JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

Lewis Acid Catalyzed Cyclization of Glycals/2-Deoxy-D-ribose with Arylamines: Additional Findings on Product Structure and Reaction Diastereoselectivity

Chengtang Du,[†,‡,∥] Fulong Li,[†,§,∥] Xuefeng Zhang,[†] Wenxiang Hu,*[,‡] Qizheng Yao,[§] and Ao Zhang*[,‡]

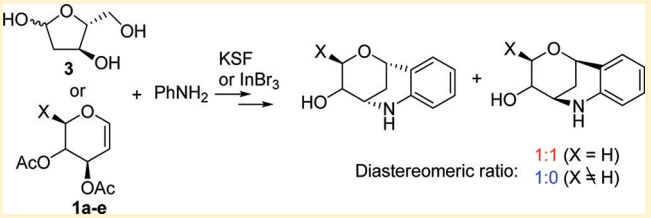
[†]Synthetic Organic & Medicinal Chemistry Laboratory (SOMCL), Shanghai Institute of Materia Medica (SIMM), Shanghai 201203, China

[‡]Chemistry Department, Capital Normal University, Beijing 100048, China

[§]Department of Medicinal Chemistry, China Pharmaceutical University, Nanjing 210009, China

Supporting Information

ABSTRACT: The cyclization reactions of arylamines with 2-deoxy-D-ribose or glycals were reinvestigated in the current report. In the montmorillonite KSF- or $InCl_3$-initiated reactions of 2-deoxy-D-ribose with arylamines, a pair of diastereomeric tetrahydro-2*H*-pyran-fused tetrahydroquinolines was obtained in a nearly 1:1 ratio where the structure of one diastereomer was incorrectly assigned in the literature. Meanwhile, the diastereoselectivity in $InBr_3$-catalyzed cyclization of glycals with arylamines was also incorrectly reported previously. It was found that high diastereomeric selectivity was achieved only when a C5-substituted glycal was used; otherwise, a pair of diastereomers was obtained in moderate yield with 1:1 diastereomeric ratio. Furthermore, tetrahydrofuran-fused tetrahydroquinolines **5b** and **5b′** were also prepared successfully by using TBDPS-protected ribose as the glycal precursor and montmorillonite KSF as the activator.



INTRODUCTION

Glycals are highly active electrophiles capable of reacting with various nucleophiles to provide diversified *C*-, *N*-, or *O*-glycosides that are generally biologically valuable building blocks.[1−6] In most cases, these reactions are initiated by an appropriate Lewis acid, such as $BF_3.Et_2O$, TMSOTf, $Bi(OTf)_3$, $YbCl_3$, $Sm(OTf)_3$, $InBr_3$, $InCl_3$, $CeCl_3$, and $FeCl_3$. In several cases, solid Lewis acids[7,8] such as montmorillonite clays (e.g., KSF), zeolites, heteropolylacids, and ion-exchange resins were also used.

Among these reactions, Lewis acid-promoted cyclizations between glycals and arylamines have attracted attention recently because of the ready construction of a C- and a N-glycoside linkage simultaneously in one step.[9−18] Specifically, Yadav and his colleagues[9] reported that reaction of D-glucal **1a** or D-xylal **1b** with aniline under 10% $InBr_3$ afforded tetrahydro-2*H*-pyran-fused tetrahydroquinolines **2a** or **2b** in high yield and excellent stereoselectivity (Scheme 1a). Interestingly, in the same year, Li et al.[10] reported that direct treatment of 2-deoxy-D-ribose **3** with aniline in the presence of 8−12% $InCl_3$ provided similar product **4a**, along with another cyclized product, tetrahydrofuran-fused tetrahydroquinolines **5a**, in almost identical yield (Scheme 1b). The unique structure of **5a** was claimed again in 2006 by the previous group[13] who conducted the same reaction but using KSF as the catalyst and obtained the same products **4a** and **5a**. Such a powerful cyclization reaction was further explored by us[15,18] more recently in the synthesis of antitumor natural product marmycin A.

It is intriguing that in our work,[15] treating 1-amino-angucyclinone **6** with D-glucal **1a** under 10% $InBr_3$ led to a pair of diastereomers **7** and **8** bearing the same tetrahydro-2*H*-pyran-fused tetrahydroquinoline skeleton in nearly 1:1 ratio (Scheme 1c), different from the results described above.[9,10,13] The discrepancy in product structure and cyclization diastereoselectivity alerted us that one of the cyclization products in the literature may be accidently overlooked and the structure of one diastereomer may be incorrectly assigned as well. In this regard, we decided to reinvestigate the cyclization reactions as reported in the literature,[9,10,13] and herein we report our findings and revision to the structure of **5a**.

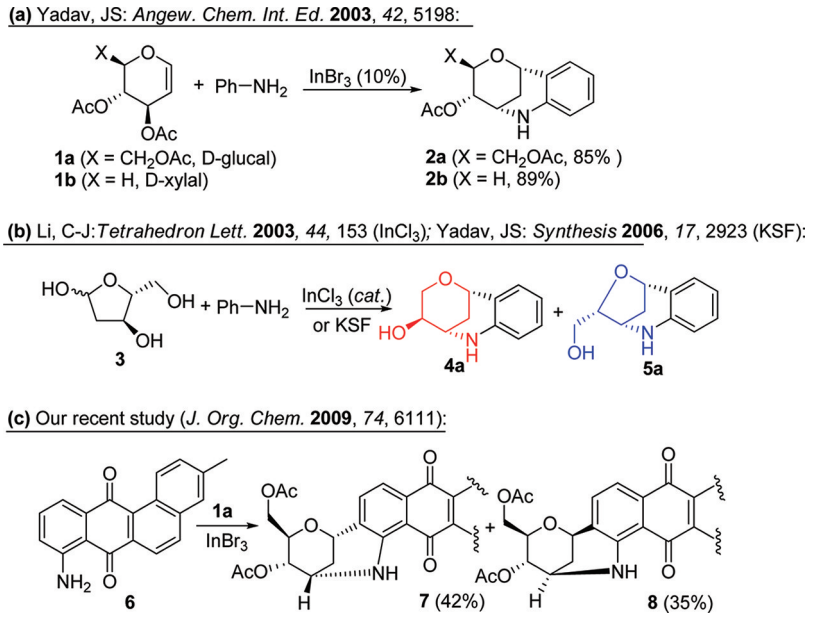
RESULTS AND DISCUSSION

Tetrahydrofuran-fused tetrahydroquinoline **5a** was assigned as the second product by both Yadav's and Li's groups in the literature,[10,13] which was different from the first product **4a** bearing a tetrahydro-2*H*-pyran-fused tetrahydroquinoline skeleton. However, product **5a** was not identified in their previous report[9] (Scheme 1a) where glycal **1a** or **1b** other than 2-deoxy-D-ribose **3** was used to react with arylamines. Compound **4a** was confirmed by X-ray analysis,[10] whereas the structure of **5a**

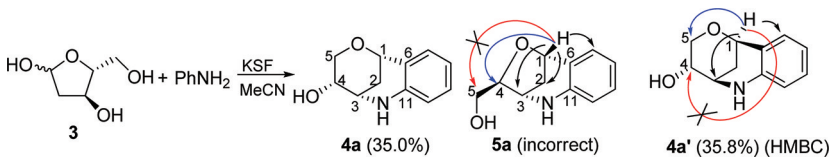
Received: July 31, 2011
Published: October 3, 2011

   dx.doi.org/10.1021/jo2015483 | *J. Org. Chem.* 2011, 76, 8833−8839

Scheme 1. Reported Cyclization of Glycals with Arylamines



Scheme 2. Reaction of Deoxy-D-ribose 3 with Aniline



was mainly assigned on the basis of a deduction from its spectroscopic data.[10,13]

To confirm the structure of **5a**, we repeated the same reaction[13] by treating 1 equiv of aniline with 2-deoxy-D-ribose (**3**) in the presence of montmorillonite KSF (a heterogeneous Lewis acid). Similar to the literature' report,[13] two products were obtained in a nearly 1:1 ratio with a combined yield of 71%. The first product gave spectroscopic data (see the Supporting Information) almost identical to that of **4a** in the literature.[13] Specifically, the H-1 and H-3 protons showed multiplicity (br s) indicating their equatorial conformations. Therefore, the carbohydrate component was assigned as a chair conformation. The *C*- and *N*-glycoside linkage was ascertained by the ^{13}C NMR where C-6 and C-11 chemical shifts were 119.9 and 145.3 ppm, respectively.

The ^{1}H and ^{13}C NMR of the second product were in agreement to the reported data[13] for compound **5a**. However, a close examination of its 2D NMR (HMBC, HSQC, and $^{1}H-^{13}C$ COSY) indicated that the correct structure of this product is compound **4a′**, other than the reported structure **5a**. In the HMBC spectra of **4a′**, a correlation between H-1 (4.73 ppm) and C-5 (63.7 ppm) was observed, whereas no correlation between H-1 and C-4 was identified. These correlations are opposite to that of structure **5a** (Scheme 2). Further evidence of the structure of **4a′** came from the CD spectrum of both **4a** and **4a′** where complete opposite Cotton effects were observed (Figure 1) indicating the opposite stereochemistry of the two carbons (C-1, C-3) adjacent to the aromatic system. Gratifyingly, X-ray crystals of both **4a** and **4a′** were obtained as hairy needles that finally secured the absolute structures of diastereomeric **4a** and **4a′** (Figure 2).

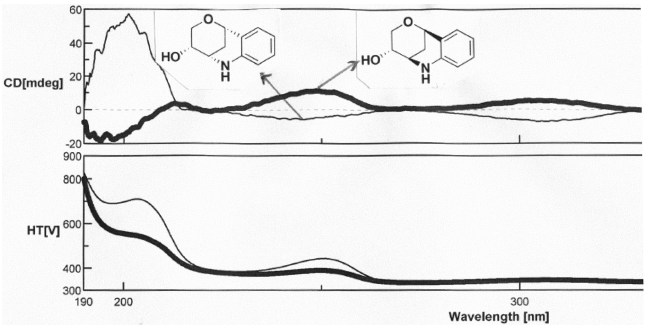


Figure 1. CD and UV spectrum of **4a** and **4a′**.

After revision of the cyclization product, $InCl_3$ (10%) was used as the replacement of montmorillonite KSF to initiate the reaction of 2-deoxy-D-ribose (**3**) with aniline, as described by Li et al.[10] It was found that the same products **4a** and **4a′** were obtained in 1:1 ratio, although the combined yield was slightly lower (68%) than when montmorillonite KSF was used as the Lewis acid. This result further confirms that the incorrect structure was reported by both groups in the literatures.[10,13] To explore the generality of this cyclization, a small series of substituted anilines were used to react with **3**, and similar products were obtained in 65−86% combined yields (Table 1). Anilines with an electron-donating substituent generally gave slightly lower yields (**4e** and **4e′**, **4f** and **4f′**). The diastereomeric relationship of the two products in each case was evidenced by comparison of their CD spectra and optical rotations (see the Supporting Information).

Although different from the literature report,[10,13] the formation of a pair of diastereomers was in agreement with

dx.doi.org/10.1021/jo2015483 | J. Org. Chem. 2011, 76, 8833−8839

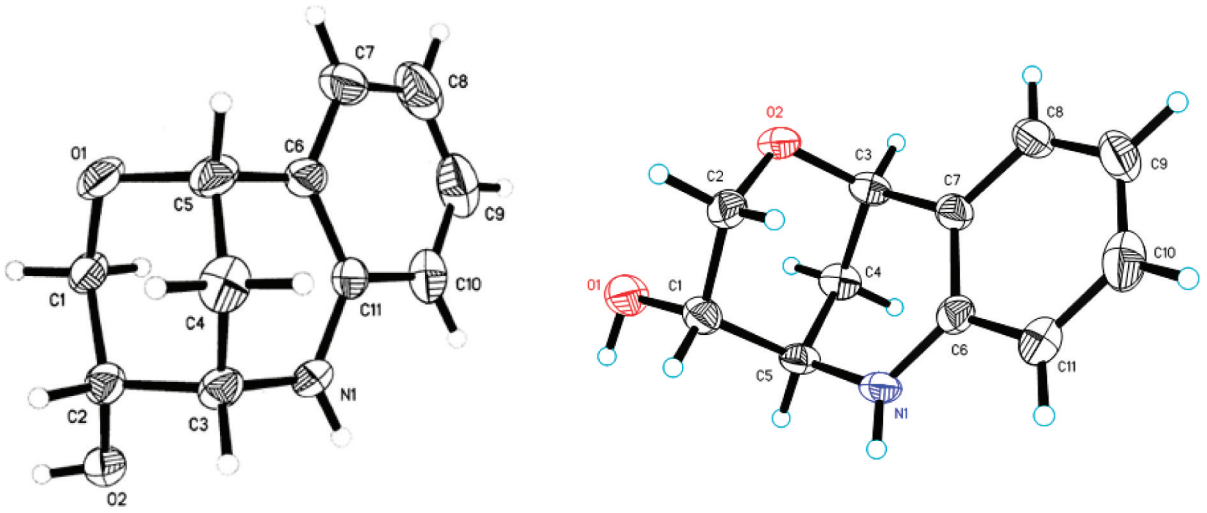
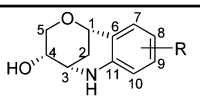
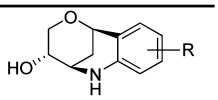


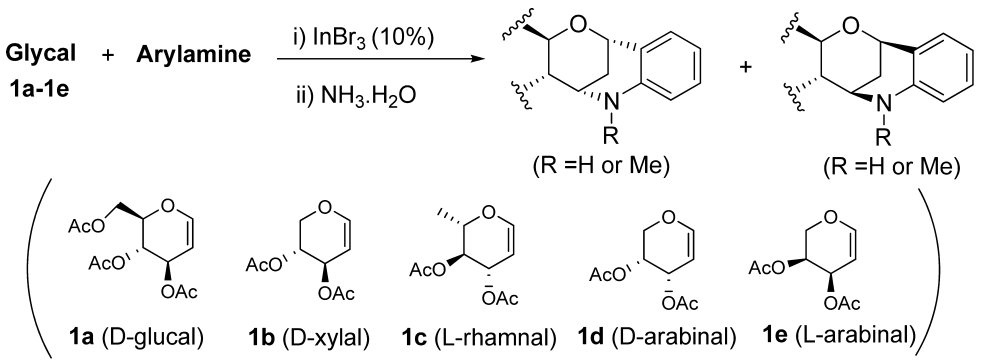
Figure 2. X-ray crystals of diastereomeric **4a** and **4a′**.

Table 1. Montmorillonite KSF-Catalyzed Cyclization of 2-Deoxy-D-ribose with Arylamines

Aryl Amine	Product		Yield[a]
			
aniline	**4a** (R = H)	**4a'** (R = H)	71%
4-chloroaniline	**4b** (R = 8-Cl)	**4b'** (R = 8-Cl)	78%
2-chloroaniline	**4c** (R = 10-Cl)	**4c'** (R = 10-Cl)	86%
3-chloroaniline	**4d** (R = 9-Cl)	**4d'** (R = 9-Cl)	72%
3-toluidine	**4e** (R = 9-CH_3)	**4e'** (R = 9-CH_3)	65%
4-toluidine	**4f** (R = 8-CH_3)	**4f'** (R = 8-CH_3)	68%

[a]Combined yield; the ratios of the two diastereomers were nearly 1:1.

Scheme 3. Reactions of Various Glycals with Arylamines



our previous report[15] in the reaction of 1-aminoangucyclinone **6** and variant glycals (Scheme 1c). This result encouraged us to reinvestigate the initial glycosidation reaction reported[9] in 2003, where several glycals reacted with variant arylamines and only one diastereomer was obtained with high stereoselectivity (Scheme 1a).

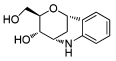
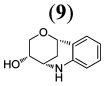
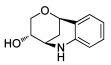
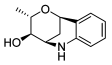
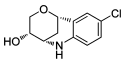
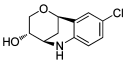
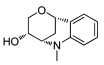
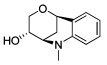
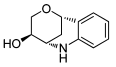
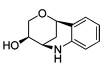
Following the same reaction protocols,[9] aniline or an appropriately substituted arylamine was reacted with equivalent

dx.doi.org/10.1021/jo2015483 | J. Org. Chem. 2011, 76, 8833–8839

of diversified glycals[15,19] (**1a**–**1e**) with 10% $InBr_3$ as the catalyst. Since the acetyl-containing glycosidation products have very similar polarity with the unreacted glycals, they were subsequently deprotected by treating with ammonia, and the final products were conveniently separated by flash chromatography (Scheme 3).[20]

First, we reinvestigated the reaction between aniline and D-glucal **1a**. Compound **9** bearing both *C*- and *N*-glycoside linkages was obtained in 50% isolated yield (entry 1, Table 2).

Table 2. Reactions of Various Glycals with Arylamines

entry	products		yield[a] (de[b])
1 (**1a**)	 (**9**)	-	50%
2 (**1b**)	 (**4a**)	 (**4a'**)	66% (1.0:1.15)
3 (**1c**)	 (**10**)	-	64%
4 (**1d**)	 (**4b**)	 (**4b'**)	66% (1.0:1.0)
5 (**1d**)	**4a**	**4a'**	62% (1.1:1.0)
6 (**1d**)	 (**11**)	 (**11'**)	46% (1.1:1.0)
7 (**1e**)	 (**12**)	 (**12'**)	69% (1.0:1.1)

[a]Combined yields. [b]Ratio of the two diastereomers determined by the isolated yields.

The structure of **9** was fully characterized by all spectroscopic data and is identical to that reported in the literature.[9] However, when D-xylal **1b** lacking the C-5 substituent was used, the reaction yielded a pair of diastereomers **4a** and **4a′** in 66% combined yield and nearly 1:1 ratio (entry 2, Table 2), different from the literature result where only one single diastereomer was produced in high yield (89%).[9] All of the spectroscopic data and optical rotation of **4a** and **4a′** are identical to that obtained in Table 1 (entry 1). Again, this finding was not in agreement with the literature report but matches the result described in Table 1 and that of our earlier report.[15] In the case of C-5 substituted L-rhamnal **1c** (entry 3, Table 2), only one diastereomer **10** was obtained in 64% yield. Another diastereomer was not produced indicating that the diastereoselectivity in the cyclization reaction was determined by the glycal C5-substituent. Such analysis was further confirmed by reactions of arylamines with C5-nonsubstituted D-**1d** and L-**1e** arabinals (entries 4–7) in which a pair of diastereomers were formed, respectively. In the case of reaction of D-arabinal **1d** with 4-chloroaniline (entry 4, Table 2), diaseteromeric **4b** and **4b′** were obtained in 66% combined yield. It has to be pointed out that reactions of aniline with D-xylal **1b** and D-arabinal **1d** led to the same pair of diastereomers **4a** and **4a′** (entries 2 and 5, Table 2). Moreover, diastereomers **12′** and **12** obtained in the reaction of aniline with L-arabinal (**1e**) (entry 7) were enantiomers of **4a** and **4a′**, respectively. The enantiomeric relationships between **12** and **4a′**, as well as **12′** and **4a**, were evidenced by their identical spectroscopic data, opposite Cotton effects in CD spectrum, and opposite optical rotations ($[\alpha]^{20}_D$: **4a**, +65 (*c* 0.6, MeOH); **12′**, −51 (*c* 0.6, MeOH); **4a′**, +118 (*c* 0.6, MeOH); **12**, −110 (*c* 0.6, MeOH)). *N*-Methyl-substituted aniline also participated in this reaction (entry 6) and afforded the corresponding diastereomers **11** and **11′** in 46% combined yield with 1.0:1.1 ratio.

The diastereochemistry in the glycosidation reaction can be rationalized by the mechanism analysis proposed in Figure 3. In

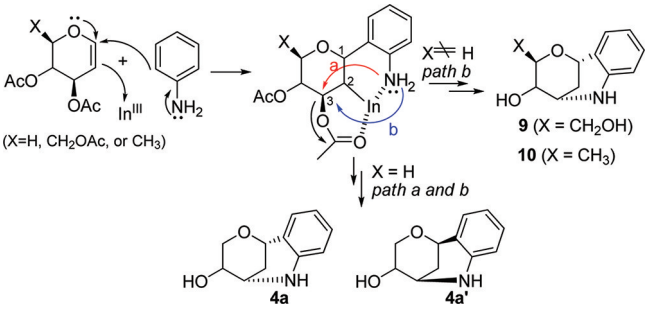


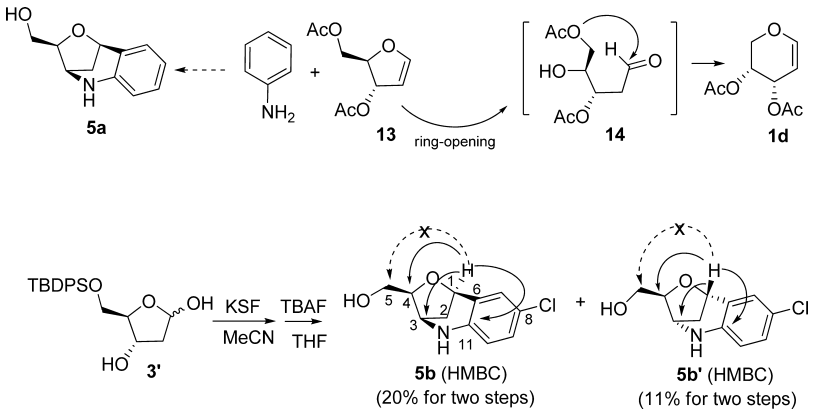
Figure 3. Mechanism analysis.

the [In^{III}] complex[9,15] formed between C3-OAc of glycals, aniline, and $InBr_3$, the amino group can attack the C-3 carbon through two paths (path a and b) leading to two diastereomers **4a** and **4a′**. while in the case of C-5-substituted glycals **1a** and **1c**, the steric effect between the C-5 substituent (**1a**: X=$AcOCH_2$; **1c**: X=CH_3) and the In^{III}-complex would disfavor the attack from path a; therefore, only one diastereomer **9** or **10** formed from the orientation opposite to C-5 substituent (path b) was obtained in high diastereoselectivity.

Although our results indicated that tetrahydrofuran-fused tetrahydroquinoline **5a** was not obtained in the reaction of aniline with either 2-deoxy-D-ribose (**3**) or glycal **1b**, its unique structure, different from tetrahydropyran analogues **4a** and **4a′**, attracted our attention. We envisioned that such structure of **5a** could be prepared through a similar manner by reaction of aniline with (3-acetoxy-2,3-dihydrofuran-2-yl)methyl acetate (**13**) under Lewis acid activation (montmorillonite KSF, InX_3) as outlined in Scheme 4. However, efforts to prepare bis-*O*-acetyl-D-ribose derivative **13** were unsuccessful because of its rapid isomerization from the 2,3-dihydrofuran skeleton to 3,4-dihydro-2*H*-pyran **1d** (Scheme 4). Indeed, the instability and readily isomerization of **13** was also observed by several groups.[21,22] In view of the fact that the ring rearrangement of **13** to **1d** generally occurs through a ring-opening mechanism to yield aldehyde intermediate **14** following by a ring-reclosure to afford the six-membered derivative **1d**, we hypothesized that replacing the 5-*O* easily off acetyl group with a more stable TBDPS group, and using TBDPS-protected 2-deoxy-D-ribose **3′** directly (instead of TBDPS analog of **13**) in the subsequent glycosidation reaction would ultimately suppress the formation of 3,4-dihydro-2*H*-pyran **1d** and give the expected tetrahydrofuran-fused tetrahydroquinoline (**5b**). To our delight, using the modest Lewis acid KSF as the promoter, the cyclization reaction of ribose **3′** and 4-chloroaniline went through smoothly, and products **5b** and **5b′** were obtained in moderate yield and 2:1 diastereomeric ratio. The diastereomeric **5b** and **5b′** were fully characterized by their spectroscopic data including 2D NMR (HSQC, HMBC, Scheme 4) and CD spectra. Specifically, in their HMBC spectra, there are

dx.doi.org/10.1021/jo2015483 | *J. Org. Chem.* 2011, 76, 8833–8839

Scheme 4. Synthesis of Compound 5b and 5b′



significant correlations between H-1 (4.81 ppm in **5b**, 4.76 ppm in **5b′**) and C-4 (89.1 ppm in **5b**, 86.8 ppm in **5b′**), whereas correlations between H-1 and C-5 which were typical characteristics in hexosides like **4a** were not detected.

■ CONCLUSION

In summary, we reinvestigated the reactions of arylamines with 2-deoxy-D-ribose or glycals catalyzed by Lewis acid montmorillonite KSF, $InCl_3$, or $InBr_3$ that were reported in the literature in 2003 and 2006, respectively. In the montmorillonite KSF- or $InCl_3$-initiated reactions of 2-deoxy-D-ribose (**3**) with arylamines, a pair of diastereomeric tetrahydro-2*H*-pyran-fused tetrahydroquinolines was obtained in nearly 1:1 ratio where one diastereomer was incorrectly assigned in the literature previously. Meanwhile, the products of $InBr_3$-catalyzed cyclization of glycals with arylamines were also incorrectly reported in the literature. It was found that high diastereoselectivity was achieved only when a C5-substituted glycal was used, otherwise a pair of diastereomers was obtained in moderate yield with 1:1 diastereomeric ratio. Furthermore, tetrahydrofuran-fused tetrahydroquinolines were also prepared successfully by using TBDPS-protected ribose as the glycal precursor and montmorillonite KSF as the activator.

■ EXPERIMENTAL SECTION

General Methods. All reactions were performed in glassware containing a Teflon-coated stir bar. CH_2Cl_2 and THF were purified and dried according to the standard methods prior to use. Methanol and acetonitrile were used without further purification. All reagents were obtained from commercial sources and used without further purifications. ^1H and ^{13}C NMR spectra were recorded with tetramethylsilane as an internal reference. Chemical shifts are expressed in ppm, and *J* values are given in hertz. Low- and high-resolution mass spectra were obtained in the EI (70 ev) mode. Flash column chromatography on silica gel (200−300 mesh) was used for the routine purification of reaction products, and a mixture of EtOAc and hexane (10%∼30%) was used as the eluent. The column output was monitored by TLC on silica gel (100−200 mesh) precoated on glass plates (10 cm ×50 cm), and spots were visualized by UV light at 254 nM or by spraying with 10% phosphomolybdic acid ($H_3PMo_{12}O_{41}$) in EtOH and charring. Montmorillonite KSF is a natural clay treated with sulfuric acid, with an acidic residue of ca. 5% in the clay. It was purchased from a commercial supplier and dried under 180 °C for 24 before use.The glycals **1a−d** were prepared according to literature procedures.[5,19]

General Procedure for Montmorillonite KSF-Catalyzed Cyclization of 2-Deoxy-D-ribose with Arylamines. A mixture of 2-deoxy-D-ribose (140 mg, 1.04 mmol), arylamine (1.56 mmol), and preactivated montmorillonite KSF (555 mg) in anhydrous MeCN (5 mL) was stirred under an atmosphere of nitrogen at rt for 8 h. The mixture was filtered and extracted with EtOAc (2 × 10 mL). The combined organic layers were dried with anhydrous Na_2SO_4, filtered, concentrated in vacuum, and purified by column chromatography (EtOAc/hexane, 10−30%) to afford the corresponding product.

Compound ***4a****:* white solid; $[\alpha]^{20}_D$ +65 (*c* 0.6, CH_3OH); ^1H NMR (300 MHz, $CDCl_3$) δ 7.16 (m, 1 H, *H*-9), 7.13 (m, 1 H, *H*-7), 6.72 (t, *J* = 7.2 Hz, 1 H, *H*-8), 6.63 (d, *J* = 8.1 Hz, 1 H, *H*-10), 4.71 (s, 1 H, *H*-1), 4.41 (br s, 1 H, N-*H*), 3.76 (m, 1 H, *H*-4), 3.73 (m, 1 H, *H*-5), 3.66 (br s, 1 H, *H*-3), 2.92 (t, *J* = 10.0 Hz, 1 H, *H*-5′), 2.14 (ddd, *J* = 13.2, 2.7, 2.4 Hz, 1 H, *H*-2), 1.94 (d, *J* = 8.4 Hz, 1 H, O-*H*), 1.92 (ddd, *J* = 12.9, 4.8, 1.8 Hz, 1 H, *H*-2′); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.3, 130.6, 129.6, 119.9, 113.7, 68.8, 67.4, 62.8, 48.7, 27.8; MS (EI-LR) 191 (M^+); HRMS (EI) calcd for $C_{11}H_{13}NO_2$ (M^+) 191.0946, found 191.0939.

Compound ***4a′****:* white solid; $[\alpha]^{20}_D$ +118 (*c* 0.6, CH_3OH); ^1H NMR (300 MHz, $CDCl_3$) δ 7.15 (m, 2 H, *H*-9, *H*-7), 6.69 (t, *J* = 7.5 Hz, 1 H, *H*-8), 6.55 (d, *J* = 8.1 Hz, 1 H, *H*-10), 4.77 (s, 1 H, *H*-1), 4.38 (br s, 1 H, N-*H*), 3.67 (br s, 1 H, *H*-3), 3.56 (m, 2 H, *H*-5, *H*-5′), 3.51 (m, 1 H, *H*-4), 2.57 (dt, *J* = 13.2, 3.0 Hz, 1 H, *H*-2), 2.33 (br s, 1 H, O-*H*), 1.59 (d, *J* = 10.5 Hz, 1 H, *H*-2′); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.4, 130.7, 129.8, 118.4, 117.0, 112.9, 70.0, 68.9, 63.7, 47.7, 23.8; MS (EI-LR) 191 (M^+); HRMS (EI) calcd for $C_{11}H_{13}NO_2$ (M^+) 191.0946, found 191.0938.

Compound ***4b****:* white solid; $[\alpha]^{20}_D$ +68 (*c* 0.6, CH_3OH); ^1H NMR (300 MHz, $CDCl_3$) δ 7.10 (m, 2 H), 6.57 (d, *J* = 13.2 Hz, 1 H), 4.64 (s, 1 H), 4.48 (br s, 1 H), 3.76 (m, 2 H), 3.65 (br s, 1 H), 2.95 (t, *J* = 8.1 Hz, 1 H), 2.13 (d, *J* = 15.2 Hz, 1 H), 1.98 (d, *J* = 6.82 Hz, 1 H), 1.86 (d, *J* = 13.2 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.9, 130.1, 129.5, 122.0, 121.0, 114.8, 68.7, 66.9, 62.7, 48.6, 27.5; MS (EI-LR) 225 (M^+); HR-MS (EI) calcd for $C_{11}H_{12}ClNO_2$ (M^+) 225.0557, found 225.0546.

Compound ***4b′****:* white solid; $[\alpha]^{20}_D$ +103 (*c* 0.6, CH_3OH); ^1H NMR (300 MHz, $CDCl_3$) δ 7.13 (m, 2 H), 6.48 (d, *J* = 8.0 Hz, 1 H), 4.69 (s, 1 H), 4.43 (br s, 1 H), 3.66 (d, *J* = 2.7 Hz, 1 H), 3.66 (br s, 1 H), 3.54 (m, 3 H), 2.57 (d, *J* = 12.6 Hz, 1 H), 2.24 (d, *J* = 6.5 Hz, 1 H), 1.54 (d, *J* = 12.3 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.1, 130.2, 129.7, 121.4, 119.6, 114.1, 69.8, 68.4, 63.7, 47.6, 23.5; MS (EI-LR) 225 (M^+); HR-MS (EI) calcd for $C_{11}H_{12}ClNO_2$ (M^+) 225.0557, found 225.0546.

Compound ***4c****:* white solid; $[\alpha]^{20}_D$ +57 (*c* 0.6, CH_3OH); ^1H NMR (300 MHz, $CDCl_3$) δ 7.24 (m, 1 H), 7.07 (d, *J* = 7.5 Hz, 1 H), 6.66 (t, *J* = 7.8 Hz, 1 H), 4.90(br s, 1 H), 4.72 (br s, 1 H), 3.74 (m, 3 H), 2.86 (t, *J* = 10.5 Hz, 1 H), 2.17 (d, *J* = 13.2 Hz, 1 H), 1.89 (br s, 1 H), 1.84 (d, *J* = 9.0 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.8, 129.5, 129.0, 117.4, 68.7, 67.2, 62.8, 48.8, 27.5; MS (EI-LR) 225 (M^+); HR-MS (EI) calcd for $C_{11}H_{12}ClNO_2$ (M^+) 225.0557, found 225.0559.

Compound ***4c′****:* white solid; $[\alpha]^{20}_D$ +120 (*c* 0.6, CH_3OH); ^1H NMR (300 MHz, $CDCl_3$) δ 7.21 (m, 1 H), 7.04 (m, 1 H), 6.58 (m, 1 H), 4.72 (br s, 1 H), 3.74 (br s, 1 H), 3.51 (m, 2 H), 3.39 (m, 1 H),

dx.doi.org/10.1021/jo2015483 | *J. Org. Chem.* 2011, 76, 8833−8839

2.59 (dd, J = 13.2, 2.7 Hz, 1 H), 1.49 (d, J = 13.5 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.8, 141.2, 129.5, 129.0, 119.7, 116.6, 69.2, 68.6, 63.5, 49.9, 47.4, 23.2; MS (EI-LR) 225 (M^+); HR-MS (EI) calcd for $C_{11}H_{12}ClNO_2$ (M^+) 225.0557, found 225.0554.

Compound ***4d****:* white solid; $[\alpha]^{20}_D$ +20 (*c* 0.6, CH_3OH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.16 (m, 1 H), 7.13 (m, 1 H), 6.72 (t, J = 7.2 Hz, 1 H), 6.63 (d, J = 8.1 Hz, 1 H), 4.64(s, 1 H), 4.47 (s, 1 H), 3.78 (d, J = 2.7 Hz, 1 H), 3.80 (d, J = 4.5 Hz, 1 H), 3.72 (m, 1 H), 2.91 (t, J = 8.1 Hz, 1 H), 2.11 (d, J = 1.8 Hz, 1 H), 2.10 (d, J = 1.8 Hz, 1 H), 1.95 (d, J = 1.8 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.2, 135.1, 131.7, 118.3, 117.8, 113.3, 68.7, 66.8, 62.6, 48.6, 27.6; MS (EI-LR) 225 (M^+). HR-MS (EI) calcd for $C_{11}H_{12}ClNO_2$ (M^+) 225.0557, found 225.0554.

Compound ***4d′****:* white solid; $[\alpha]^{20}_D$ +69 (*c* 0.6, CH_3OH); ^{1}H NMR (300 MHz, $CDCl_3$ + CD_3OD) δ 6.96 (d, J = 8.1 Hz, 1 H), 6.54 (dd, J = 8.1 Hz, 1.8 Hz, 1 H), 6.49 (d, J = 1.8 Hz, 1 H), 4.63 (s, 1 H), 3.52 (br s, 1 H), 3.48 (s, 1 H), 3.40 (br s, 1 H), 2.55 (dt, J = 12.9, 3.0 Hz, 1 H), 1.43 (d, J = 12.3 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.7, 135.0, 131.5, 116.4, 116.3, 112.2, 69.3, 69.1, 68.2, 63.2, 47.0, 23.2; MS (EI-LR) 225 (M^+). HR-MS (EI) calcd for $C_{11}H_{12}ClNO_2$ (M^+) 225.0557, found 225.0554.

Compound ***4e****:* white solid; $[\alpha]^{20}_D$ +75 (*c* 0.6, CH_3OH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.01 (d, J = 7.8 Hz, 1 H), 6.55 (d, J = 7.5 Hz, 1 H), 6.45 (s, 1 H), 4.68(s, 1 H), 4.68 (s, 1 H), 4.40 (br s, 1 H), 3.73 (m, 2 H), 3.62 (br s, 1 H), 2.92 (t, J = 9.9 Hz, 1 H), 2.27 (s, 3 H), 2.19 (d, J = 8.4 Hz, 1 H), 2.11 (d, J = 13.2 Hz, 1 H), 1.87 (dd, J = 13.2, 4.5 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.2, 139.6, 130.4, 118.7, 117.0, 114.0, 68.8, 67.2, 62.6, 48.6, 27.9, 21.4; MS (EI-LR) 205 (M^+); HR-MS (EI) calcd for $C_{12}H_{15}NO_2$ (M^+) 205.1103, found 205.1108.

Compound ***4e′****:* white solid; $[\alpha]^{20}_D$ +110 (*c* 0.6, CH_3OH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.95 (d, J = 7.8 Hz, 1 H), 6.43 (d, J = 7.5 Hz, 1 H), 6.32 (s, 1 H), 4.64 (s, 1 H), 3.52 (br s, 1 H), 3.46 (m, 2 H), 3.41 (m, 1 H), 2.52 (dt, J = 13.2, 3.0 Hz, 1 H), 2.20 (s, 3 H), 1.48 (d, J = 12.9 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$ + CD_3OD) δ 144.5, 139.6, 130.3, 117.6, 115.2, 113.1, 69.6, 68.6, 63.2, 47.4, 23.7, 21.2; MS (EI-LR) 205 (M^+); HR-MS (EI) calcd for $C_{12}H_{15}NO_2$ (M^+) 205.1103, found 205.1106.

Compound ***4f****:* white solid; $[\alpha]^{20}_D$ +35 (*c* 0.6, CH_3OH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.95 (m, 2 H), 6.56 (d, J = 7.8 Hz, 1 H), 4.66 (s, 1 H), 4.33 (br s, 1 H), 3.74 (m, 2 H), 3.61 (br s, 1 H), 2.92 (t, J = 9.6 Hz, 1 H), 2.24 (s, 3 H), 2.11 (ddd, J = 12.9, 3.6, 2.4 Hz, 1 H,), 1.87 (ddd, J = 13.5, 4.5, 2.1 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.9, 130.8, 130.3, 126.9, 119.8, 113.8, 68.7, 67.5, 62.7, 48.6, 27.8, 20.3; MS (EI-LR) 205 (M^+); HR-MS (EI) calcd for $C_{12}H_{15}NO_2$ (M^+) 205.1103, found 205.1108.

Compound ***4f′****:* white solid; $[\alpha]^{20}_D$ +99 (*c* 0.6, CH_3OH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6. 97(m, 2 H), 6.48 (d, J = 8.7 Hz, 1 H), 4.70 (s, 1 H), 4.24 (br s, 1 H), 3.64 (br s, 1 H), 3.52 (m, 3 H), 2.55 (d, J = 12.9 Hz, 1 H), 2.24 (s, 3 H), 1.58 (d, J = 12.3 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.2, 131.0, 130.5, 126.2, 118.3, 112.9, 70.2, 69.0, 63.7, 47.8, 24.0, 20.3; MS (EI-LR) 205 (M^+); HR-MS (EI) calcd for $C_{12}H_{15}NO_2$ (M^+) 205.1103, found 205.1108.

*Synthesis of 5-((tert-Butyldiphenylsilyloxy)methyl)-tetrahydrofuran-2,4-diol (****3′****).* To a solution of 2-deoxy-D-ribose (370 mg, 2.76 mmol), imidazole (207 mg, 3.04 mmol), and DMAP (44 mg, 0.36 mmol) in DMF/CH_2Cl_2 (1:1, 28 mL) at 0 °C was added dropwise *tert*-butyldiphenylchlorosilane (TBDPSCl, 681 mg, 2.5 mmol). The mixture was stirred at rt overnight, concentrated in vacuum, and purified by column chromatography on silica gel (EtOAc/hexane 1:4) to afford **3′** as a white solid (484 mg, 71% yield): ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.64 (m, 4H), 7.42 (m, 6H), 5.57 (m, 1H), 4.40 (m, 1H), 4.30 (m, 1H), 3.71 (m, 1H), 3.57 (m, 1H), 3.43 (d, J = 4.5 Hz, 1H), 2.77 (d, J = 7.8 Hz, 1H), 2.16 (m, 1H), 2.03 (m, 1H), 1.08 (m, 9H).

Synthesis of Compounds 5b and 5b′. Compounds **5b** and **5b′** were prepared following the general procedure described above in 41% yield as yellow solid from ribose **3′** (484 mg, 1.30 mmol) followed by deprotection with TBAF (1 M in THF) at 0 °C.

Compound ***5b****:* yellow solid; $[\alpha]^{20}_D$ +49.6 (*c* 0.23, CH_3OH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.02 (dd, J = 2.3 Hz, J = 8.4 Hz, 1H, *H*-9), 6.97 (d, J = 2.4 Hz, 1H, *H*-7), 6.46 (d, J = 8.4 Hz, 1H, *H*-10), 4.81 (d, J = 4.5 Hz, 1H, *H*-1), 4.30 (t, J = 5.1 Hz, 1H, *H*-4), 3.76 (d, J = 3.6 Hz, 1H, *H*-3), 3.54 (d, J = 5.1 Hz, 2H, *H*-5), 2.17 (m, 2H, *H*-2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.5, 129.1, 127.3, 127.2, 122.3, 115.9, 89.1, 76.2, 63.6, 54.8, 30.5; MS (EI-LR) 225 (M^+); HRMS calcd for $C_{11}H_{12}ClNO_2$ (M^+) 225.0557, found 225.0557.

Compound ***5b′****:* yellow solid; $[\alpha]^{20}_D$ −70.1 (*c* 0.24, CH_3OH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.98 (d, J = 8.1 Hz, 1H, *H*-9), 6.91 (s, 1H, *H*-7), 6.43 (d, J = 8.4 Hz, 1H, *H*-10), 4.76 (d, J = 4.8 Hz, 1H, *H*-1), 4.25 (m, 1H, *H*-4), 4.11 (m, 1H, *H*-3), 3.84 (m, 1H, *H*-5), 3.71 (m, 1H, *H*-5), 2.29 (m, 2H, *H*-2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 141.9, 129.0, 128.6, 126.8, 121.8, 114.8, 86.8, 75.8, 62.9, 53.2, 31.5; MS (EI-LR) 225 (M^+); HRMS calcd for $C_{11}H_{12}ClNO_2$ (M^+) 225.0557, found 225.0559.

General Procedure for $InBr_3$-Catalyzed Glycosidation of Various Glycals with Arylamines. A mixture of an appropriate glycal (50 mg, 0.25 mmol), arylamine (0.25 mmol), and $InBr_3$ (27 mg, 0.07 mmol) in anhydrous CH_2Cl_2 (4 mL) was stirred under N_2 at rt overnight. After completion of the reaction as indicated by TLC, the mixture was quenched with water and then extracted with CH_2Cl_2 (2 × 10 mL). The combined organic layers were washed with water and brine and then dried over anhydrous Na_2SO_4 and concentrated in vacuo to afford the crude cyclic acetates.

The mixture of the crude acetate, ammonia solution (1 mL) and methanol (5 mL) was stirred for 6 h at rt. After completion of the reaction, the solvent was removed under vacuum and then extracted with CH_2Cl_2 (2 × 10 mL), dried over anhydrous Na_2SO_4, concentrated in vacuum, and purified by column chromatography (EtOAc/hexane = 1:1) to afford a pair of diastereomers.

Compound ***9****:* white solid; $[\alpha]^{20}_D$ +18 (*c* 0.6, CH_3OH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.13 (m, 2 H), 6.72 (t, J = 7.8 Hz, 1 H), 6.65 (d, J = 8.1 Hz, 1 H), 4.75 (s, 1 H), 4.46 (br s, 2 H), 3.68 (m, 2 H), 3.13 (m, 1 H), 2.35 (d, J = 8.7 Hz, 1 H), 2.14 (d, J = 12.9 Hz, 1 H), 1.94 (m, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.4, 130.0, 129.5, 119.3, 116.6, 113.2, 71.7, 69.6, 68.3, 62.1, 48.7, 27.8; MS (EI-LR) 221 (M^+); HR-MS (EI) calcd for $C_{12}H_{15}NO_3$ (M^+) 221.1052, found 221.1050.

Compound ***10****:* white solid; $[\alpha]^{20}_D$ −10 (*c* 0.6, CH_3OH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.14 (m, 2 H), 6.73 (t, J = 7.5 Hz, 1 H), 6.63 (d, J = 8.1 Hz, 1 H), 4.71 (s, 1 H), 4.38 (br s, 1 H), 3.26 (t, J = 3.3 Hz, 1 H), 3.12 (m, 1 H), 2.16 (dt, J = 13.5, 2.4 Hz, 1 H), 1.99 (d, J = 9.6 Hz, 1 H), 1.90 (ddd, J = 12.6, 4.8, 2.1 Hz, 1 H), 1.22 (d, J = 6 Hz, 3 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.0, 130.6, 129.5, 120.7, 117.6, 113.7, 75.2, 68.5, 68.2, 49.0, 28.3, 18.2; MS (EI-LR) 205 (M^+); HR-MS (EI) calcd for $C_{12}H_{15}NO_2$ (M^+) 205.1102, found 205.1100.

Compound ***11****:* white solid; $[\alpha]^{20}_D$ +68 (*c* 0.45, CH_3OH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (m, 1 H), 7.17 (d, J = 7.5 Hz, 1 H), 6.69 (t, J = 7.2 Hz, 1 H), 6.60 (d, J = 8.1 Hz, 1 H), 4.74 (s, 1 H), 3.66 (br s, 1 H), 3.57 (m, 2 H), 3.36 (d, J = 13.2 Hz, 1 H), 3.08 (s, 3 H), 2.54 (dt, J = 13.2, 3.3 Hz, 1 H), 2.19 (d, J = 7.2 Hz, 1 H), 1.61 (d, J = 8.4 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.0, 130.5, 130.1, 118.7, 115.8, 109.4, 69.5, 66.2, 63.7, 56.6, 37.7, 24.0; MS (EI-LR) 205 (M^+); HR-MS (EI) calcd for $C_{12}H_{15}NO_2$ (M^+) 205.1102, found 205.1102.

Compound ***11′****.* white solid; $[\alpha]^{20}_D$ +56 (*c* 0.26, CH_3OH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (m, 1 H), 7.15 (d, J = 7.5 Hz, 1 H), 6.69 (m, 2 H), 4.68 (s, 1 H), 3.87 (br s, 1 H), 3.69 (m, 2 H), 3.20 (d, J = 3.6 Hz, 3 H), 2.91 (td, J = 10.8, 3.3 Hz, 1 H), 1.97 (d, J = 13.2 Hz, 1 H), 1.87 (d, J = 11.7 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.2, 130.5, 130.0, 119.7, 116.2, 110.1, 70.7, 68.2, 62.9, 58.3, 41.0, 27.2; MS (EI-LR) 205 (M^+); HR-MS (EI) calcd for $C_{12}H_{15}NO_2$ (M^+) 205.1102, found 205.1101.

Compound ***12****:* white solid; $[\alpha]^{20}_D$ −110 (*c* 0.6, CH_3OH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.14 (m, 2 H), 6.70 (t, J = 7.2 Hz, 1 H), 6.56 (d, J = 8.1 Hz, 1 H), 4.74 (s, 1 H), 4.38 (br s, 1 H), 3.66 (br s, 1 H), 3.54 (m, 3 H), 2.57 (d, J = 13.2 Hz, 1 H), 2.33 (br s, 1 H), 1.59 (d, J = 14.1 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 130.5, 129.7, 118.0, 116.6, 112.7, 69.6, 68.9, 63.4, 47.4, 23.5; MS (EI-LR) 191 (M^+); HRMS (EI) calcd for $C_{11}H_{13}NO_2$ (M^+) 191.0946, found 191.0939.

Compound ***12′****:* white solid; $[\alpha]^{20}_D$ −51 (*c* 0.6, CH_3OH); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.15 (m, 2 H), 6.73 (td, J = 7.5, 0.9 Hz, 1 H), 6.62 (d, J = 8.1 Hz, 1 H), 4.70 (s, 1 H), 4.48 (br s, 1 H), 3.73 (m,

2 H), 3.63 (br s, 1 H), 3.56 (m, 2 H), 2.92 (t, J = 10.2 Hz,1 H), 2.24 (d, J = 8.1 Hz, 1 H), 2.12 (ddd, J = 13.2, 3.3, 2.4 Hz, 1 H), 1.88 (ddd, J = 13.2, 4.2, 1.5 Hz, 1 H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 145.4, 130.5, 129.6, 119.6, 117.5, 113.5, 68.8, 67.4, 62.6, 48.6, 27.7; MS (EI-LR) 191 (M^+); HRMS (EI) calcd for $C_{11}H_{13}NO_2$ (M^+) 191.0946, found 191.0938.

■ ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR, HSQC, HMBC, and CD spectra for all final compounds and X-ray crystallographic data of compounds **4a** and **4a′** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: (W.H.) huwx66@163.com; (A.Z.) aozhang@mail.shcnc.ac.cn.

Author Contributions

‖These authors contributed equally to this work.

■ ACKNOWLEDGMENTS

We are grateful to the Chinese National Science Foundation (81072528), Shanghai Commission of Science and Technology (10410702600, 10JC1417100, and 10dz1910104), and National Science & Technology Major Project on "Key New Drug Creation and Manufacturing Program" (2012ZX09101, 2009ZX09301-001, and 2009ZX09103-062). A grant from the Key Laboratory of Pesticide & Chemical Biology, Central China Normal University (201005A02) is also appreciated.

■ REFERENCES

(1) Postema, M. H. D. *Tetrahedron* **1992**, *48*, 8545.
(2) Ferrier, R. J.; Prasad, N. J. *Chem. Commun.* **1969**, *20*, 570.
(3) Ferrier, R. J.; Zubkov, O. A. *Org. React.* **2003**, *62*, 569.
(4) Ferrier, R. J. *Top. Curr. Chem.* **2001**, *215*, 153.
(5) Brawn, R. A.; Panek, J. S. *Org. Lett.* **2010**, *12*, 4624.
(6) Yeager, A. R.; Min, G. K.; Porco, J. A. Jr.; Schaus, S. E. *Org. Lett.* **2006**, *8*, 5065.
(7) Clark, J. H. *Acc. Chem. Res.* **2002**, *35*, 791.
(8) Minzuno, N.; Misono, M. *Chem. Rev.* **1998**, *98*, 199.
(9) Yadav, J. S.; Reddy, B. V. S.; Rao, K. V.; Raj, K. S.; Prasad, A. R.; Kumar, S. K.; Kunwar, A. C.; Jayaprakash, P.; Jagannath, B. *Angew. Chem., Int. Ed.* **2003**, *42*, 5198.
(10) Li, Z.; Zhang, J.; Li, C. *Tetrahedron Lett.* **2003**, *44*, 153.
(11) Yadav, J. S.; Reddy, B. V. S.; Srinivas, M.; Padmavani, B. *Tetrahedron* **2004**, *60*, 3261.
(12) Yadav, J. S.; Reddy, B. V. S.; Parimala, G.; Raju, A. K. *Tetrahedron Lett.* **2004**, *45*, 1543.
(13) Yadav, J. S.; Reddy, B. V. S.; Srinivas, M.; Vishnumurthy, P.; Narsimulu, K.; Kunwar, A. C. *Synthesis* **2006**, *17*, 2923.
(14) Rafiee, E.; Azad, A. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 2756.
(15) Ding, C.; Tu, S.; Li, F.; Wang, Y.; Yao, Q.; Hu, W.; Xie, H.; Meng, L.; Zhang, A. *J. Org. Chem.* **2009**, *74*, 6111.
(16) Maugel, N.; Snider, B. *Org. Lett.* **2009**, *11*, 4926.
(17) Ding, C.; Tu, S.; Yao, Q.; Li, F.; Wang, Y.; Hu, W.; Zhang, A. *Adv. Synth. Catal.* **2010**, *352*, 847.
(18) Li, F.; Ding, C.; Wang, M.; Yao, Q.; Zhang, A. *J. Org. Chem.* **2011**, *76*, 2820.
(19) Shull, B. K.; Wu, Z.; Koreeda, M. *J. Carbohydr. Chem.* **1996**, *15*, 955.
(20) It should be pointed out that the products were isolated directly as acetates in ref 9 instead of hydrolysis to their corresponding alcohols as in our experiment.
(21) Leibeling, M.; Koester, D. C.; Pawliczek, M.; Kratzert, D.; Dittrich, B.; Werz, D. B. *Bioorg. Med. Chem.* **2010**, *18*, 3656.
(22) Brawn, R. A.; Panek, J. S. *Org. Lett.* **2010**, *12*, 4624; *Org. Lett.* **2010**, *12*, 5600 The authors originally reported their success in preparation of furanose **13**, but later they revised the structure as pyranose **1d**.