-Boc group was reduced to the corresponding methylamino group. Reprotection of the methylamino group as the Boc derivative led to problems during the consummate deprotection due to the sensitivity of the 2-deoxypyranoside linkage.[46] Instead, the methylamino group of disaccharide **24** was then protected as the *N*-trimethylsilylethyl carbamate (Teoc) derivative.

With the disaccharide in hand, elaboration to AT2433-B1 was undertaken. Debenzylation with palladium and hydrogen provided the deprotected disaccharide **26** (not shown). Refluxing of lactol **26** with 3 equiv of (±)-**7a** in methanol for 72 h gave 84% yield of glycosylated product. Oxidative aromatization of the mixture of diastereomers with DDQ led to the protected natural product **27** in 80% yield. Finally, deprotection of the Teoc carbamate with TBAF provided AT2433-B1 in good yield (Scheme 9).

V. Mannich Cyclization Studies on Chlorinated Substrates

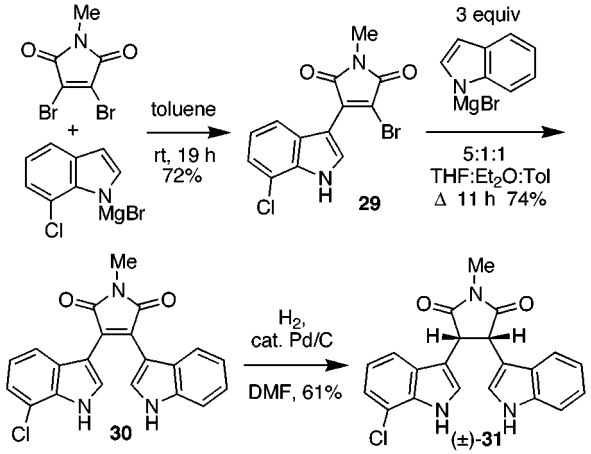
The synthesis of the chlorinated indolocarbazoles presents a more dramatic problem of selectivity. AT2433-A1 and A2 both possess a chlorine atom at the 1-position of the indolocarbazole. Building on previous work with the tjipanazole natural products, we envisioned that the electron withdrawing chlorine atom would allow selective Mannich cyclization of an unsymmetrical bis-indole. Toward this end, an unsymmetrical bisindolylmaleimide was synthesized.

The Grignard anion of 7-chloroindole was added to 1 equiv of *N*-methyl dibromomaleimide to provide the monoaddition product **29**. The second addition of indolylmagnesium bromide required more vigorous conditions, but also proceeded smoothly (Scheme 10).[33]

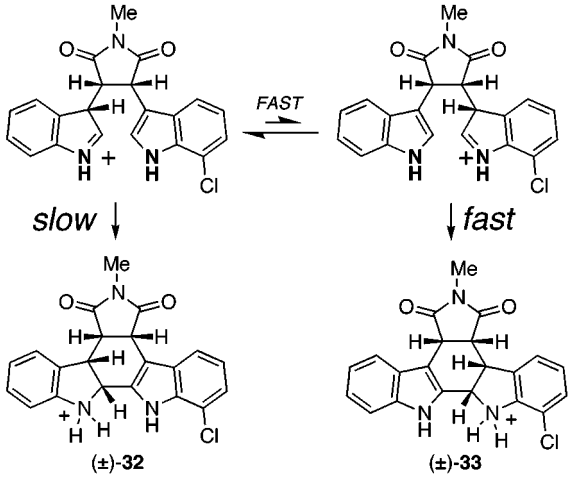
As expected, hydrogenation of the tetrasubstituted maleimide double bond proved to be problematic. The rate of hydrogenation of tetrasubstituted double bonds known to be slow while hydrogenolysis of aryl halides is facile.[53] Heterogeneous ruthenium and iridium catalysts proved to be unreactive, whereas rhodium on carbon or alumina gave mixtures of the *meso* and *dl* succinimides. In contrast, hydrogenation with palladium on carbon in DMF afforded a 60% yield of the meso succinimide, the balance of the material having been de-chlorinated. Attempts to slow hydrogenolysis of the aryl chloride bond with less polar solvents (THF/MeOH mixtures) only slowed the reaction, without changing slowing the hydrogenolysis side reaction.

(53) Rylander, P. N. *Hydrogenation Methods*; Academic Press: San Diego, 1985.

Scheme 10



Scheme 11



Two products are possible in the Mannich cyclization of unsymmetrical bis-indoles such as (±)-**31**: the chloroindole regioisomer (±)-**32** and the chloroindoline regioisomer (±)-**33**. In previous studies of simple tethered indoles,[29] it was demonstrated that Mannich cyclization was reversible in neat trifluoroacetic acid, but essentially irreversible with camphorsulfonic acid in chloroform. Mannich cyclization of the chlorinated bisindolylsuccinimide (±)-**31** with methanesulfonic acid in chloroform provided isomer (±)-**33** with high regio- and stereoselectivity. The regioselectivity is readily rationalized based on classical Curtin-Hammett conditions (Scheme 11). The 7-chloro group in bis-indole **31** is expected to exert a powerful inductive effect during the key cyclization event and probably makes the less stable indolenium ion cyclize faster (Scheme 11). However, the resulting product (±)-**33**, is probably destabilized by the same inductive effect, making it less stable than the alternative product (±)-**32**. A dramatic reversal in regiochemistry is achieved by carrying out the cyclization in refluxing trifluoroacetic acid. Under these conditions, the more stable product (±)-**32** is obtained with excellent selectivity, although the yield is somewhat diminished due to decomposition (Table 2).

The stereochemistry of indolylindolines (±)-**32** and (±)-**33** were verified using NOE experiments. Significant

Table 2. Mannich Cyclization of Unsymmetrical Bis-Indolylsuccinimide (±)-31

conditions	time (h)	ratio (**32**:**33**)	yield (%)
MSA (5 equiv), $CHCl_3$	2	<1:20	94
MSA (5 equiv), $CHCl_3$	24	<1:20	93
TFA (neat)	.25	1:9	90
TFA (neat)	24	1:5	90
TFA (neat)	72	1:3	93
TFA (neat), reflux	2	4:1	90
TFA (neat), reflux	12	>20:1	82

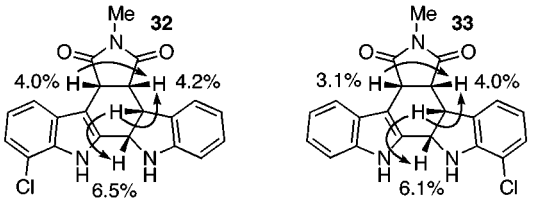
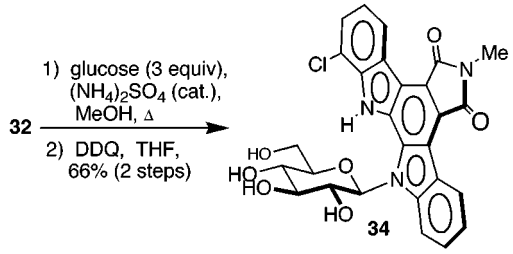


Figure 2. DPFGSE-NOEs (t_{mix} = 1 s) establish the stereochemistry of the indolylindolines (±)-**32** and (±)-**33**.

Scheme 12



NOE enhancements were seen upon irradiation of the same protons as in the nonchlorinated systems.

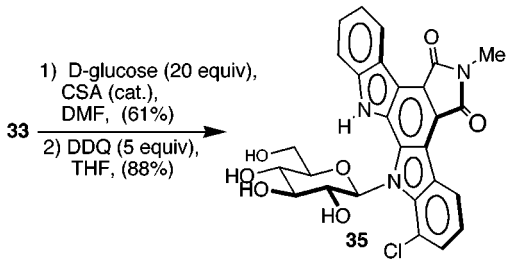
As with Mannich products (±)-**4** and (±)-**5**, the relative stereochemistry of the hexacyclic products (±)-**32** and (±)-**33** was assigned on the basis of double pulsed field gradient spin−echo-NOEs (DPFGSE-NOEs). Irradiation of H4b in diastereomer produced moderate enhancements to the signals from protons H4c and H12b, confirming a syn relationship between protons H4b, H4c, and H12b. Proton H7c is also on the same face since irradiation leads to enhancement of H4c (Figure 2).

VI. Carbohydrate Capture by Chlorinated Substrates

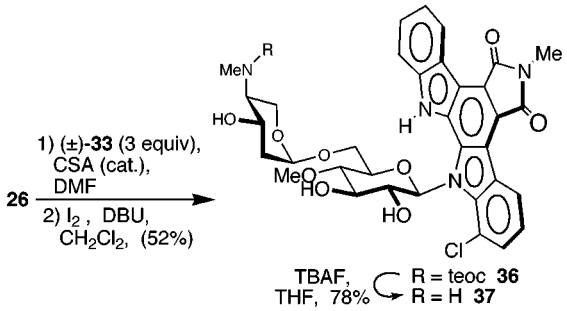
With both regioisomers available using Mannich chemistry, we began to elaborate the chlorinated indolines (±)-**32** and (±)-**33** into indolocarbazole glycosides. Mannich cyclization product (±)-**32** showed similar reactivity to the non-chlorinated aglycon, (±)-**7a**. Glycosylation and oxidation under standard conditions provided the fully functionalized, regioselectively chlorinated indolocarbazole glycoside **34** in 66% overall yield (Scheme 12).

Elaboration of the racemic indolylindoline (±)-**33** proved much more challenging. The addition of the sterically encumbering, electron withdrawing chloride atom ortho to the reactive amine nitrogen decimated the reactivity of the center. No product was observed using the standard glycosylation conditions: refluxing methanol, 3 equiv of D-glucose, and catalytic $(NH_4)_2SO_4$. After some experimentation, alternative conditions for the glycosylation were found. Glycosylation could be effected with 0.33 equiv of *d*-10-camphorsulfonic acid (CSA) in DMF at room temperature using 3 equiv D-glucose, albeit in 31% yield. Both enantiomers of the aglycon react and the

Scheme 13



Scheme 14



β-glucoside is obtained as a 1:1 mixture of diastereomers. By using 20 equiv of D-glucose the yield could be increased to 61%. When the product is resubmitted to the reaction conditions (0.33 equiv CSA in wet DMF) it is observed to hydrolyze, suggesting that the yield is ultimately limited by the thermodynamic stability of the product. Glycosylation of the non-chlorinated aglycon (±)-**7a** with 3 equiv of D-glucose gave 85% yield under the same conditions, speaking to the detrimental effect of the chlorine atom.

The presence of the chlorine substituent peri to the glucosyl moiety makes the oxidative aromatization laggardly, but the combination of excess DDQ (5 equiv) and long reaction times (5 days) provided reasonable yields of the fully aromatic chlorinated indolocarbazole **35**. With the ability to glycosylate and aromatize aglycon **33**, attention was focused on elaboration into AT2433-A1 (Scheme 13).

VII. Synthesis of AT2433-A1

The aminodisaccharide **26**, used in the synthesis of AT2433-B1, was condensed with 3 equiv of aglycon (±)-**33** in 35% yield. Both starting materials could be recovered unchanged and recycled. After two more cycles, an overall yield of 75% was obtained for the diastereomeric mixture of glycosylated products. Surprisingly, oxidative aromatization again proved very difficult. After 5 days with 5 equiv of DDQ only an 8% yield of the oxidized product was realized. This demanded a search for other conditions that could effect this transformation. Ultimately, dehydrohalogenation could be accomplished with DBU and iodine in methylene chloride. While this procedure gave lower yields than DDQ in other cases, here a 52% yield was obtained in a much shorter reaction time (4 h). Finally, deprotection of the teoc group with TBAF provided material that matched AT2433-A1 (Scheme 14).

This work has capitalized upon a Mannich cyclization/glycosylation route for the synthesis of indolocarbazole glycosides. The pentacyclic indoline intermediates prepared by Mannich cyclization are readily glycosylated

with unactivated sugars without protection of the sugar hydroxyl groups or the imide moiety of the aglycon. The regiochemistry of the Mannich cyclization can be precisely controlled using kinetic or thermodynamic conditions. This strategy has culminated in the first synthesis of the antitumor antibiotic AT2433-A1.

Experimental Section

General experimental procedures may be found in the Supporting Information of another publication.[54]

1-Methyl-*trans*-3,4-bis(3-indolyl)-2,5-pyrrolidinedione, 3. Bisindolylmaleimide **1a** (350 mg, 1.02 mmol) was suspended in 10 mL of dry MeOH. Mg turnings (450 mg, 18.5 mmol) were then added, and the reaction was heated to reflux. After 20 min, the reaction was cooled to room temperature and poured into 50 mL of 1 N HCl. The reaction was then extracted with EtOAc (3×), and the extracts were dried (Na_2SO_4) and concentrated. Purification by silica gel chromatography (50% EtOAc/hexanes) provided 325 mg (93%) of the *trans*-bisindolylsuccinimide **3** as a buff foam.

3: mp 196−198 °C (EtOAc); $R_f = 0.14$ (40% EtOAc/hexanes); IR (KBr) 3388, 3069, 2900, 1779, 1694 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz) δ 11.08 (s, 2H), 7.40−7.44 (m, 4H), 7.11 (td, 2H, $J = 7.9$, 0.8 Hz), 6.98 (td, 2H, $J = 8.0$, 0.8 Hz), 4.62 (s, 2H), 3.10 (s, 3H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 177.1, 136.5, 126.3, 124.1, 121.3, 118.8, 118.6, 111.7, 109.8, 45.9, 25.0; MS (CI+) 343; HRMS (CI+) calcd for $C_{21}H_{17}N_3O_2$ 343.1320, found 343.1307. Anal. Calcd for $C_{21}H_{17}N_3O_2$: C, 73.45; H, 4.99; N, 12.24. Found: C, 73.39; H, 5.03; N, 12.12.

(4b*R*,4c*S*,7a*R*,12b*S*)-*rel*-6-Methyl-4b,4c,6,7,7a,12,12b,13-octahydroindolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione (±)-4 and (4b*R*,4c*R*,7a*S*,12b*S*)-*rel*-6-Methyl-4b,4c,6,7,-7a,12,12b,13-octahydroindolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione (±)-5. *trans*-Bisindolylsuccinimide **3** (536 mg, 0.326 mmol) was dissolved in 6 mL (78 mmol) of TFA and protected from light with aluminum foil. After 26 h, the reaction mixture was poured into 200 mL of 1 N NaOH and extracted with EtOAc (3×). The extracts were then dried (Na_2SO_4) and concentrated. Purification by silica gel chromatography provided 145 mg (27%) of the anti-anti-syn indoline (±)-**4** and 318 mg (59%) of the anti-syn-syn indoline (±)-**5**. Both compounds are off-white foams which quickly undergo oxidation in EtOAc or acetone solution.

(±)-4: mp 228−230 °C (acetone); $R_f = 0.59$ (50% EtOAc/hexanes); IR (KBr) 3385, 3268, 3181, 2902, 1776, 1654 cm^{-1}; ^1H NMR (acetone-d_6, 500 MHz) δ 10.23 (s, 1H), 8.43 (d, 1H, $J = 8.0$ Hz), 7.78 (d, 1H, $J = 7.5$ Hz), 7.38 (d, 1H, $J = 8.0$ Hz), 6.98−7.12 (m, 3H), 6.72 (t, 1H, $J = 7.4$ Hz), 6.62 (d, 1H, $J = 7.8$ Hz), 5.41 (s, 1H), 5.12 (bd, 1H, $J = 8.4$ Hz), 4.27 (d, 1H, $J = 10.7$ Hz), 4.01 (dd, 1H, $J = 11.6$, 8.5 Hz), 3.19 (t, 1H, $J = 11.1$ Hz); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 175.7, 174.4, 150.7, 135.8, 135.4, 128.5, 128.0, 127.8, 126.0, 124.3, 121.5, 121.2, 119.0, 117.5, 111.3, 109.1, 106.0, 56.0, 46.4, 43.3, 41.6, 23.9; MS (CI+) 343; HRMS (CI+) calcd for $C_{21}H_{17}N_3O_2$ 343.1320, found 343.1309. Anal. Calcd for $C_{21}H_{17}N_3O_2$: C, 73.45; H, 4.99; N, 12.24. Found: C, 73.33; H, 5.08; N, 12.21.

(±)-5: mp 196−198 °C (MeOH); $R_f = 0.34$ (50% EtOAc/hexanes); IR (KBr) 3382, 3043, 2902, 1773, 1603 cm^{-1}; ^1H NMR (acetone-d_6, 500 MHz) δ 11.10 (s, 1H), 8.13 (d, 1H, $J = 8.0$ Hz), 7.33 (d, 1H, $J = 8.0$ Hz), 7.06 (t, 1H, $J = 7.7$ Hz), 6.98 (t, 1H, $J = 7.7$ Hz), 6.86−6.93 (m, 2H), 6.54 (t, 1H, $J = 7.4$ Hz), 6.51 (d, 1H, $J = 7.8$ Hz), 5.80 (s, 1H), 5.15 (d, 1H, $J = 8.9$ Hz), 4.40 (dd, 1H, $J = 8.8$, 2.8 Hz), 3.86 (d, 1H, $J = 10.8$ Hz), 3.67 (dd, 1H, $J = 10.8$, 3.1 Hz), 2.94 (s, 3H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 175.3, 174.8, 152.3, 137.6, 135.8, 128.1, 125.3, 124.4, 124.3, 121.3, 121.2, 119.0, 117.6, 111.3, 109.7, 106.6, 56.5, 47.7, 39.7, 30.4, 24.2; MS (CI+) 343; HRMS (CI+) calcd for $C_{21}H_{17}N_3O_2$ 343.1320, found 343.1326. Anal. Calcd for $C_{21}H_{17}N_3O_2$: C, 73.45; H, 4.99; N, 12.24. Found: C, 73.20; H, 4.99; N, 12.13.

(54) Gilbert, E. J.; Chisholm, J. D.; Van Vranken, D. L. *J. Org. Chem.* **1999**, *64*, 5670.

1-Methyl-*cis*-3,4-bis(3-indolyl)-2,5-pyrrolidinedione 6a. Bisindolylmaleimide **1a** (1.056 g, 3.09 mmol) was dissolved in 20 mL of DMF. 10% Palladium on carbon (0.411 g, 0.38 mmol) was then added, and the reaction mixture was shaken in a parr shaker under 50 psi of hydrogen. After 13 h, the reaction was filtered through Celite with ethanol and concentrated in vacuo (the DMF being removed by distillation under hi-vac). The residue was purified using silica gel chromatography (50% EtOAc/50% hexanes) to give 0.980 g (93%) of *cis*-succinimide **6a** as an orange foam.

6a: mp 250−252 °C (crystals from EtOAc); $R_f = 0.22$ in 50% EtOAc/hexanes; IR (film) 3402, 1692 cm^{-1}; ^1H NMR (acetone-d_6, 500 MHz) δ 9.81 (s, 2H), 7.40 (d, 2H, $J = 7.6$ Hz), 7.14 (d, 2H, $J = 8.0$ Hz), 6.93 (t, 2H, $J = 8.1$ Hz), 6.87 (m, 4H), 5.00 (s, 2H), 3.17 (s, 3H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 178.3, 135.4, 126.9, 124.5, 120.7, 118.4, 118.3, 111.3, 108.1, 45.5, 24.8; MS (CI+) 343; HRMS (CI+) calcd for $C_{21}H_{17}N_3O_2$ 343.1320, found 343.1318. Anal. Calcd for $C_{21}H_{17}N_3O_2$: C, 73.45; H, 4.99; N, 12.24. Found: C, 73.33; H, 5.12; N, 12.02.

(4b*R*,4c*R*,7a*R*,12b*S*)-*rel*-6-Methyl-4b,4c,6,7,7a,12,12b,-13-octahydroindolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione (±)-7a. *cis*-*N*-Methyl-2,3-bis(3-indolyl)succinimide **6a** (0.836 g, 2.43 mmol) was dissolved in 20 mL of trifluoroacetic acid. After 30 min, the TFA was removed in vacuo and the reaction mixture taken up in 50 mL of EtOAc. The reaction mixture was then poured into 150 mL of saturated aqueous $NaHCO_3$. The layers were separated, and the aqueous layerwas extracted with EtOAc (3 × 50 mL). The combined organic layers were then dried (Na_2SO_4) and concentrated. Purification by silica gel chromatography (40% EtOAc/hexanes) afforded (±)-**7a** (0.760 g, 91% yield) as an orange foam.

(±)-7a: mp 178−182 °C; $R_f = 0.36$ (40% EtOAc/hexanes); IR (film) 3368, 1607 cm^{-1}; ^1H NMR (CD_3CN, 500 MHz) δ 9.19 (s, 1H), 7.82 (d, 1H, $J = 7.6$ Hz), 7.30 (d, 1H, $J = 8.0$ Hz), 7.16 (d, 1H, $J = 7.6$ Hz), 7.10 (t, 1H, $J = 7.6$ Hz), 7.02 (t, 1H, $J = 7.6$ Hz), 6.94 (t, 1H, $J = 7.6$ Hz), 6.67 (t, 1H, $J = 7.6$, Hz), 6.56 (d, 1H, $J = 7.6$ Hz), 4.97 (s, 1H), 4.80 (d, 1H, $J = 7.6$ Hz), 4.30 (d, 1H, $J = 7.2$ Hz), 4.20 (d, 1H, $J = 7.6$ Hz), 4.01 (dd, 1H, $J = 7.6$, 2.0 Hz), 2.82 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 179.3, 177.9, 150.6, 137.4, 135.2, 130.1, 129.0, 126.8, 123.6, 123.3, 121.4, 120.4, 119.6, 111.9, 110.8, 106.4, 54.5, 41.1, 40.7, 38.8, 25.1; MS (CI+) 343; HRMS (CI+) calcd for $C_{21}H_{17}N_3O_2$ 343.1321, found 343.1320. Anal. Calcd for $C_{21}H_{17}N_3O_2$: C, 73.45; H, 4.99; N, 12.24. Found: C, 73.51; H, 5.04; N, 12.27.

(4b*R*,4c*R*,7a*R*,12b*S*)-*rel*-4b,4c,6,7,7a,12,12b,13-octahydroindolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione (±)-7b. Bisindolylsuccinimide **6b** (962 mg, 2.92 mmol) was suspended in 30 mL of $CHCl_3$. Trifluoroacetic acid (2.25 mL, 29.2 mmol) was then added. After 1 h, the reaction was quenched by pouring it into 100 mL of 1 N NaOH. The mixture was then extracted with EtOAc (3×). The combined extracts were then dried (Na_2SO_4) and concentrated. Purification by silica gel chromatography (45% EtOAc/hexanes) provided pure (±)-**7b** (916 mg, 95% yield) as an off-white solid.

(±)-7b: mp 300−302 °C (EtOAc); $R_f = 0.28$ (50% EtOAc/hexanes); IR (KBr) 3418, 3351, 3284, 3056, 2908, 1706, 1606 cm^{-1}; ^1H NMR (acetone-d_6, 500 MHz) δ 10.14 (s, 1H), 9.96 (bs, 1H), 7.88 (d, 1H, $J = 8.0$ Hz), 7.29 (d, 1H, $J = 8.4$ Hz), 7.25 (d, 1H, $J = 7.6$ Hz), 7.64 (dt, 1H, $J = 7.6$, 1.0 Hz), 6.99 (dt, 1H, $J = 8.0$, 0.8 Hz), 6.90 (t, 1H, $J = 7.6$ Hz), 6.64 (t, 1H, $J = 7.6$ Hz), 6.53 (d, 1H, $J = 7.6$ Hz), 5.50 (bs, 1H), 4.93 (d, 1H, $J = 8.0$ Hz), 4.34 (m, 1H), 4.31 (dd, 1H, $J = 7.5$, 2.9 Hz), 4.22 (dd, 1H, $J = 7.5$, 1.2 Hz); ^{13}C NMR (acetone-d_6, 125 MHz) δ 179.7, 177.8, 150.8, 137.7, 135.3, 129.9, 128.7, 127.1, 123.3, 122.9, 121.6, 120.1, 119.3, 111.7, 110.6, 106.3, 54.4, 42.6, 40.5, 40.3; MS (CI+) 329; HRMS (CI+) calcd for $C_{20}H_{15}N_3O_2$ 329.1164, found 329.1160. Anal. Calcd for $C_{20}H_{15}N_3O_2$: C, 72.94; H, 4.59; N, 12.76. Found: C, 72.79; H, 4.70; N, 12.58.

1-Trifluoromethanesulfonyl-6-methyl-4b,4c,6,7,7a,12,-12b,13-octahydroindolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione (±)-9. Aglycon indolylindoline (±)-**7a** (117 mg, 0.341 mmol) was dissolved in 10 mL of dry CH_2Cl_2. Triethylamine (150 μL, 1.08 mmol) was added, and the reaction was cooled to −78 °C in a dry ice/acetone bath. Triflic anhydride (125 μL, 0.750 mmol) was then added. After 1 h, the reaction was

quenched with 5 mL of saturated aqueous $NaHCO_3$ and poured into 5 mL of CH_2Cl_2. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were dried (Na_2SO_4) and concentrated in vacuo. Purification via silica gel chromatography (30% EtOAc/hexanes) gave 105 mg (69%) of (±)-**9** as a white foam.

(±)-9: mp 262−264 °C (CH_3CN); R_f = 0.28 (30% EtOAc/hexanes); IR (KBr) 3359, 3059, 2945, 1700 cm^{-1}; ^1H NMR (acetone-d_6, 500 MHz) δ 9.33 (s, 1H), 7.85 (d, 1H, J = 8.0 Hz), 7.44 (m, 1H), 7.42 (d, 1H, J = 6.3 Hz), 7.39 (m, 1H), 7.37 (m, 2H), 7.24 (t, 1H, J = 1.0 Hz), 7.23 (t, 1H, J = 2.2 Hz), 7.15 (dt, 1H, J = 1.2, 7.2 Hz), 7.05 (dt, 1H, J = 7.8, 0.8 Hz), 5.76 (d, 1H, J = 7.5 Hz), 4.75 (d, 1H, J = 7.4 Hz), 4.27 (dd, 1H, J = 7.6, 1.2 Hz), 4.14 (dd, 1H, J = 2.0, 7.6 Hz), 2.83 (s, 3H); ^{13}C NMR (acetone-d_6, 125 MHz) δ 178.1, 177.2, 138.4, 138.2, 134.7, 130.1, 129.3, 128.0, 126.4, 125.0, 124.3, 121.8, 120.9, 117.6, 112.6, 112.5, 108.5, 61.1, 40.3, 40.1, 38.0, 25.3; MS (CI+) 475; HRMS (CI+) calcd for $C_{22}H_{16}N_3O_4SF_3$ 475.0813, found 475.0806. Anal. Calcd for $C_{22}H_{16}N_3O_4SF_3$: C, 55.57; H, 3.39; N, 8.84. Found: C, 55.65; H, 3.37; N, 8.77.

6-Methyl-12-[β-D-glucopyranosyl]-6,7,12,13-tetrahydroindolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione (+)-10a. (±)-**7a** (101 mg, 0.292 mmol) was dissolved in 3 mL of methanol. α-D-Glucose (158 mg, 0.876 mmol) was then added, and the reaction mixture was heated to reflux. After 60 h, the reaction mixture was allowed to cool to room temperature and purified by silica gel chromatography (9% MeOH/$CHCl_3$) to give a 1:1 mixture of diastereomers by ^1H NMR (0.128 g, 87%). This was dissolved in 2 mL of 1,4-dioxane, and DDQ (127 mg, 0.56 mmol) was added. After 24 h, the reaction mixture was taken up in 40 mL of EtOAc and washed with saturated $NaHCO_3$ solution (3 × 40 mL). The organic layer was then dried (Na_2SO_4) and concentrated. Purification using silica gel chromatography (3% MeOH/EtOAc) gave (±)-**10a** (107 mg, 84%) as an orange solid.

(+)-10a: mp 331 °C dec; $[\alpha]_D$ +198.5 (*c* 0.90, THF); R_f = 0.38 (5% MeOH/EtOAc); IR (film) 3341, 2990, 1688 cm^{-1}; ^1H NMR (acetone-d_6, 500 MHz) δ 11.30 (s, 1H), 9.08 (d, 1H, J = 7.6), 8.84 (d, 1H, J = 8.0), 7.79 (d, 1H, J = 8.3), 7.51 (d, 1H, J = 8.3), 7.48 (t, 1H, J = 7.7), 7.36 (t, 1H, J = 8.2), 7.27 (t, 1H, J = 7.6), 7.22 (t, 1H, J = 7.6), 6.30 (d, 1H, J = 9.2), 5.11 (t, 1H, J = 3.7), 4.77 (s, 1H), 4.66 (s, 1H), 4.48 (d, 1H, J = 5.2), 4.38 (dd, 1H, J = 9.6, 3.6), 4.08−4.11 (m, 3H), 3.90−3.94 (m, 2H), 2.79 (s, 3H); ^{13}C NMR (acetone-d_6, 125 MHz) δ 170.4, 170.3, 143.2, 142.1, 130.8, 129.2, 127.6, 125.8, 125.4, 122.7, 122.6, 121.4, 121.1,121.0, 119.7, 119.1, 118.7, 112.6, 112.5, 111.8, 86.1, 80.1, 78.2, 74.6, 69.0, 60.1, 23.5; MS (FAB+) 517, 501, 339; HRMS (FAB+) calcd for $C_{27}H_{23}N_3O_7$ 501.1536, found 501.1522. Anal. Calcd for $C_{27}H_{23}N_3O_7 + H_2O$: C, 62.42; H, 4.85; N, 8.09. Found: C, 62.46; H, 4.84; N, 8.03.

12-[β-D-glucopyranosyl]-6,7,12,13-tetrahydroindolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione (+)-10b. Indolylindoline (±)-**7b** (218 mg, 0.658 mmol) and α-D-glucose (355 mg, 1.975 mmol) were refluxed in 2 mL of MeOH for 79 h. The reaction mixture was then preadsorbed on silica gel and purified by silica gel chromatography (12% MeOH/$CHCl_3$) to give 250 mg (77%) of a 1:1 mixture of glycosylated diastereomers. The mixture of diastereomers was then dissolved in 4 mL of 1,4-dioxane. DDQ (242 mg, 1.06 mmol) was then added. After 24 h, the reaction mixture was poured into 100 mL of EtOAc and washed with saturated aqueous $NaHCO_3$ (3×), dried (Na_2SO_4), and concentrated. Purification by silica gel chromatography (3% MeOH/EtOAc) provided 168 mg (68%, 52% from (±)-**7b**) of (+)-**10b** as an orange solid.

(+)-10b: mp 340−342 °C dec (methanol); $[\alpha]_D$ +187.1 (*c* 0.30, DMSO); R_f = 0.55 (5% methanol/EtOAc); IR (KBr) 3334, 3218, 2920, 1694 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz) δ 11.67 (s, 1H), 11.12 (s, 1H), 9.16 (d, 1H, J = 8.0 Hz), 9.08 (d, 1H, J = 8.0 Hz), 7.97 (d, 1H, J = 8.7 Hz), 7.69 (d, 1H, J = 8.0 Hz), 7.54−7.60 (m, 2H), 7.36 (aq, 2H, J = 6.8 Hz), 6.28 (d, 1H, J = 8.8 Hz), 6.01 (t, 1H, J = 4.0 Hz), 5.40 (d, 1H, J = 5.2 Hz), 5.15 (d, 1H, J = 5.2 Hz), 4.92 (d, 1H, J = 5.3 Hz), 4.06−4.12 (m, 2H), 3.95−4.01 (m, 2H), 3.81−3.84 (m, 1H), 3.54−3.59 (m, 1H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 171.1, 171.0, 142.1, 140.8, 129.7, 128.4, 127.0, 126.8, 124.5, 121.4, 121.1, 121.0, 120.7, 120.4, 119.4, 118.4, 116.9, 112.1, 111.8, 84.5, 78.5, 76.6, 73.0, 67.5, 58.3; MS (FAB+) 487; HRMS (FAB+) calcd for $C_{26}H_{21}N_3O_7$ 487.1379, found 487.1371. Anal. Calcd for $C_{26}H_{21}N_3O_7 + H_2O$: C, 61.78; H, 4.59; N, 8.31. Found: C, 62.20; H, 4.75; N, 7.97.

6-Methyl-12-[β-D-xylosyl]-6,7,12,13-tetrahydroindolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione (+)-11. Indolylindoline (±)-**7a** (201 mg, 0.585 mmol) and D-xylose (263 mg, 1.76 mmol) were refluxed in 4 mL of MeOH for 8 h. The reaction mixture was then preadsorbed on silica gel and purified by silica gel chromatography (7% MeOH/$CHCl_3$) to give 236 mg (85%) of a 1:1 mixture of glycosylated diastereomers. The mixture of diastereomers was then dissolved in 4 mL of 1,4-dioxane. DDQ (242 mg, 1.06 mmol) was then added. After 48 h, the reaction mixture was poured into 100 mL of EtOAc and washed with saturated aqueous $NaHCO_3$ (3×), dried (Na_2SO_4), and concentrated. Purification by silica gel chromatography (50% EtOAc/hexanes) provided 174 mg (74%, 63% from (±)-**7a**) of (+)-**11** as an orange solid.

(+)-11: mp 345 °C dec (EtOAc); $[\alpha]_D$ +103.2 (*c* 0.45, DMSO); R_f = 0.10 (50% acetone/hexanes); IR (KBr) 3372, 3052, 2923, 1749, 1693 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz, 398K) δ 10.86 (s, 1H), 9.21 (d, 1H, J = 8.0 Hz), 9.13 (d, 1H, J = 8.0 Hz), 7.92 (d, 1H, J = 8.5 Hz), 7.82 (d, 1H, J = 8.5 Hz), 7.53−7.59 (m, 2H), 7.35−7.39 (m, 2H), 6.16 (d, 1H, J = 9.0 Hz), 4.40−4.80 (bs, 3H), 4.33 (dd, 1H, J = 10.8, 5.0 Hz), 3.93−3.97 (m, 2H), 3.86 (t, 1H, J = 10.8 Hz), 3.70 (t, 1H, J = 8.7 Hz), 3.23 (s, 3H); ^{13}C NMR (DMSO-d_6, 125 MHz, 300K, 2 sets of signals) δ 169.6, 142.4, 140.8, 140.4, 139.3, 130.1, 129.2, 128.1, 127.2, 127.0, 126.0, 124.6, 124.2, 122.8, 121.4, 120.9, 120.8, 120.6, 120.4, 120.0, 119.3, 118.6, 117.8, 117.1, 116.6, 114.5, 112.9, 111.8, 111.7, 87.5, 85.8, 77.6, 76.9, 72.9, 70.8, 69.4, 69.2, 68.3, 23.7; MS (FAB+) 472, 391, 339; HRMS (FAB+) calcd for $C_{26}H_{21}N_3O_6$ 471.1430, found 471.1430. Anal. Calcd for $C_{26}H_{21}N_3O_6 + H_2O$: C, 63.79; H, 4.74; N, 8.58. Found: C, 63.39; H, 4.48; N, 8.30.

6-Methyl-12-[*O*-(α-D-glucopyranosyl)−(1→4)-β-D-glucopyranosyl]-6,7,12,13-tetrahydroindolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione, (+)-12. Aglycon indolylindoline (±)-**7a** (0.589 mmol, 202 mg), maltose (1.78 mmol, 636 mg), and $(NH_4)_2SO_4$ (0.04 mmol, 1 mg) were suspended in 7 mL of methanol and warmed to reflux. After 25 h, the reaction was preabsorbed on silica gel and purified by silica gel chromatography (20% methanol/chloroform) to give a mixture of diastereomers (389 mg, 96%). This mixture was dissolved in 10 mL of THF and DDQ (1.34 mmol, 304 mg) was added. After 44 h the reaction was concentrated in vacuo and purified by silica gel chromatography (20% methanol/chloroform). The product of this purification was contaminated with silica gel, but this was removed by filtratation through an HPLC filter with 7% MeOH/THF to give 286 mg (69% from (±)-**7a**) of the indolocarbazole (+)-**12**.

(+)-12: mp 345 °C dec; $[\alpha]_D$ = +151.0 (*c* 0.05, 1:1 MeOH/DMF); R_f = 0.22 (25% MeOH/$CHCl_3$); IR (KBr) 3329, 2922, 1745, 1690 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) δ 11.62 (s, 1H), 9.17 (d,1H, J = 8.0 Hz), 9.10 (d, 1H, J = 8.0 Hz), 7.96 (d,1H, J = 8.5 Hz), 7.75 (d, 1H, J = 8.1 Hz), 7.55−7.61 (m, 2H), 7.36−7.40 (m, 2H), 6.36 (d, 1H, J = 9.0 Hz), 6.04 (bs, 1H), 5.72 (bs, 1H), 5.54 (bs, 1H), 5.30 (d, 1H, J = 3.5 Hz), 5.10−5.21 (m, 3H), 4.69 (bs, 1H), 4.26 (bd, 1H, J = 9.6 Hz), 4.16−4.21 (m, 2H), 3.92 (t, 1H, J = 8.4 Hz), 3.84 (bd, 1H, J = 10.7 Hz), 3.78 (d, 1H, J = 11.0 Hz), 3.66−3.69 (m, 1H), 3.55−3.63 (m, 3H), 3.50 (t, 1H, J = 9.1 Hz), 3.34−3.36 (m, 1H), 3.15 (t, 1H, J = 9.4 Hz); ^{13}C NMR (DMSO-d_6, 125 MHZ) δ 169.7, 169.6, 142.2, 140.9, 129.5, 128.0, 127.1, 126.9, 124.3, 124.2, 121.4, 121.0, 120.7, 120.5, 120.1, 118.5, 118.4, 117.2, 112.4, 111.8, 100.9, 84.0, 77.8, 77.0, 76.0, 73.8, 73.4, 72.5, 70.0, 61.1, 58.4, 23.7; MS(FAB+) 686 (M + Na); HRMS (FAB+) calcd for $C_{33}H_{37}N_3O_{14}$ 663.2064, found 663.2081.

6-Methyl-12-[*O*-(α-D-galacotopyranosyl)-(1→6)-β-D-glucopyranosyl]-6,7,12,13-tetrahydroindolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione, (+)-13. Indolylindoline (±)-**7a** (230 mg, 0.67 mmol), melibiose hydrate (0.72 g, 2.01 mmol), and $(NH_4)_2SO_4$ (7 mg, 0.05 mmol) were suspended in 4 mL of MeOH and warmed to reflux. After 72 h, the reaction mixture was adsorbed on silica gel and purified (30% MeOH/$CHCl_3$,

isolated the UV active streak at $R_f = 0.5$ in 30% MeOH/$CHCl_3$). The resulting mixture of diatereomers was suspended in 10 mL of 1,4-dioxane, and DDQ (276 mg, 1.22 mmol) was added. After 70 h the dioxane was evaporated and the residue purified by RPHPLC (60% MeOH/40% 50 mM pH 9.0 NH_4OAc). The product was then purified by silica gel chromatography (15% MeOH/EtOAc) to remove the NH_4OAc. The product of this purification was contaminated with silica gel, and was therefore dissolved in 5% MeOH/THF and filtered through an HPLC filter. This provided pure (+)-**13** (214 mg, 47% yield from (±)-**7a**) as an orange amorphous solid.

(+)-13: mp 296−298 °C (MeOH/$CHCl_3$); $[\alpha]_D$ +99.0 (*c* 0.40, DMSO); $R_f = 0.16$ (20% MeOH/$CHCl_3$); IR (KBr) 3391, 2933, 1745, 1680 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz, 423K) δ 9.22 (d, 1H, $J = 8.0$ Hz), 9.13 (d, 1H, $J = 8.0$ Hz), 8.02 (d, 1H, $J = 8.3$ Hz), 7.84 (d, 1H, $J = 8.2$ Hz), 7.53−7.57 (m, 2H), 7.35 (aq, 2H, $J = 8.1$ Hz), 6.36 (d, 1H, $J = 8.5$ Hz), 4.87 (bs, 1H), 4.15−4.18 (m, 1H), 4.09 (dd, 1H, $J = 11.5$, 4.7 Hz), 4.05 (bt, 1H, $J = 8.8$ Hz), 3.94 (dd, 1H, $J = 11.5$, 2.2 Hz), 3.84−3.86 (m, 2H), 3.79−3.81 (m, 2H), 3.69 (bd, 2H, $J = 1.4$ Hz), 3.57 (dd, 1H, $J = 11.1$, 5.6 Hz), 3.50 (dd, 1H, $J = 11.1$, 5.8 Hz), 3.24 (s, 3H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 1169.8, 169.7, 141.0, 139.4, 130.0, 128.1, 127.2, 127.0, 124.4, 124.3, 122.7, 120.9, 120.8, 120.4, 119.3, 118.6, 117.7, 116.7, 115.4, 112.0, 99.0, 86.7, 77.5, 76.4, 71.1, 69.7, 69.3, 69.0, 68.5, 65.6, 60.7, 23.8; MS (CI+) 686 (M + Na), 663; HRMS (CI+) calcd for $C_{33}H_{33}N_3O_{12}$ 663.2064, found 663.2078.

6-Methyl-12-[*O*-(α-D-glucopyranosyl)-(1→4)-*O*-(α-D-glucopyranosyl)−(1→4)-*β*-D-glucopyranosyl]-6,7,12,13-tetrahydroindolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione, (+)-14. Indolylindoline (±)-**7a** (378 mg, 1.10 mmol), maltotriose hydrate (1.66 g, 3.30 mmol), and $(NH_4)_2SO_4$ (7 mg, 0.05 mmol) were suspended in 11 mL of MeOH and warmed to reflux. After 32 h, the reaction mixture was adsorbed on silica gel and purified (10−30% MeOH/$CHCl_3$, isolated the UV active streak at $R_f = 0.5$ in 20% MeOH/$CHCl_3$). The resulting mixture of diatereomers was suspended in 25 mL of 1,4-dioxane, and DDQ (500 mg, 2.2 mmol) was added. After 72 h, the dioxane was evaporated and 100 mL of saturated aqueous $NaHCO_3$ was added. The reaction was stirred vigorously for 1 h and then filtered. The filtrate was then purified by silica gel chromatography (30% MeOH/$CHCl_3$). The product of this purification was contaminated with silica gel, and was therefore dissolved in 10% MeOH/THF and filtered through an HPLC filter. This provided pure (+)-**14** (583 mg, 64% yield from (±)-**7a**) as an orange amorphous solid.

(+)-112: mp 300−304 °C (THF/MeOH); $[\alpha]_D$ +151.5 (*c* 0.60, DMSO); $R_f = 0.10$ (30% MeOH/$CHCl_3$); IR (KBr) 3331, 2923, 1745, 1680 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz) δ 11.60 (s, 1H), 9.16 (d, 1H, $J = 8.1$ Hz), 9.09 (d, 1H, $J = 8.0$ Hz), 7.94 (d, 1H, $J = 8.5$ Hz), 7.73 (d, 1H, $J = 8.2$ Hz), 7.54−7.61 (m, 2H), 7.35−7.39 (m, 2H), 6.33 (d, 1H, $J = 9.1$ Hz), 6.06 (t, 1H, $J = 3.8$ Hz), 5.70 (d, 1H, $J = 3.6$ Hz), 5.62 (d, 1H, $J = 6.4$ Hz), 5.53 (d, 1H, $J = 3.2$ Hz), 5.50 (d, 1H, $J = 6.2$ Hz), 5.29 (d, 1H, $J = 3.6$ Hz), 5.09 (d, 1H, $J = 5.7$ Hz), 5.05 (d, 1H, $J = 3.7$ Hz), 4.93 (d, 1H, $J = 6.1$ Hz), 4.91 (d, 1H, $J = 6.1$ Hz), 4.68 (t, 1H, $J = 5.5$ Hz), 4.55 (t, 1H, $J = 5.6$ Hz), 3.90 (td, 1H, $J = 8.3$, 3.3 Hz), 4.15−4.20 (m, 3H), 3.64−3.84 (m, 7H), 3.59 (ddd, 1H, $J = 14.7$, 9.0, 5.7 Hz), 3.36−3.54 (m, 3H), 3.24−3.29 (m, 2H), 3.20 (s, 3H), 3.09 (ddd, 1H, $J = 14.9$, 9.2, 5.7 Hz); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 169.7, 169.6, 142.2, 140.9, 129.6, 128.1, 127.1, 127.0, 124.9, 124.4, 124.3, 121.4, 121.1, 120.8, 120.5, 120.2, 118.6, 118.5, 117.2, 112.4, 111.8, 100.8, 100.7, 84.1, 79.6, 77.9, 76.9, 76.0, 73.5, 73.4, 73.3, 72.5, 72.1, 69.9, 60.9, 60.6, 58.5, 23.7 (One resonance was not resolved); MS (FAB+) 848, 825; HRMS (FAB+) calcd for $C_{39}H_{43}N_3O_{17}$ 825.2592, found 825.2599. Anal. Calcd for $C_{39}H_{43}N_3O_{17} + H_2O$ C, 55.51; H, 5.38; N, 4.98. Found: C, 55.51; H, 5.61; N, 4.56.

6-*O*-*p*-Methoxybenzyl-4-*O*-methyl-1,2,3-*O*-benzyl-*β*-D-glucopyranoside, 16. Protected glucoside **15** (2.23 g, 3.90 mmol) was dissolved in 20 mL of THF. Sodium hydride (60% oil dispersion, 0.47 g, 11.7 mmol) was added followed by methyl iodide (1.1 mL, 11.7 mmol). After 90 min, the reaction was quenched with 10 mL of saturated aqueous NH_4Cl and poured into 100 mL of brine. The mixture was extracted with EtOAc (3 × 80 mL), the extracts combined, dried (Na_2SO_4), and concentrated. Purification by silica gel chromatography (30% EtOAc/hexanes) gave 2.26 g (99%) of benzyl ether **16** as a clear syrup.

16: $[\alpha]_D$ +1.4 (*c* 0.85, $CHCl_3$); $R_f = 0.55$ (30% EtOAc/hexanes); IR 3017, 2908 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.37 (d, 1H, $J = 8.0$ Hz), 7.15−7.32 (m, 16H), 6.86 (d, 2H, $J = 8.8$ Hz), 4.96 (d, 1H, $J = 11.9$ Hz), 4.94 (d, 1H, $J = 9.6$ Hz), 4.88 (d, 1H, $J = 10.7$ Hz), 4.77 (d, 1H, $J = 10.7$ Hz), 4.70 (d, 1H, $J = 9.9$ Hz), 4.65 (d, 1H, $J = 11.9$ Hz), 4.59 (d, 1H, $J = 11.5$ Hz), 4.51 (d, 1H, $J = 11.9$ Hz), 4.48 (dd, 1H, $J = 7.6$, 1.2 Hz), 3.76 (s, 3H), 3.75 (m, 1H), 3.66−3.69 (m, 1H), 3.49−3.55 (m, 2H), 3.47 (s, 3H), 3.35−3.37 (m, 1H), 3.30 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 159.1, 138.6, 138.4, 137.4, 130.2, 129.2, 128.3, 128.2, 128.1, 128.0, 127.8, 127.6, 127.5, 113.6, 102.4, 84.5, 82.0, 79.7, 75.4, 74.9, 74.8, 73.0, 70.9, 68.6, 60.5, 55.1; MS (FAB+) 607; HRMS (FAB+) calcd for $C_{36}H_{40}O_7Na$ $(M + Na)^+$ 607.2672, found 607.2683. Anal. Calcd for $C_{36}H_{40}O_7$: C, 73.95; H, 6.90. Found: C, 73.74; H, 6.90.

4-*O*-Methyl-1,2,3-*O*-benzyl-*β*-D-glucopyranoside, 17. Protected glucoside **16** (54 mg, 0.92 mmol) was dissolved in 2 mL of CH_2Cl_2, and 0.2 mL of H_2O was added. DDQ (22 mg, 0.10 mmol) was then added. After 5 h, the reaction was poured into 15 mL of saturated aqueous $NaHCO_3$ and extracted with CH_2Cl_2 (3 × 15 mL). The extracts were dried (Na_2SO_4) and concentrated. Purification by silica gel chromatography (30% EtOAc/hexanes) gave 27 mg (63% yield) of alcohol **17**.

17: mp 92−94 °C; $[\alpha]_D$ +10.8 (*c* 1.05, $CHCl_3$); $R_f = 0.47$ (40% EtOAc/hexanes); IR (film) 3391, 3308, 2960 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.25−7.37 (m, 15 H), 4.93 (d, 1H, $J = 8.7$ Hz), 4.90 (d, 1H, $J = 9.5$ Hz), 4.88 (d, 1H, $J = 10.7$ Hz), 4.77 (d, 1H, $J = 11.1$ Hz), 4.71 (d, 1H, $J = 11.1$ Hz), 4.68 (d, 1H, $J = 11.9$ Hz), 4.54 (d, 1H, $J = 8.0$ Hz), 3.88 (m, 1H), 3.73 (m, 1H), 3.55 (s, 3H), 3.52−3.54 (m, 2H), 3.43 (dd, 1H, $J = 9.2$ Hz), 3.28 (m, 2H), 1.95 (m, 1H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 138.5, 138.3, 137.3, 128.5, 128.3, 128.1, 127.9, 127.6, 127.5, 102.7, 84.4, 82.1, 79.7, 75.6, 75.1, 75.0, 71.6, 62.0, 60.8; MS (CI+) 357, 265; HRMS (CI+) calcd for $C_{28}H_{32}O_6$ 464.2198, found 464.2186. Anal. Calcd for $C_{28}H_{32}O_6$: C, 72.39; H, 6.94. Found: C, 72.54; H,0.7.04.

***tert*-Butyl (4*R*,1′*R*)-2,2-Dimethyl-4-(1′-benzyloxy-3-butenyl)oxazolidine-3-carboxylate, 19.** Homoallylic alcohol **18** (1.51 g, 5.57 mmol) was dissolved in 20 mL of dry DMF. Sodium hydride (60% suspension, 0.450 g, 11.14 mmol) was added followed by benzyl bromide (1.35 mL, 11.14 mmol). After 90 min, the reaction was quenched with the addition of 5 mL of saturated aqueous NH_4Cl and taken up in 100 mL of EtOAc. The organic layer was washed with water (50 mL), and brine (2 × 50 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification by silica gel chromatography (8% EtOAc/hexanes) afforded 1.60 g (80% yield) of **19** as a clear syrup.

19: $[\alpha]_D$ +21.5 (*c* 0.85, $CHCl_3$); $R_f = 0.47$ (20% EtOAc/hexanes); IR (neat) 3069, 2977, 2935, 1701 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz, 80 °C) δ 7.30−7.35 (m, 4H), 7.26−7.28 (m, 1H), 5.85−5.91 (m, 1H), 5.08 (d, 1H, $J = 17.1$ Hz), 5.02 (d, 1H, $J = 11.1$ Hz), 4.58 (d, 1H, $J = 11.9$ Hz), 4.53 (d, 1H, $J = 11.9$ Hz), 4.14 (bs, 1H), 3.99 (d, 1H, $J = 7.2$ Hz), 3.95 (t, 1H, $J = 15.4$ Hz), 3.84 (m, 1H), 2.30−2.32 (m, 1H), 2.19−2.24 (m, 1H), 1.53 (s, 3H), 1.42 (s, 3H), 1.41 (s, 9H); ^{13}C NMR (DMSO-d_6, 125 MHz, 80 °C) δ 151.4, 138.3, 135.5, 127.6, 126.9, 126.8, 115.8, 78.9, 77.7, 71.1, 62.8, 57.1, 35.8, 33.2, 27.7, 27.6; MS (CI+) 362; HRMS (CI+) calcd for $C_{21}H_{32}NO_4$ $(M + H)^+$ 362.2332, found 362.2325. Anal. Calcd for $C_{21}H_{32}NO_4$: C, 69.76; H, 8.65; N, 3.88. Found: C, 69.52; H, 8.59; N, 3.82.

***tert*-Butyl (4*R*,1′*R*)-2,2-Dimethyl-4-(1′-benzyloxy-3′-aldehydo)oxazolidine-3-carboxylate 20.** Homoallyl ether **19** (2.46 g, 6.82 mmol) was dissolved in 40 mL of acetone. *N*-Morpholine *N*-oxide (0.76 g, 7.50 mmol) was added followed by OsO_4 (2.5% solution in tBuOH, 1.22 mL, 0.095 mmol). The reaction mixture turned yellow. After 2 h, the reaction was concentrated in vacuo, taken up in EtOAc (50 mL), and washed with 0.1 N HCl (3 × 50 mL). The organic layer was then dried (Na_2SO_4) and concentrated. Purification by silica gel chromatagraphy (70% EtOAc/hexanes) gave a mixture of diol diastereomers that was dissolved in 50 mL of THF. To this solution

was added sodium (meta)periodonate (6.4 mmol, 1.37 g) in 10 mL of water. After 1 h, the reaction was concentrated in vacuo and poured into 50 mL of H_2O. The water was extracted with CH_2Cl_2 (3 × 50 mL) and the combined organic extracts dried (Na_2SO_4) and concentrated. Purification by silica gel chromatography (15% ethyl actetate/hexanes) gave 1.22 g (58%) of aldehyde **20** as a clear oil and 0.17 g (8%) of the other diastereomer at C-1′.

20: $[\alpha]_D$ −14.5 (*c* 1.40, $CHCl_3$); R_f = 0.43 (20% EtOAc/hexanes); IR (neat) 2978, 2882, 2724, 1727, 1698 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz, 80 °C) δ 9.68 (s, 1H), 7.24−7.34 (m, 5H), 4.59 (d, 1H, *J* = 11.8 Hz), 4.54 (d, 1H, *J* = 11.8 Hz), 4.39 (m, 1H), 4.18 (m, 1H), 3.93−3.99 (m, 2H), 2.60 (dd, 2H, *J* = 1.9, 7.1 Hz), 1.50 (s, 3H), 1.42 (s, 9H), 1.40 (s, 3H); ^{13}C NMR (DMSO-d_6, 125 MHz, 80 °C) δ 201.0, 151.5, 138.0, 127.7, 127.0, 93.4, 79.3, 70.9, 62.6, 56.7, 43.3, 40.0, 27.6, 25.9, 25.8; MS (CI+) 364, 306, 262, 200, 144; HRMS (CI+) calcd for $C_{20}H_{30}NO_5$ $(M + H)^+$ 364.2124, found 364.2120. Anal. Calcd for $C_{20}H_{30}NO_5$: C, 66.08; H, 8.05; N, 3.86. Found: C, 65.81; H, 8.10; N, 3.82.

3-*O*-Benzyl-4-(*tert*-butoxycarboxamido)-2,4-dideoxy-D-xylose, (+)-21. Aldehyde **20** (1.028 g, 2.82 mmol) was dissolved in 27 mL of dioxane. Three milliliters of water was added followed by toluenesulfonic acid monohydrate (538 mg, 2.82 mmol). After 21 h at room temperature, the reaction was poured into 100 mL of saturated aqueous $NaHCO_3$ and extracted with EtOAc (3 × 100 mL). The extracts were then dried (Na_2SO_4) and concentrated in vacuo. Purification via silica gel chromatography (40% EtOAc/hexanes) gave 738 mg (81%) of (+)-**21** as a 1:1 mixture of anomers and a mixture of partially hydrolyzed products (163 mg, 15% recovered).

(+)-21: mp 119−120 °C ($CHCl_3$); $[\alpha]_D$ = +25.4 (*c* 0.90, $CHCl_3$); R_f = 0.36 (50% EtOAc/hexanes); ^1H NMR ($CDCl_3$, 500 MHz) δ 7.24−7.36 (m, 5H), 5.31 (d, 0.5 H, *J* = 6.3 Hz), 5.21 (d, 0.5 H, *J* = 6.0 Hz), 5.10 (dd, 0.5 H, *J* = 6.6, 3.3 Hz), 5.03 (bs, 1H), 4.70 (d, 0.5 H, *J* = 11.5 Hz), 4.61 (d, 1H, *J* = 11.7 Hz), 4.59 (bs, 1H), 4.37 (d, 0.5 H, *J* = 11.8 Hz), 4.00 (d, 1H, *J* = 9.2 Hz), 3.79 (bd, 1H, *J* = 14.3 Hz), 3.64−3.71 (m, 1.5 H), 2.08 (d, 0.5 H, *J* = 14.0 Hz), 1.83−1.93 (m, 1 1/2 H), 1.44 (s, 9H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 155.3, 138.3, 137.3, 128.7, 128.6, 128.4, 128.0, 127.8, 127.6, 127.5, 127.4, 92.7, 92.1, 79.8, 79.6, 74.4, 73.9, 71.9, 70.9, 63.8, 58.6, 47.9, 46.9, 34.1, 31.4, 28.2, 27.9; MS(CI+) 324; HRMS (CI+) calcd for $C_{17}H_{25}NO_5$ 324.1808, found 324.1811. Anal. Calcd for $C_{17}H_{25}NO_5$: C, 63.14; H, 7.79; N, 4.33. Found: C, 63.12; H, 7.72; N, 4.34.

Benzyl-*O*-[3-*O*-benzyl-4-methylamino-2,4-dideoxy-β-L-xylopyranosyl]-(1→6)-2,3-di-*O*-benzyl-4-*O*-methyl-β-D-glucopyranoside, 24, and Benzyl-*O*-[3-*O*-benzyl-4-methylamino-2,4-dideoxy-α-L-xylopyranosyl]-(1→6)-2,3-di-*O*-benzyl-4-*O*-methyl-β-D-glucopyranoside, 23. Lactol **21** (3.25 mmol, 1.051 g) and 4 Å mol sieves (400 mg) were suspended in 20 mL of THF and cooled to −78 °C. DAST (8.13 mmol, 1.08 mL) was then added. After 20 min, the reaction was warmed to 0 °C. Thirty minutes later, the reaction was filtered through Celite with Et_2O and washed with ice-cold $NaHCO_3$ (3 × 50 mL). The organic layer was then dried ($MgSO_4$) and concentrated to give the unstable glycosyl fluoride as a yellow solid (942 mg, 89% yield). The glycosyl fluoride **22** and glucoside **17** were dissolved in 25 mL of THF and added to a slurry of $AgClO_4$ (3.07 mmol, 1.43 g), $SnCl_2$ (6.14 mmol, 1.16 g), and 4 Å mol sieves (500 mg) in THF at −78 °C (the $AgClO_4$ and $SnCl_2$ were dried by azeotropic removal of benzene followed by the addtion of the mol sieves). The reaction was allowed to slowly warm to −15 °C over 6 h. The mixture was then filtered through Celite with ether, which was then washed with $NaHCO_3$ (3 × 100 mL), brine (100 mL), dried ($MgSO_4$), and concentrated. The residue was then purified by silica gel chromatography (40% EtOAc/60% hexanes) to give 1.68 g of a mixture of anomers inseparable by chromatography (75%) and 286 mg (20%) of recovered **17**. The mixture of isomers were then dissolved in 20 mL of THF. $LiAlH_4$ (1M in THF, 4 mL, 4 mmol) was then added and the reaction warmed to reflux. After 1 h, the reaction was cooled to room temperature and quenched with the sequential addition of 500 μL of water, 500 μL of 15% NaOH, and 1.5 mL of water. The reaction was then stirred for 2 h, filtered and concentrated. Purification of the residue by silica gel chromatography (5% MeOH/EtOAc) provided amine **24** (525 mg, 35%) and amine **23** (897 mg, 60%) as yellow oils.

24: $[\alpha]_D$ −13.5 (*c* 0.65, $CHCl_3$); R_f = 0.55 (5% MeOH/EtOAc); IR (KBr) 3340, 3063, 2880 cm^{-1}; ^1H NMR ($CDCl_3$ 500 MHz) δ 7.24−7.41 (m, 20H), 4.97 (bt, 1H, *J* = 2.5 Hz), 4.94 (d, 1H, *J* = 10.9 Hz), 4.92 (d, 1H, *J* = 11.9), 4.89 (d, 1H, *J* = 10.9 Hz), 4.76 (d, 1H, *J* = 10.9 Hz), 4.71 (d, 1H, *J* = 10.9 Hz), 4.65 (d, 1H, *J* = 12.0 Hz), 4.61 (d, 1H, *J* = 11.4 Hz), 4.46−4.48 (m, 2H), 3.94 (dd, 1H, *J* = 1.8, 11.0 Hz), 3.74−3.81 (m, 2H), 3.52−3.59 (m, 4H), 3.51 (s, 3H), 3.45 (dd, 1H, *J* = 9.0, 2.3 Hz), 3.37 (ddd, 1H, *J* = 9.8, 6.1, 1.6 Hz), 3.18 (t, 1H, *J* = 9.1 Hz), 2.63 (ddd, 1H, *J* = 9.5, 4.6, 4.4 Hz), 2.40 (s, 3H), 2.23 (ddd, 1H, *J* = 12.8, 4.5, 1.8 Hz), 1.66 (ddd, 1H, *J* = 13.3, 10.4, 3.5 Hz); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 138.6, 138.4, 138.3, 137.3, 128.5, 128.4, 128.3, 128.2, 128.1, 128.0, 127.9, 127.8, 127.7, 127.6, 102.2, 98.5, 84.5, 82.1, 80.1, 75.6, 75.5, 74.8, 74.5, 70.9, 70.8, 66.6, 61.7, 60.7, 60.5, 34.6, 34.3; MS (FAB+) 684; HRMS (FAB+) calcd for $C_{41}H_{49}NO_8$: 684.3537 $(M + H)^+$, found 684.3541 $(M + H)^+$. Anal. Calcd for $C_{41}H_{49}NO_8$: C, 72.01; H, 7.22; N, 2.05. Found: C, 72.05; H, 7.30; N, 2.11.

23: $[\alpha]_D$ +52.3 (*c* 0.9, $CHCl_3$); R_f = 0.30 (5% MeOH/EtOAc); IR (KBr) 3342, 3030, 2862 cm^{-1}; ^1H NMR ($CDCl_3$, 500 MHz) δ 7.25−7.40 (m, 20H), 4.94 (d, 1H, *J* = 5.4 Hz), 4.92 (d, 1H, *J* = 6.4 Hz), 4.87 (d, 1H, *J* = 10.9), 4.78 (d, 1H, *J* = 10.9 Hz), 4.71 (d, 1H, *J* = 11.0 Hz), 4.66 (d, 1H, *J* = 11.4 Hz), 4.65 (d, 1H, *J* = 12.0 Hz), 4.52 (dd, 1H, *J* = 6.6, 2.7 Hz), 4.46 (d, 1H, *J* = 7.7 Hz), 4.40 (d, 1H, *J* = 11.4 Hz), 4.12 (dd, 1H, *J* = 11.6, 4.6 Hz), 4.07 (dd, 1H, *J* = 11.5, 3.8 Hz), 3.76 (dd, 1H, *J* = 11.5, 1.5 Hz), 3.56 (s, 3H), 3.53 (t, 1H, *J* = 9.0 Hz), 3.45 (t, 1H, *J* = 8.0 Hz), 3.35−3.40 (m, 2H), 3.28−3.30 (m, 1H), 3.09 (dd, 1H, *J* = 11.6, 9.7 Hz), 2.59 (ddd, 1H, *J* = 9.2, 9.2, 4.6 Hz), 2.41−2.44 (m, 1H), 2.40 (s, 3H), 1.59 (ddd, 1H, *J* = 12.4, 10.6, 9.1 Hz); ^{13}C NMR ($CDCl_3$ 125 MHz) δ 138.6, 138.4, 138.0, 137.4, 128.5, 128.4, 128.3, 128.1, 127.9, 127.8, 127.7, 127.6, 127.5, 127.4, 102.5, 100.7, 84.5, 82.0, 79.3, 77.1, 75.6, 74.8, 74.6, 71.1, 70.3, 66.9, 64.7, 60.7, 60.4, 35.0, 34.5; MS (FAB+) 684; HRMS (CI+) calcd for $C_{41}H_{49}NO_8$ 684.3537 $(M + H)^+$, found 684.3535 $(M + H)^+$. Anal. Calcd for$C_{41}H_{49}NO_8$: C, 72.01; H, 7.22; N, 2.05. Found: C, 72.25; H, 7.28; N, 2.03.

Benzyl-*O*-[3-*O*-benzyl-4-(2-trimethylsilyloxycarbonyl)-methylamino-2,4-dideoxy-β-L-xylopyranosyl]-(1→6)-2,3-di-*O*-benzyl-4-*O*-methyl-β-D-glucopyranoside 25. Protected disaccharide**24** (400 mg, 0.584 mmol), *p*-nitrophenyl trimethylsilylethyl carbonate (292 mg, 1.03 mmol), and DMAP (126 mg, 1.03 mmol) were dissolved in 5 mL of NMP and warmed to 75 °C. After 3 h, the reaction was taken up in EtOAc and washed with 1 N NaOH (3×), dried (Na_2SO_4), and conc**e**ntrated. Purification by silica gel chromatography (40% EtOAc/hexane) provided 452 mg (93%) of Teoc carbamate 25 as a colorless syrup.

25: $[\alpha]_D$ −8.5 (*c* 1.2, MeOH); R_f = 0.31 (30% EtOAc/hexanes); IR (KBr) 3507, 3088, 2951, 1697 cm^{-1}; ^1H NMR (DMSO-d_6, 500 MHz) δ 7.25−7.33 (m, 20H), 4.97 (bs, 1H), 4.77−4.82 (m, 3H), 4.71 (d, 1H, *J* = 11.2 Hz), 4.64 (d, 1H, *J* = 11.4 Hz), 4.60 (d, 1H, *J* = 12.1 Hz), 4.53−4.57 (m, 2H), 4.39 (dd, 1H, *J* = 11.6, 4.6 Hz), 4.05−4.12 (m, 2H), 3.93−3.98 (m, 2H), 3.74−3.79 (m, 2H), 3.57 (dd, 1H, *J* = 10.3, 4.7 Hz), 3.54 (t, 1H, *J* = 9.1 Hz), 3.45 (s, 3H), 3.37−3.41 (m, 2H), 3.23 (t, 1H, *J* = 8.3 Hz), 3.17 (t, 1H, *J* = 9.4 Hz), 2.61 (s, 1.5H), 2.57 (s, 1.5H), 2.34 (d, 1H, *J* = 12.5 Hz), 1.46−1.51 (m, 1H), 0.89−0.93 (m, 2H), −0.01 (s, 9H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 156.0, 138.7, 138.5, 138.4, 137.6, 128.2, 128.1, 127.6, 127.5, 101.6, 97.1, 83.6, 81.6, 79.4, 74.4, 73.7, 73.5, 70.1, 69.3, 69.1, 69.0, 65.2, 62.7, 59.8, 59.5, 58.2, 56.3, 35.2, 17.2, −1.5; MS (FAB+) 850, 486; HRMS (FAB+) calcd for $C_{47}H_{61}N_4O_{10}Si$ 850.3962
$(M + Na)^+$, found 850.3977. Anal. Calcd for $C_{47}H_{61}N_4O_{10}Si$: C, 68.17; H, 7.43; N, 1.69. Found: C, 68.12; H, 7.52; N, 1.75.

***O*-[4-(2-Trimethylsilyloxycarbonyl)methylamino-2,4-dideoxy-β-L-xylopyranosyl]-(1→6)-4-*O*-methyl-D-glucopyranose 26.** Protected disaccharide **25** (442 mg, 0.533 mmol) was dissolved in 3 mL of EtOH and 3 mL of EtOAc. Pd/C (10%, 227 mg, 0.213 mmol) was added. The reaction was then stirred

under a balloon of H_2 for 90 min. The reaction was then filtered through Celite with EtOAc and concentrated in vacuo. The residue was purified by silica gel chromatography (10% methanol/EtOAc) to give 240 mg (96%) of Teoc-protected aminodisaccharide **26**.

26: mp 41 °C (MeOH); R_f = 0.26 (10% MeOH/EtOAc); IR (KBr) 3426, 2955, 1676 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 6.67 (d, 0.4H, J = 3.5 Hz), 6.32 (d, 0.6H, J = 4.0 Hz), 5.03 (d, 0.6H, J = 4.9 Hz), 4.94−4.97 (m, 1H), 4.84−4.87 (m, 1.8H), 4.81 (bs, 1H), 4.57 (d, 0.6H, J = 6.5 Hz), 4.26 (t, 0.4H, J = 6.4 Hz), 4.00−4.12 (m, 1.6H), 3.91−3.95 (m, 1.4H), 3.51−3.77 (m, 3.6 Hz), 3.41 (s, 3H), 3.23−3.37 (m, 2H), 3.09−3.14 (m, 1H), 2.84 (t, 2H, J = 9.6 Hz), 2.73 (s, 1.5H), 2.72 (s, 1.5H), 1.98 (bd, 1H, J = 9.8 Hz), 1.44−1.53 (m, 1H), 0.93 (t, 2H, J = 8.1 Hz), 0.01 (s, 9H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 156.1, 97.4, 97.3, 96.6, 92.2, 80.2, 79.9, 76.4, 75.0, 73.5, 72.9, 72.5, 69.0, 66.3, 66.2, 62.7, 62.6, 61.7, 61.5, 59.6, 58.4, 58.1, 29.1, 29.0, 17.3, −1.4; MS (FAB+) 490; HRMS (FAB+) calcd for $C_{19}H_{37}NO_{10}Si$ 490.2084 (M + Na)$^+$, found 490.2091 Anal. Calcd for $C_{19}H_{37}NO_{10}Si$: C, 48.81; H, 7.98; N, 3.00. Found: C, 48.60; H, 8.03; N, 3.14.

6-Methyl-12-[*O*-[4-(2-trimethylsilyloxycarbonyl)methylamino-2,4-dideoxy-β-L-xylopyranosyl]-(1→6)-4-*O*-methyl-β-D-glucopyranosyl]-6,7,12,13-tetrahydroindolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione 27. The debenzylated Teoc-protected disaccharide **26** (93 mg, 0.200 mmol) and indolylindoline (±)-**7a** (206 mg, 0.600 mmol) were suspended in 3 mL of MeOH. $(NH_4)_2SO_4$ (4 mg, 0.04 mmol) was then added, and the reaction was warmed to reflux. After 72 h, the reaction mixture was adsorbed on silica gel and purified by silica gel chromatography (5% MeOH/EtOAc, isolated compounds at R_f = 0.5). The mixture of diastereomers (135 mg, 0.170 mmol, 85% yield) was dissolved in 3 mL of 1,4-dioxane. DDQ (135 mg, 0.511 mmol) was added, and the reaction mixture was stirred at room temperature for 45 h. The reaction mixture was evaporated and taken up in EtOAc. The EtOAc was washed with 0.1 N NaOH (3×), dried (Na_2SO_4), and concentrated. Purification by silica gel chomatography (50% hexane/acetone) gave 110 mg (82%, 70% from **26**) of **27** as a yellow solid.

27: mp 320 °C dec; $[\alpha]_D$ +76.2 (*c* 0.5, THF); R_f = 0.40 (50% acetone/hexane); IR (KBr) 3363, 2939, 1747, 1694 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz, 398K) δ 10.83 (s, 1H), 9.22 (d, 1H, J = 7.9 Hz), 9.15 (d, 1H, J = 8.2 Hz), 7.98 (d, 1H, J = 8.2 Hz), 7.78 (d, 1H, J = 8.2 Hz), 7.59 (t, 1H, J = 8.2 Hz), 7.54 (t, 1H, J = 8.3 Hz), 7.35−7.38 (m, 2H), 6.27 (d, 1H, J = 8.5 Hz), 4.0.91 (bs, 1H), 4.79 (bs, 2H), 4.16−4.19 (m, 1H), 4.01−4.06 (m, 5H), 3.93 (at, 2H, J = 8.4 Hz), 3.80−3.85 (m, 1H), 3.67 (s, 3H), 3.55−3.65 (m, 2H), 3.53 (t, 1H, J = 6.9 Hz), 3.50 (dd, 1H, J = 10.7, 5.0 Hz), 3.24 (s, 3H), 2.34 (s, 3H), 2.15 (dd, 1H, J = 17.7, 4.4 Hz), 1.53−1.58 (m, 1H), 0.89 (t, 2H, J = 8.0 Hz), −0.01 (s, 9H); ^{13}C NMR (DMSO-d_6, 125 MHz, 2 sets of signals) δ 169.9, 169.5, 169.4, 169.3, 155.9, 155.8, 140.8, 140.0, 139.4, 139.2, 129.9, 128.9, 128.0, 127.8, 127.7, 127.3, 127.1, 126.6, 124.8, 124.5, 124.4, 122.9, 121.5, 121.0, 120.8, 120.4, 119.9, 119.4, 119.0, 118.6, 118.3, 117.9, 117.2, 116.7, 114.4, 112.2, 111.7, 111.5, 98.1, 97.9, 86.6, 84.8, 79.5, 79.3, 79.0, 77.1, 76.5, 76.0, 73.2, 71.0, 66.6, 66.4, 62.7, 62.6, 61.9, 61.7, 61.6, 60.3, 60.2, 58.6, 58.3, 58.0, 55.8, 29.6, 28.7, 23.7, 17.2, −1.4, −1.5; MS (FAB+) 788, 339; HRMS (FAB+) calcd for $C_{40}H_{48}N_4O_{11}Si$ 788.3088, found 788.3088. Anal. Calcd for $C_{40}H_{48}N_4O_{11}Si$: C, 60.90; H, 6.13; N, 7.10. Found: C, 61.22; H, 6.39; N, 6.76.

AT2433-B1 (28). Teoc-protected indolocarbazole glycoside **27** (30 mg, 0.038 mmol) was dissolved in 2 mL of THF. 4 Å mol sieves (200 mg) and TBAF (1 M in THF, 100 μL, 0.10 mmol) were then added. After 4 h, the reaction was filtered, adsorbed on silica gel, and purified by silica gel chromatography (10% MeOH/1% NH_4OH/89% $CHCl_3$). This provided 21 mg (86%) of **AT2433-B1 (28)** as a yellow solid.

28: mp 245 °C ($CHCl_3$); $[\alpha]_D$ +115.7 (*c* 0.50, 1:1 methanol/$CHCl_3$); R_f = 0.34 (20% MeOH/$CHCl_3$); IR (KBr) 3357, 2922, 1750, 1691 cm^{-1}; ^{1}H NMR (DMSO-d_6, 423 K, 500 MHz) δ 9.22 (d, 1H, J = 8.0 Hz), 9.15 (d, 1H, J = 8.1 Hz), 7.99 (d, 1H, J = 8.4 Hz), 7.80 (d, 1H, J = 8.2 Hz), 7.55−7.60 (m, 2H), 7.35−7.39 (m, 2H), 6.27 (d, 1H, J = 8.6 Hz), 4.91 (dd, 1H, J = 3.4, 3.2 Hz), 4.80 (bs, 1H), 4.16 (ddd, 1H, J = 9.7, 6.5, 1.8 Hz), 4.00−4.05 (m, 2H), 3.96 (t, 1H, J = 8.6 Hz), 3.83 (dd, 1H, J = 11.5, 4.9 Hz), 3.70−3.72 (M, 1H), 3.68 (S, 3H), 3.62−3.65 (M, 1H), 3.60 (dd, 1H, J = 11.1, 4.4 Hz), 3.34 (dd, 1H, J = 11.1, 9.0 Hz), 3.23 (s, 3H), 2.27 (dt, 1H, J = 8.4, 4.2 Hz), 2.24 (s, 3H), 2.03 (td, 1H, J = 13.1, 4.2 Hz), 1.58 (ddd, 1H, J = 9.9, 9.6, 3.4 Hz); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 169.6, 169.5, 169.4, 142.2, 140.8, 140.0, 139.3, 129.9, 129.0, 128.1, 127.9, 127.4, 127.2, 127.0, 126.8, 124.5, 124.4, 124.2, 122.8, 121.4, 120.9, 120.7, 120.3, 120.0, 119.3, 118.9, 118.6, 118.4, 117.8, 117.1, 116.6, 114.7, 112.2, 111.8, 111.6, 98.6, 97.8, 86.5, 84.8, 79.1, 78.6, 77.2, 77.0, 76.2, 76.0, 73.1, 71.2, 66.4, 66.1, 65.7, 62.7, 61.5, 61.4, 61.1, 60.1, 60.0, 38.1, 36.7, 34.1, 33.7, 23.7; MS (FAB+) 667, 645, 339; HRMS (FAB+) calcd for $C_{34}H_{36}N_4O_8$ 645.2561 (M + H)$^+$, found 645.2554.

2-Bromo-3-(7-chloro-1*H*-indol-3-yl)-*N*-methylmaleimide, 29. 7-Chloroindole (5.54 g, 34.45 mmol) was dissolved in 60 mL of toluene. Ethylmagnesium bromide (3 M in Et_2O, 11.5 mL, 34.45 mmol) was then slowly added. After 30 min, *N*-methyl dibromomaleimide (10.2 g, 37.9 mmol, in 50 mL of toluene) was then cannulated into the indole solution. After 19 h, the reaction was poured into 200 mL of saturated aqueous NH_4Cl and extracted with EtOAc (3×). The combined organic extracts were then dried (Na_2SO_4) and concentrated. Purification by silica gel chromatography (20−40% EtOAc/hexane) provided 8.37 g (72%) of the mixed maleimide **29** as a yellow solid. (Note: the column must be run quickly in order to avoid decomposition, the product being sensitive to silica gel).

29: mp 176−178 °C (acetone); R_f = 0.23 (30% EtOAc/hexanes); IR (KBr) 3400, 3137, 2930, 1707, 1602 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 12.45 (s, 1H), 8.01 (d, 1H, J = 3.0 Hz), 7.82 (d, 1H, J = 8.1 Hz), 7.30 (d, 1H, J = 7.6 Hz), 7.15 (t, 1H, J = 7.9 Hz), 3.00 (s, 3H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 168.8, 166.3, 137.0, 133.3, 131.3, 126.3, 122.0, 121.3, 121.1, 116.5, 115.8, 104.8, 24.6; MS (CI+) 337; HRMS (CI+) calcd for $C_{13}H_8N_2O_2BrCl$ 337.9458, found 337.9463.

2-(7-Chloro-1*H*-indol-3-yl)-3-(1*H*-indol-3-yl)-*N*-methylmaleimide, 30. Indole (3.80 g, 32.25 mmol) was dissolved in 60 mL of toluene, and ethylmagnesium bromide (3 M in Et_2O, 10.75 mL, 32.25 mmol) was added. The reaction was then warmed to 50 °C for 30 min. The solution of indole Grignard was then cannulated into a solution of bromomaleimide **29** (3.66 g, 10.75 mmol) in 15 mL of THF, 15 mL of toluene, and 3 mL of Et_2O. The reaction mixture was then heated to reflux for 21 h. The reaction was then allowed to cool to room temperature and quenched with 50 mL of saturated aqueous NH_4Cl. The reaction mixture was then poured into 200 mL of brine and extracted with EtOAc (3×). The extracts were then dried (Na_2SO_4) and concentrated. Purification by silica gel chromatography (5% acetone/CH_2Cl_2) gave 3.13 g (77%) of the unsymmetrical bisindole **30** as a red foam.

30: mp 246−250 °C (acetone); R_f = 0.32 (30% EtOAc/hexanes); IR (KBr) 3409, 3317, 2973, 1682 cm^{-1}; ^{1}H NMR (acetone-d_6, 500 MHz) δ 11.09 (bs, 1H), 10.87 (bs, 1H), 7.92 (s, 1H), 7.88 (s, 1H), 7.41 (d, 1H, J = 8.0 Hz), 7.04 (d, 1H, J = 7.6 Hz), 6.98 (t, 1H, J = 7.2 Hz), 6.90 (d, 1H, J = 8.0 Hz), 6.85 (d, 1H, J = 8.0 Hz), 6.61−6.65 (m, 2H), 3.10 (s, 3H); ^{13}C NMR (acetone-d_6, 125 MHz) δ 172.5, 137.2, 134.0, 130.3, 130.2, 130.1, 129.5, 128.6, 127.0, 126.4, 122.8, 122.2, 122.0, 121.2, 121.1, 120.5, 117.0, 112.4, 108.6, 107.1, 24.1; MS (CI+) 375, 329; HRMS (CI+) calcd for $C_{21}H_{14}N_3O_2Cl$ 375.0774, found 375.0776. Anal. Calcd for $C_{21}H_{14}N_3O_2Cl$: C, 67.19; H, 3.76; N, 11.20. Found: C, 67.4; H, 3.93; N, 10.93.

1-Methyl-*cis*-3-(7-chloro-1H-indol-3-yl)-4-(1H-indol-3-yl)-2,5-pyrrolidinedione (±)-31. Unsymmetrical maleimide **30** (2.35 g, 6.25 mmol) and palladium on carbon (10%, 665 mg, 0.626 mmol) were suspended in 40 mL of DMF. The reaction mixture was then shaken on a Parr shaker under 50 psi of H_2 for 26 h. The reaction was then filtered through Celite with EtOAc, washed with water (1×) and brine (2×), dried (Na_2SO_4), and concentrated. Purification by silica gel chromatography (50% EtOAc) provided (±)-**31** (1.44 g, 61%) as an off-white solid.

(±)-31: mp 118−122 °C (EtOAc); R_f = 0.23 (40% EtOAc/hexanes); IR (KBr) 3386, 3055, 2863, 1773, 1697 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 11.01 (s, 1H), 10.67 (s, 1H), 7.31 (d, 1H, J = 8.0 Hz), 7.28 (d, 1H, J = 7.9 Hz), 7.13 (d, 1H, J = 8.1 Hz), 7.01 (d, 1H, J = 7.0 Hz), 6.84−6.95 (m, 5H), 4.97 (d, 1H, J = 9.0 Hz), 4.93 (d, 1H, J = 9.0 Hz), 3.12 (s, 3H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 178.1, 178.0, 135.4, 132.2, 129.0, 126.7, 125.7, 124.5, 120.7, 120.3, 119.4, 118.4, 118.2, 117.5, 115.5, 111.3, 109.5, 108.1, 43.5, 43.4, 24.8; MS (CI+) 379, 377, 292; HRMS (CI+) calcd for $C_{21}H_{16}N_3O_2Cl$ 377.0931, found 377.0930. Anal. Calcd for $C_{21}H_{16}N_3O_2Cl$: C, 66.76; H, 4.27; N, 11.12. Found: C, 66.47; H, 4.34; N, 11.02.

(4b*R*,4c*R*,7a*R*,12b*S*)-*rel*-6-Methyl-11-chloro-4b,4c,6,7,-7a,12,12b,13-octahydroindolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione, (±)-32. Unsymmetrical bisindolylsuccinimide (±)-**31** (298 mg, 0.784 mmol) was dissolved in TFA (5 mL, 64.9 mmol) and heated to reflux. After 12 h, the reaction was cooled to room temperature and taken up in EtOAc. The reaction was then washed with 1 N NaOH (3×), dried (Na_2SO_4), and concentrated. Purification by silica gel chromatography (3% acetone/CH_2Cl_2) provided chlorinated indolylindoline (±)-**32** (248 mg, 82% yield) as a buff foam.

(±)-32: mp 288−290 °C (acetone); R_f = 0.33 (4% acetone/CH_2Cl_2); IR (KBr) 3379, 3031, 2922, 1774, 1690 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 11.22 (s, 1H), 7.74 (d, 1H, J = 8.0 Hz), 7.17 (d, 1H, J = 7.3 Hz), 7.14 (d, 1H, J = 7.6 Hz), 6.99 (t, 1H, J = 7.9 Hz), 6.89 (t, 1H, J = 7.6 Hz), 6.59 (t, 1H, J = 7.4 Hz), 6.53 (d, 1H, J = 7.7 Hz), 6.06 (s, 1H), 4.75 (d, 1H, J = 7.8 Hz), 4.29 (dd, 1H, J = 7.7, 1.8 Hz), 4.17 (bd, 2H, J = 7.6 Hz), 2.80 (s, 3H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 178.3, 176.6, 149.6, 135.9, 133.1, 128.4, 127.9, 127.4, 122.5, 121.1, 120.1, 119.3, 117.9, 115.5, 109.1, 105.9, 53.2, 39.4, 39.1, 37.7, 24.6; MS (CI+) 379, 377; HRMS (CI+) calcd for $C_{21}H_{16}N_3O_2Cl$ 377.0931, found 377.0939. Anal. Calcd for $C_{21}H_{16}N_3O_2Cl$: C, 66.76; H, 4.27; N, 11.12. Found: C, 66.79; H, 4.39; N, 10.92.

(4b*R*,4c*R*,7a*R*,12b*S*)-*rel*-1-Chloro-6-methyl-4b,4c,6,7,-7a,12,12b,13-octahydroindolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione, (±)-33. Unsymmetrical bisindolylsuccinimide (±)-**31** (1.37 g, 3.59 mmol) was dissolved in 50 mL of $CHCl_3$, and methanesulfonic acid (1.16 mL, 18 mmol) was added. After 3 h, the reaction was taken up in EtOAc and washed with 1 N NaOH (3×), dried (Na_2SO_4), and concentrated. Purification by silica gel chromatography (4% acetone/CH_2Cl_2) provided chlorinated indolylindoline (±)-**33** (1.29 g, 94% yield) as a buff foam.

(±)-33: mp 172−175 °C (acetone); R_f = 0.44 (4% acetone/CH_2Cl_2); IR (KBr) 3370, 3062, 2932, 1774, 1695 cm^{-1}; ^{1}H NMR (acetone-d_6, 500 MHz) δ 10.26 (s, 1H), 7.89 (d, 1H, J = 8.0 Hz), 7.29 (d, 1H, J = 8.0 Hz), 7.23 (d, 1H, J = 7.3 Hz), 7.08 (t, 1H, J = 7.2 Hz), 7.00 (t, 1H, J = 7.9 Hz), 6.95 (d, 1H, J = 8.6 Hz), 6.65 (t, 1H, J = 7.8 Hz), 5.67 (s, 1H), 4.99 (d, 1H, J = 7.9 Hz), 4.46 (bd, 1H, J = 7.9 Hz), 4.28 (d, 1H, J = 7.7 Hz), 4.25 (dd, 1H, J = 9.9, 2.3 Hz), 2.85 (s, 3H); ^{13}C NMR (acetone-d_6, 125 MHz) δ 178.6, 177.1, 147.6, 137.7, 134.3, 132.0, 128.6, 127.0, 123.2, 122.1, 121.7, 120.4, 120.2, 115.4, 111.8, 106.5, 54.5, 41.3, 41.2, 39.0, 24.9; MS (CI+) 379, 378, 377, 319, 266; HRMS (CI+) calcd for $C_{21}H_{16}N_3O_2Cl$ 377.0931, found 377.0932. Anal. Calcd for $C_{21}H_{16}N_3O_2Cl$: C, 66.76; H, 4.27; N, 11.12. Found: C, 66.97; H, 4.39; N, 10.93.

6-Methyl-11-chloro-12-[β-D-glucopyranosyl]-6,7,12,13-tetrahydroindolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione, (+)-34. Chlorinated indolylindoline (±)-**32** (248 mg, 0.650 mmol), α-D-glucose (351 mg, 1.95 mmol), and $(NH_4)_2SO_4$ (1 mg, 0.007 mmol) were refluxed in 6 mL of MeOH for 26 h. The reaction mixture was then preadsorbed on silica gel and purified by silica gel chromatography (8% MeOH/$CHCl_3$) to give 301 mg (85%) of a 1:1 mixture of glycosylated diastereomers. The mixture of diastereomers was then dissolved in 6 mL of THF. DDQ (315 mg, 1.38 mmol) was then added. After 26 h the reaction mixture was poured into 100 mL of saturated aqueous $NaHCO_3$ and stirred vigorously. The reaction was then filtered and the filtrate purified by silica gel chromatography (10% MeOH/$CHCl_3$) provided 229 mg (77%, 66% from (±)-**32**) of chlorinated indolocarbazole (+)-**34** as a yellow solid.

(+)-34: mp 342 °C dec (THF/MeOH); $[\alpha]_D$ +166.4 (*c* 0.60, THF); R_f = 0.10 (10% MeOH/$CHCl_3$); IR (KBr) 3370, 2922, 1748, 1691 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 10.59 (s, 1H), 9.11 (d, 1H, J = 7.5 Hz), 9.03 (d, 1H, J = 8.0 Hz), 8.05 (d, 1H, J = 8.5 Hz), 7.68 (d, 1H, J = 7.7 Hz), 7.59 (t, 1H, J = 7.9 Hz), 7.41 (t, 1H, J = 7.9 Hz), 7.35 (t, 1H, J = 7.5 Hz), 6.29 (d, 1H, J = 9.5 Hz), 5.51 (d, 1H, J = 5.0 Hz), 5.33 (d, 1H, J = 5.0 Hz), 5.04−5.08 (m, 2H), 4.02−4.05 (m, 1H), 3.92−3.95 (m, 2H), 3.88 (td, 1H, J = 9.1, 5.2 Hz), 3.79 (td, 1H, J = 9.0, 5.8 Hz), 3.64 (td, 1H, J = 8.8, 5.4 Hz), 3.17 (s, 3H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 169.3, 169.2, 142.1, 137.1, 128.8, 128.0, 127.0, 126.5, 124.2, 123.5, 123.2, 121.8, 120.7, 120.6, 119.8, 119.6, 118.6, 117.1, 116.0, 111.7, 84.7, 81.0, 77.1, 73.3, 70.0, 60.6, 23.7; MS (CI+) 535, 373; HRMS (FAB+) calcd for $C_{27}H_{22}N_3O_7Cl$ 535.1146, found 535.1142. Anal. Calcd for $C_{27}H_{22}N_3O_7Cl+H_2O$: C, 58.54; H, 4.37; N, 7.59. Found: C, 58.43; H, 4.33; N, 7.48.

1-Chloro-6-methyl-12-[β-D-glucopyranosyl]-6,7,12,13-tetrahydroindolo[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione, (+)-35. Chlorinated indolylindoline (±)-**33** (30 mg, 0.078 mmol), α-D-glucose (281 mg, 1.56 mmol) and CSA (18 mg, 0.078 mmol) were suspended in 1 mL of DMF for 65 h. The reaction mixture was then taken up in EtOAc and washed with saturated aqueous $NaHCO_3$ (3×), dried (Na_2SO_4), and concentrated. Purification by silica gel chromatography (8% MeOH/$CHCl_3$) gave 28 mg (66%) of a 1:1 mixture of glycosylated diastereomers. The mixture of diastereomers was then dissolved in 1 mL of THF. DDQ (54 mg, 0.239 mmol) was then added. After 5 days the reaction mixture was poured into saturated aqueous $NaHCO_3$ and extracted with EtOAc (3×), dried (Na_2SO_4) and concentrated. Purification by silica gel chromatography (10% MeOH/$CHCl_3$) provided 24 mg (86%, 57% from (±)-**33**) of indolocarbazole glycoside (+)-**35** as a yellow solid.

(+)-35: mp 348 °C dec (THF/MeOH); $[\alpha]_D$ +173.1 (*c* 0.35, DMSO); R_f = 0.20 (10% MeOH/$CHCl_3$); IR (KBr) 3453, 3313, 3070, 2939, 1744, 1694 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 11.85 (s, 1H), 9.24 (d, 1H, J = 8.0 Hz), 9.10 (d, 1H, J = 8.0 Hz), 7.72 (d, 1H, J = 8.1 Hz), 7.64 (d, 1H, J = 7.7 Hz), 7.59 (t, 1H, J = 7.7 Hz), 7.39 (aq, 2H, J = 8.0 Hz), 6.91 (d, 1H, J = 8.3 Hz), 6.15 (bt, 1H, J = 3.5 Hz), 5.30 (d, 1H, J = 5.5 Hz), 5.08 (d, 1H, J = 5.0 Hz), 4.83 (d, 1H, J = 4.5 Hz), 4.11 (dd, 1H, J = 10.8, 3.3 Hz), 3.96 (bd, 1H, J = 10.6 Hz), 3.85−3.90 (m, 1H), 3.84 (t, 1H, J = 9.0 Hz), 3.32−3.41 (m, 2H), 3.20 (s, 3H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 169.4, 169.3, 140.8, 138.2, 130.3, 129.8, 129.6, 127.4, 125.5, 124.5, 123.8, 122.3, 121.7, 121.0, 120.6, 119.3, 118.1, 117.4, 116.5, 112.1, 84.0, 79.0, 76.9, 72.0, 67.4, 58.4, 23.8; MS (FAB+) 535, 373; HRMS (FAB+) calcd for $C_{27}H_{22}N_3O_7Cl$ 535.1146, found 535.1148. Anal. Calcd for $C_{27}H_{22}N_3O_7Cl+H_2O$: C, 58.54; H, 4.37; N, 7.59. Found: C, 58.54; H, 4.32; N, 7.45.

1-Chloro-6-methyl-12-[*O*-[4-(2-trimethylsilyloxycarbonyl)methylamino-2,4-dideoxy-β-L-xylopyranosyl]-(1→6)-4-*O*-methyl-β-D-glucopyranosyl]-6,7,12,13-tetrahydroindolo-[2,3-*a*]pyrrolo[3,4-*c*]carbazole-5,7-dione 36. Chlorinated indolylindoline (±)-**33** (860 mg, 2.24 mmol), Teoc-protected aminodisaccharide **26** (349 mg, 0.747 mmol), and CSA (58 mg, 0.247 mmol) were suspended in 4 mL of DMF for 67 h. The reaction mixture was then quenched with NH_4OH and concentrated in vacuo. The residue was then purified by silica gel chromatography (5% MeOH/EtOAc) to give 219 mg (35%) of a 1:1 mixture of glycosylated diastereomers. The mixture of diastereomers was then dissolved in 2 mL of CH_2Cl_2. DBU (120 μL, 0.789 mmol) was then added followed by I_2 (201 mg, 0.789 mmol). After 23 h the reaction mixture was poured into saturated aqueous $NaHCO_3$ and extracted with EtOAc (3x), dried (Na_2SO_4) and concentrated. Purification by silica gel chromatography (5% MeOH/EtOAc) provided 113 mg (52%) of indolocarbazole glycoside **36** as a yellow solid.

36: mp 330 °C dec; $[\alpha]_D$ +110.3 (*c* 0.85, THF); R_f = 0.55 (50% hexane/acetone); IR (KBr) 3445, 3359, 2952, 1748, 1698 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz, 323 K) δ 10.53 (s, 1H), 9.08 (d, 1H, J = 7.9 Hz), 7.79 (d, 1H, J = 8.0 Hz), 7.64−7.68 (m, 2H), 7.41 (aq, 2H, J = 7.1 Hz), 6.89 (d, 1H, J = 9.2 Hz), 5.40 (d, 1H, J = 5.9 Hz), 5.07 (bs, 1H), 5.01 (d, 1H, J = 5.8

Hz), 4.60 (bs, 1H), 4.10 (d, 1H, J = 11.5 Hz), 4.04 (bd, 1H, J = 9.4 Hz), 3.90−3.98 (m, 3H), 3.81 (bs, 1H), 3.62 (s, 3H), 3.54−3.59 (m, 3H), 3.30−3.32 (m, 1H), 3.18 (s, 3H), 2.31 (dd, 1H, J = 13.0, 4.0 Hz), 2.08 (s, 3H), 1.62−1.65 (m, 1H), 0.80−0.86 (m, 2H), −0.05−0.03 (m, 2H), −0.09 (s, 9H); ^{13}C NMR (acetone-d_6, 125 MHz) δ 169.0, 168.9, 155.8, 139.9, 137.8, 125.2, 124.5, 123.8, 122.4, 121.4, 121.1, 121.0, 119.0, 118.6, 117.6, 116.2, 112.0, 98.3, 84.6, 78.8, 77.8, 77.4, 72.0, 65.7, 65.5, 62.6, 62.5, 61.7, 60.2, 58.4, 57.9, 55.8, 38.5, 32.1, 29.6, 28.2, 23.6, 17.1, −1.5; MS (FAB+) 824, 822; HRMS (FAB+) calcd for $C_{40}H_{47}N_4O_{11}ClSi$ 822.2698, found 822.2685. Anal. Calcd for $C_{40}H_{47}N_4O_{11}ClSi$: C, 58.35; H, 5.75; N, 6.80. Found: C, 58.11; H, 5.77; N, 6.56.

AT2433-A1, 37. Teoc-protected indolocarbazole glycoside **36** (58 mg, 0.070 mmol) was dissolved in 2 mL of THF. Molecular sieves (4 Å) (200 mg) and TBAF (1 M in THF, 200 μL, 0.20 mmol) were then added. After 3 h, the reaction was filtered, adsorbed on silica gel, and purified by silica gel chromatography (10% MeOH/1% NH_4OH/89% $CHCl_3$). This provided 39 mg (82%) of **AT2433-A1 (37)** as a yellow solid.

37: mp 330 °C dec; $[\alpha]_D$ +104.0 (c 0.3, DMSO); R_f = 0.43 (10% MeOH/$CHCl_3$); IR (KBr) 3422, 2927, 1745, 1694 cm^{-1}; ^{1}H NMR (DMSO-d_6, 500 MHz) δ 10.55 (s, 1H), 9.22 (d, 1H, J = 8.0 Hz), 9.10 (d, 1H, J = 7.8 Hz), 9.10 (d, 1H, J = 7.8 Hz), 7.79 (d, 1H, J = 8.3 Hz), 7.62−7.70 (m, 2H), 7.41−7.46 (m, 2H), 6.83 (d, 1H, J = 8.8 Hz), 5.38 (d, 1H, J = 5.8 Hz), 5.05 (t, 1H, J = 1.8 Hz), 4.98 (d, 1H, J = 5.4 Hz), 4.91 (bs, 1H), 4.12 (d, 1H, J = 10.4 Hz), 4.01 (bd, 1H, J = 9.6 Hz), 3.92 (dd, 1H, J = 11.6, 3.1 Hz), 3.74 (dd, 1H, J = 11.1, 3.7 Hz), 3.61−3.68 (m, 2H), 3.60 (s, 3H), 3.52−3.57 (m, 3H), 3.37−3.41 (m, 1H), 3.20 (s, 3H), 2.38 (bs, 1H), 2.21 (s, 3H), 2.19−2.20 (m, 1H), 1.69−01.74 (m, 1H); ^{13}C NMR (DMSO-d_6, 125 MHz) δ 169.1, 169.0, 140.0, 138.1, 129.8, 129.6, 129.4, 127.8, 125.3, 124.5, 123.8, 122.5, 121.5, 121.1, 121.0, 119.1, 118.6, 117.5, 116.4, 112.1, 98.7, 84.5, 78.4, 77.8, 77.3, 72.0, 66.3, 65.6, 61.7, 61.5, 60.1, 57.5, 338., 23.7; MS (FAB+) 679; HRMS (FAB+) calcd for $C_{34}H_{35}N_4O_9Cl$ (M + H) 679.2170, found 679.2170.

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Supporting Information Available: ^{1}H NMR spectra for compounds **12**, **13**, **28**, **29**, and **37**. This material is available free of charge via the Internet at http://pubs.acs.org.

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