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Azidation of anomeric nitro sugars: application in the synthesis of spiroaminals as glycosidase inhibitors

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ABSTRACT

6,5-Fused sugar-derived spiroaminals have been synthesized from the azido esters obtained via the nucleophilic substitution reactions of unstable Michael adducts derived from 1-nitro sugars. Most of the spiroaminals synthesized showed moderate but selective inhibitory activities toward some glycosidases.

Nitro compounds are versatile intermediates in organic synthesis due to their easy availability and transformation into a wide variety of functionalities.[1] Carbohydrate chemists have long recognized nitro sugars as both novel compounds and synthetically useful intermediates.[2] Both saturated and unsaturated nitro groups have been used in the synthesis of a number of useful compounds.[3]

In 1-nitro sugars, having a nitro group at the anomeric carbon, the strong electron-withdrawing property of the nitro group can facilitate an easy removal of the anomeric proton under mild basic conditions. The stabilized glycosyl anions can easily react with different electrophiles like Michael acceptors and carbonyl compounds leading to the generation of useful *C*-glycosyl adducts. By utilizing these properties of 1-nitro sugars, Vasella and co-workers synthesized several molecules such as *N*-acetylneuraminic acid and their analogues,[4] sialidase inhibitors, 6-amino-6-deoxysialic acids,[5] and various biologically important carbohydrates such as methyl shikimate and diethyl phosphashikimate.[6]

It is well known in the literature[7] that in an aliphatic compound a nitro group can be easily replaced by various nucleophiles via $S_{RN}1$ or ionic processes. In some cases, it has also been observed that the nitro group of C-glycosylated-1-nitro sugars can be easily replaced by a hydroxy group during solvolysis. Thus, Vasella[8] replaced nitro group present in C-glycosylated-1-nitropyranoses and furanoses with sodium salt of nitromethane (Kornblum reaction) for the synthesis of branched sugars. Further, Vasella and co-workers[9] have also reported S_N1-type substitution of C-glycosylated-1-nitro furanoses (α-nitro ether link) with hydroxy group under solvolytic condition and also with 2,4-bis(trimethylsilyloxy)-pyrimidine in the presence of $FeCl_3$ in CH_3CN at higher temperatures for the synthesis[10] of ketose-derived nucleosides. Because of diverse applications and also due to our continued interest[11] in exploring the chemistry of nitro sugars we hereby report on the functionalization of 1-nitro sugars and its application in the synthesis of some spiro-compounds which are moderate glycosidase inhibitors. Toward this purpose, we have utilized the chemistry of 1-nitro sugars **1** and **4** (Table 1)[12] derived from D-glucose and D-mannose, respectively.

Reaction of nitro sugar **1** with methyl acrylate in the presence of a catalytic amount of *n*-tetrabutylammonium fluoride (TBAF), at 0 °C presumably gave the adduct **2a** (Table 1), as was observed by its IR spectrum immediately after work-up (with an intense peak at 1554 cm^{-1} indicating the presence of a nitro group), whose purification by column chromatography led only to the formation of the hydroxyl derivative **3a** in 83% yield. Further, it was observed that the adduct **2a** was not only unstable on silica gel but it slowly got converted into **3a** by merely keeping it at room temperature (Table 1). The ^1H NMR spectrum of **3a** showed a characteristic peak of -OMe as a singlet at δ 3.66 and the methylene protons as multiplets at δ 2.63–1.74. The Michael addition with acrylonitrile also gave the hydroxyl compound viz. hydroxy nitrile **3b** whose structure was easily established from its spectral analysis and NOE data. The treatment of **1** with ethyl propiolate in CH_2Cl_2 with Et_3N at −30 °C gave the unsaturated *trans* ester **3c** in 51% yield along with a complex mixture of products. The ^1H NMR spectrum of **3c** showed the presence of two olefinic protons at δ 6.83 and δ 6.19

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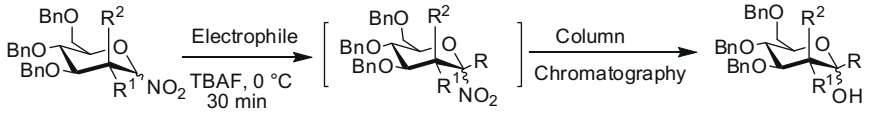
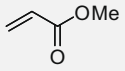
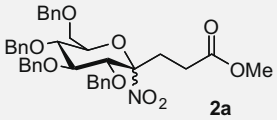
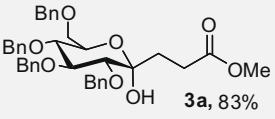
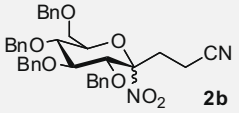
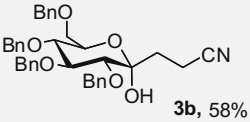
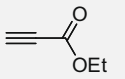
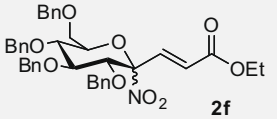
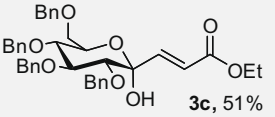
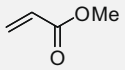
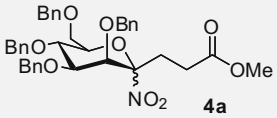
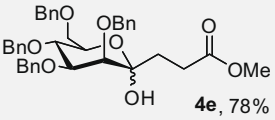
Table 1
Michael additions using nitro sugars **1** and **4**



1 R^1 = OBn, R^2 = H
4 R^1 = H, R^2 = OBn

2a,2b, 2f R^1 = OBn, R^2 = H
4a R^1 = H, R^2 = OBn

3a-3c R^1 = OBn, R^2 = H
4e R^1 = H, R^2 = OBn

Entry	Nitro sugar	Electrophiles	Michael adducts	Hydrolyzed products
1	**1**		 **2a**	 **3a**, 83%
2	**1**		 **2b**	 **3b**, 58%
3	**1**		 **2f**	 **3c**, 51%
4	**4**		 **4a**	 **4e**, 78%

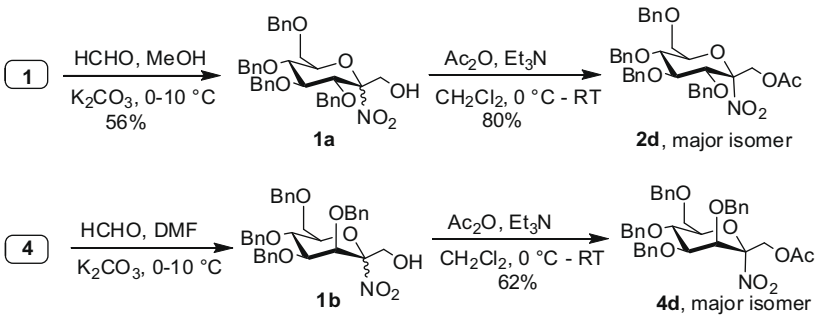
with J = 15.6 Hz confirming that the geometry of the double bond is trans. Reaction of mannosyl nitro sugar **4** with methyl acrylate also gave the ketose **4e** (Table 1) in 78% yield. Although its structure was confirmed by spectral means,[13a] the stereochemistry at the anomeric center could not be established. In contrast with these Michael adducts, the aldol products[13b] **1a**, **1b**, **2d**, and **4d** (Scheme 1) were found to be more stable at room temperature and also on silica gel during column chromatography. These results clearly suggest that a nitro group at the anomeric carbon having certain substituents, as discussed above, is a rather labile leaving group. We, therefore, explored the efficiency of the anomeric nitro group as a leaving group in reactions with azide as a nucleophile in C-glycosylated-1-nitro sugars.

Our initial attempts for the azidation of the crude Michael adducts **2a–d** with sodium azide in DMF at higher temperatures led to the formation of a mixture of two products, the hydrolyzed products and the desired glycosyl azides in almost 1:1 ratio.

Next, we investigated the azidation of the Michael adducts by Lewis acid activation. Gratifyingly, the formation of the undesired hydrolysis products was completely suppressed under Lewis acid conditions and glycosyl azides were formed as single isomers. Thus, the treatment of the Michael adduct **2a** in CH_2Cl_2 with $TMSN_3$ in the presence of TMSOTf and 4 Å powdered molecular sieves at 0 °C produced the desired glycosyl azide **5a** (Table 2) in 91% yield. Use of $BF_3.OEt_2$ at −40 °C and −78 °C also produced the desired product, but the yields were poor. Best results were obtained by using 50 mol % of TMSOTf in CH_2Cl_2 at 0 °C to room temperature. Reduction in catalyst loading was ineffective as it led to longer reaction time and reduction in chemical yield due to the formation of undesired products.

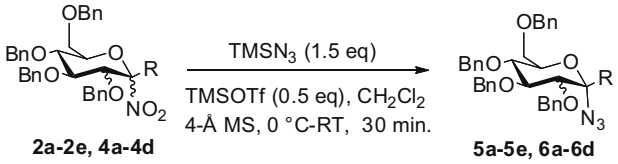
Using these optimized reaction conditions we prepared the glycosyl azides **5b**, **5c**, and **5e** from the corresponding Michael adducts in good to moderate yields. But in the case of nitro acetate **2d**, one mole equivalent of the catalyst was needed to get the azido acetate **5d**. The stereochemistry of the newly generated anomeric center was determined by ^1H NMR spectroscopic analysis, COSY, and NOE experiments.

Utilization of the optimized conditions, vide supra, for the conversion of nitro sugars **4a–c**, derived from D-mannose, led to the desired azides **6a–c** as single isomers in 72%, 80%, and 78% yields,



Scheme 1. Henry reactions of nitro sugars **1** and **4** with formaldehyde.

Table 2
Azidation of Michael adducts in the presence of $TMSN_3$ and TMSOTf at lower temperatures (0 °C to rt)



2a-2e, 4a-4d → **5a-5e, 6a-6d**

Entry	Michael adducts	Tertiary anomeric azides	Yield (%)
1	**2a**	**5a**	90
2	**2b**	**5b**	85
3	**2c**	**5c**	79
4	**2d**	**5d**	86
5	**2e**	**5e**	83
6	**4a**	**6a**	72
7	**4b**	**6b**	80
8	**4c**	**6c**	78
9	**4d**	**6d**	80

respectively. Further, similar to nitro acetate **2d**, the mannose-derived nitro acetate **4d** was also found to be less reactive. The reaction of this acetate with $TMSN_3$ also required 1.0 equiv of TMSOTf to afford the desired azido acetate **6d** in 80% yield. Compound **6d** was a single isomer as it showed the presence of only one -$OCOCH_3$ group in its ^1H NMR spectrum at δ 2.02 as a singlet suggesting that only one anomer was present. Unfortunately, the stereochemistry at the anomeric center could not be confirmed by NOE experiments. However, based on literature analogy,[14] we presume that the azide group in this molecule is axially oriented.

The stereochemistry at the anomeric center of ketoses and anomeric azides was confirmed by NOE experiments. Thus, in NOE experiments for ketose **3a** (Fig. 1) irradiation of H-3 proton at δ 3.34 enhanced the signal for H-3′ methylene proton at δ 1.75 (3.4% NOE), whereas irradiation of H-4 at δ 4.02 and H-6 at δ 3.97 protons did not show any enhancement in H-3′ methylene protons signal. These results indicated that the hydroxy group has occupied axial position. In a similar manner, the stereochemistry of ketoses **3b** and **3c** was also established. Irradiation of H-3 proton at δ 3.45 in compound **5a** showed enhancement of H-3′ methylene protons signal at δ 2.26 and δ 2.1 (2.0% and 3.0% NOE, respectively, Fig. 1). In contrast, irradiation of H-4 proton signal at δ 3.99 did not show any enhancement of H-3′ methylene protons signal, clearly indicating that azide occupies the axial position.

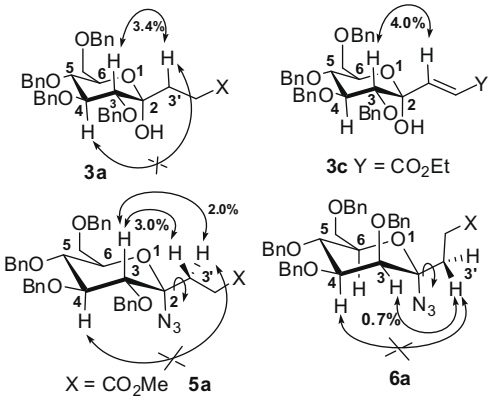


Figure 1. NOE correlations of compounds **3a**, **3c**, **5a**, and **6a**.

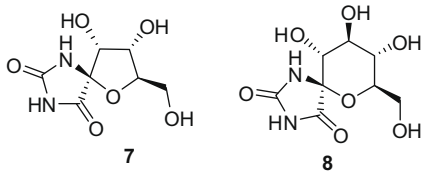
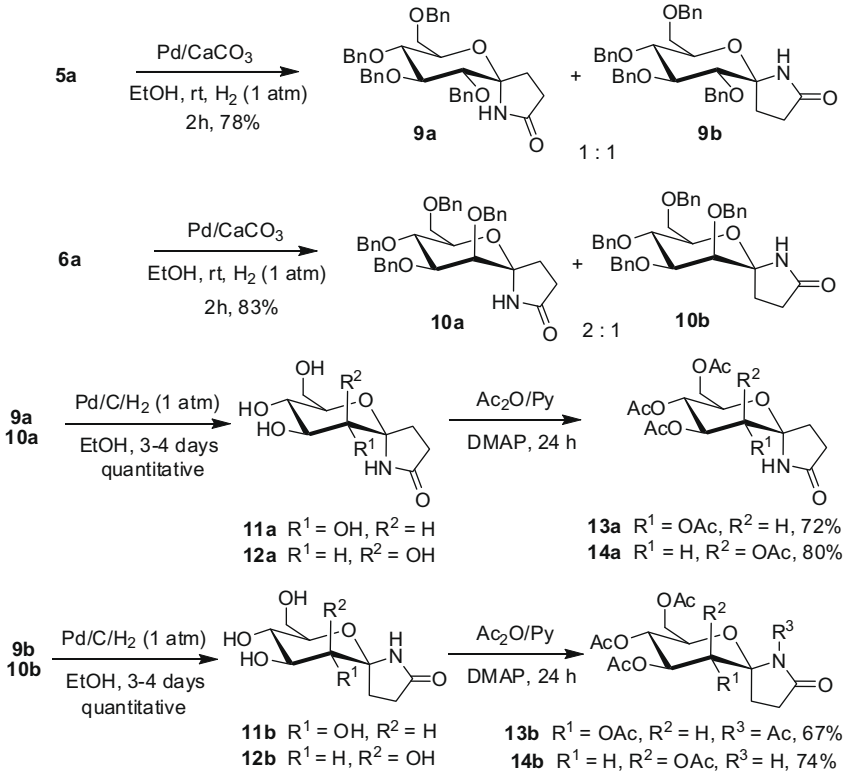


Figure 2. Hydantocidin and D-glucopyranose analogue of hydantocidin.

Likewise, based on NOE experiments the anomeric configurations of azides **5b**, **5c**, **5d**, and **5e** were confirmed. Further, irradiation of H-4 proton at δ 4.05 in **6a** did not show any enhancement of H-3′ methylene protons signal at δ 2.18, but enhancement was observed for H-3′ signals when irradiation of equatorial proton H-3 at δ 3.57 was done and, as expected,[15] the enhancement was small (0.7% only). These results clearly establish the axial orientation of the azide group in compound **6a**. In a similar manner, the stereochemistry of azides **6b** and **6c** was also established.

For the past few years, we have been interested in developing synthesis of novel carbohydrate entities such as hybrids of D-galactose with 1-deoxynojirimycin analogues,[11c] sugar-carbamino sugar hybrids,[16a] hybrids of nojirimycin δ-lactam D-galactose[11d], and pyrrolidine-based imino sugars,[16b] natural products L-(+)-swainsonine[16c], and (+)-lentiginosine.[16d] In connection with our program of developing novel carbohydrate molecules as glycosidase inhibitors, we became interested in making sugar-derived spiroaminals as glycosidase inhibitors. Spiroaminals, also called as oxa-aza spirobicyclic frameworks, are the substructures present in a number of biologically active compounds viz. pandamarilactone,[17a] hydantocidin, azaspiracid-1,[17b] immunosuppressant sanglifehrin,[17c] and a spironucleoside as a potent glycosidase inhibitor.[17d] Because of the unique structural features and potent herbicidal properties of the natural product hydantocidin **7**, several reports[18] have appeared for its synthesis and also a wide range of analogues. The D-glucopyranose analogue of hydantocidin[19a,b] viz. compound **8** (Fig. 2) is a powerful inhibitor of glycogen phosphorylase (GP). Keeping these activities in mind we planned to synthesize sugar-derived spiroaminals.[19c]

To convert 1-*C*-alkyl-1-azido sugars into spirolactams, we studied their reductions under different conditions. There are only few reports in the literature regarding the reduction of C-glycosylated-1-azido sugars.[20a–d] Our initial attempts for the reduction of azide **5a** with PPh_3 along with H_2O[21] and Zn-AcOH[20a] conditions were unsuccessful. Treatment of ester **5a** with Zn-AcOH at room temperature gave a complex mixture, which is not surprising as earlier reports[20a] for the reduction of anomeric azides with Zn-AcOH have led to *N*,*O*-acetals in less yields. Dondoni et al.[20d] have reported the reduction of C-glycosylated-1-azido sugars with Pd/C-H_2 in ^{t}BuOH·H_2O. But, the use of these conditions in the reduction of



Scheme 2. Synthesis of 6,5-fused bicyclic spirolactams.

5a led to a mixture of products. To overcome these problems we chose to utilize $Pd/CaCO_3$ as a catalyst[22] for the reduction of such azides. Thus, the treatment of azide **5a** with $Pd/CaCO_3$ in EtOH in the presence of H_2 (1 atm) at room temperature afforded the spiroaminals **9a** and **9b** (Scheme 2) in 1:1 ratio and in 78% yield. It is likely that under these conditions the azide group will first be reduced[19a] to a free amine which will undergo tautomerization accompanied by pyranose ring opening to form a species having a free alcohol and an imine. Reclosure to form pyranose ring will lead to two anomeric amines each of which will cyclize leading to two spiroaminals viz. **9a** and **9b**. Likewise, reduction of the mannose-derived azido ester **6a** in the presence of $Pd/CaCO_3$ gave 2:1 ratio of products **10a** and **10b** in 83% yield. These benzylated spirolactams **9a**, **9b**, **10a**, and **10b** were deprotected using Pd/C in EtOH in the presence of H_2 (1 atm) at room temperature to afford fully deprotected spirolactams **11a**, **11b**, **12a**, and **12b**, respectively, in quantitative yields, whose structures were confirmed by the spectral analysis of the corresponding acetates obtained from acetylation with Ac_2O/Py. Interestingly, while compound **11b** produced a pentaacetate **13b**, other compounds **11a**, **12a**, and **12b** gave the amides **13a**, **14a**, and **14b**, respectively. All these compounds were characterized by ^1H, ^{13}C NMR and COSY, and spectral data.[13a]

The stereochemistry at the anomeric center of spiroaminals was confirmed by NOE experiments. Thus in glucose-derived spiroaminal **13a**, irradiation of H-9 proton at δ 5.40 and H-7 proton at δ 3.84 enhanced -NH proton signal at δ 8.24 (4.6% and 5.1% NOE, respectively, Fig. 3). Similarly, we confirmed the stereochemistry of spiroaminals **14a** as an isomer having -NH group in axial position. In case of compound **14b**, irradiation of H-7 proton at δ 3.80 and H-9 proton at δ 5.11 enhanced H-4 proton signal at δ 2.40 (6.0% and 3.0% NOE, respectively, Fig. 3), clearly indicating the equatorial orientation of –NH position in compound **14b**. The stereochemistry of spiroaminal **13b**, as isomer with -NAc group in equatorial position was also confirmed in an analogous manner.

The inhibitory activities of compounds **11a**, **11b**, **12a**, **12b** were tested against five commercially available enzymes and the results are summarized in Table 3. The spiroaminals **11a** and **11b** showed good inhibition against galactosidases. Compound **11b** showed inhibition against α-galactosidase (coffee beans) at a concentration of 77 μM as a non-selective glycosidase inhibitor, whereas compound **11a** was found to be a highly selective β-galactosidase inhibitor and showed a considerable inhibition at a concentration of 207 μM. But, mannose-derived spirolactam **12a** did not show any activity against all tested enzymes, only compound **12b** showed activity against β-galactosidase at 0.4 mM concentration. These results suggest that these spiroaminals are inhibitors of glycosidases and structural variations of these molecules may improve the activity and selectivity of inhibition.

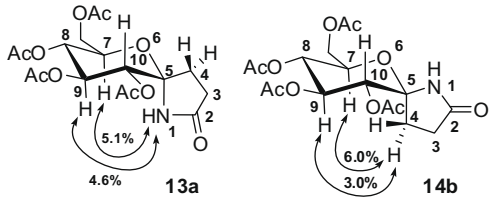


Figure 3. NOE correlations of compounds 1**3a** and **6a**.

Table 3
IC_{50} (μM) values for compounds **11a**, **11b**, **12a**, and **12b**

Entry	Enzyme	11a	11b	12a	12b
1	α-Glucosidase (yeast)	NI[a]	NI	NI	NI
2	β-Glucosidase (almonds)	NI	200	NI	NI
3	α-Galactosidase (coffee beans)	NI	77	NI	NI
4	β-Galactosidase (bovine)	207	160	NI	400
5	α-Mannosidase (Jack beans)	NI	NI	NI	NI

[a] NI: no inhibition at 3 mM concentrations, inhibition studies were carried out at 0.1–0.5 mM concentrations.

In conclusion, we have developed a method for the direct conversion of unstable nitro precursors viz. 1-*C*-alkyl-1-nitro sugars into stable amino precursors viz. 1-*C*-alkyl-1-azido sugars. We have studied hydrolysis behavior of Michael adducts of 1-nitro sugars and also S_N2-type of azidation reactions. This methodology gave an easy access to 6,5-fused spiroaminals. Because of the occurrence of spiroaminal frameworks in natural products of pharmacological importance, we studied the enzyme inhibition activities of hydroxy spiroaminals, in which lactam **11a** was found to be selective β-galactosidase inhibitors. Further work to extend the scope of the present study is in progress.

Acknowledgments

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2010.03.003.

References and notes

1. Nonboru, O. In *The Nitro Group in Organic Synthesis*; Feuer, H., Ed.; Organic Nitro Chemistry Series; Wiley-VCH, 2001.
2. (a) Wade, P. A.; Giuliano, R. M. The Role of Nitro Group in Carbohydrate Chemistry. In *Organic Nitro Chemistry Series*; Feuer, H., Nielsen, A. T., Eds.; Wiley-VCH, 1990; (b) Aebischer, B.; Vasella, A. *Helv. Chim. Acta* **1982**, *65*, 621–634; (c) Baumberger, F.; Beer, D.; Christen, M.; Prewo, R.; Vasella, A. *Helv. Chim. Acta* **1986**, *69*, 1191–1204; (d) Brade, W.; Vasella, A. *Helv. Chim. Acta* **1990**, *73*, 1923–1930; (e) Dupuis, J.; Giese, B.; Hartung, J.; Leising, M. *J. Am. Chem. Soc.* **1985**, *107*, 4332–4333; (f) Winterfeld, G. A.; Schmidt, R. R. *Angew.Chem., Int Ed.* **2001**, *40*, 2654–2657; (g) Geiger, J.; Gopal Reddy, B.; Winterfeld, G. A.; Weber, R.; Przybylski, M.; Schmidt, R. R. *J. Org. Chem.* **2007**, *72*, 4367–4377; (h) Sakakibara, T.; Tokuda, K.; Hayakawa, T.; Seta, A. *Carbohydr. Res.* **2000**, *327*, 489–496; (i) Sakakibara, T.; Narumi, S.; Matsuo, I.; Okada, S.; Nakamura, T. *Carbohydr. Res.* **2007**, *342*, 2339–2353; (j) Lemieux, R. U.; Nagabhushan, T. L.; O'Neill, I. K. *Can. J. Chem.* **1968**, *46*, 413–418.
3. (a) Somsak, L. *Chem. Rev.* **2001**, *101*, 81–135 (In this review see Vasella et al. references regarding 1-nitro sugars chemistry); (b) Das, J.; Schmidt, R. R. *Eur. J. Org. Chem.* **1998**, 1609–1613; (c) Khodair, A. I.; Winterfeld, G. A.; Schmidt, R. R. *Eur. J. Org. Chem.* **2003**, 1847–1852; (d) Balamurugan, R.; Pachamuthu, K.; Schmidt, R. R. *Synlett* **2005**, 134–138; (e) Barroca, N.; Schmidt, R. R. *Org. Lett.* **2004**, *6*, 1551–1554; (f) Peseke, K.; Ambrosi, H. D. *Carbohydr. Res.* **1989**, *194*, 87–93; (g) Kobertz, W. R.; Carolyn, R.; Bertozzi, C. R.; Bednarski, M. D. *J. Org. Chem.* **1996**, *61*, 1894–1897.
4. (a) Baumberger, F.; Vasella, A. *Helv. Chim. Acta* **1986**, *69*, 1205–1215; (b) Baumberger, F.; Vasella, A. *Helv. Chim. Acta* **1986**, *69*, 1535–1541.
5. Baumberger, F.; Vasella, A.; Schauer, R. *Helv. Chim. Acta* **1988**, *71*, 429–445.
6. Mirza, S.; Vasella, A. *Helv. Chim. Acta* **1984**, *67*, 1562–1567.
7. (a) Tamura, R.; Hegedus, L. S. *J. Am. Chem. Soc.* **1982**, *104*, 3727–3729; (b) Ono, N.; Hamamoto, I.; Kaji, A. *J. Chem. Soc., Chem. Commun.* **1982**, 821–822; (c) Ono, N.; Yanai, T.; Kamimura, A.; Kaji, A. *J. Chem. Soc., Chem. Commun.* **1986**, 1285–1287; (d) Ono, N.; Hamamoto, I.; Kaji, A. *Synthesis* **1985**, 950–952; (e) Chung, J. Y. L.; Grabowski, E. J. J.; Reider, P. J. *Org. Lett.* **1999**, *1*, 1783–1785; (f) Tamura, R.; Watabe, K.; Ono, N.; Yamamoto, Y. *J. Org. Chem.* **1993**, *58*, 4471–4472; (g) Ono, N.; Jun, T. X.; Hashimoto, T.; Kaji, A. *J. Chem. Soc., Chem. Commun.* **1987**, 947–948.
8. Vasella, A. *Pure Appl. Chem.* **1991**, *63*, 507–518.
9. Aebischer, B.; Bieri, J. H.; Prewo, R.; Vasella, A. *Helv. Chim. Acta* **1982**, *65*, 2251–2271.
10. Mahmood, K.; Vasella, A.; Bernet, B. *Helv. Chim. Acta* **1991**, *74*, 1555–1584.
11. (a) Pachamuthu, K.; Gupta, A.; Das, J.; Schmidt, R. R.; Vankar, Y. D. *Eur. J. Org. Chem.* **2002**, 1479–1483; (b) Gopal Reddy, B.; Vankar, Y. D. *Tetrahedron Lett.* **2003**, *44*, 4765–4767; (c) Gopal Reddy, B.; Vankar, Y. D. *Angew. Chem., Int. Ed.* **2005**, *44*, 2001–2004; (d) Jayakanthan, K.; Vankar, Y. D. *Tetrahedron Lett.* **2006**, *47*, 8667–8671; (e) Schmidt, R. R.; Vankar, Y. D. *Acc. Chem. Res.* **2008**, *41*, 1059–1073; (f) Kumar, A.; Rawal, G. K.; Vankar, Y. D. *Tetrahedron* **2008**, *64*, 2379–2390.
12. Aebischer, B.; Vasella, A. *Helv. Chim. Acta* **1983**, *66*, 789–794.
13. (a) See the Supplementary data for experimental and spectral details.; (b) Baumberger, F.; Vasella, A. *Helv. Chim. Acta* **1983**, *66*, 2210–2222.

14. Oda, Y.; Yamanoi, T. *Synthesis* **2007**, 3021–3031.
15. (a) Bell, R. A.; Osakwe, E. N. C. *Chem. Commun.* **1968**, 1093–1094; (b) Liu, S. L.; Shi, X. X.; Xu, Y. L.; Xu, W.; Dong, J. *Tetrahedron: Asymmetry* **2009**, *20*, 78–83.
16. (a) Jayakanthan, K.; Vankar, Y. D. *Org. Lett.* **2005**, *7*, 5441–5444; (b) Doddi, V. R.; Vankar, Y. D. *Eur. J. Org. Chem.* **2007**, 5583–5589; (c) Alam, M. A.; Kumar, A.; Vankar, Y. D. *Eur. J. Org. Chem.* **2008**, 4972–4980; (d) Alam, M. A.; Vankar, Y. D. *Tetrahedron Lett.* **2008**, *49*, 5534–5536.
17. (a) Karmer, R. M.; Johansen, B.; Hession, C.; Pepinnsky, R. B. *Adv. Exp. Med. Biol.* **1990**, *275*, 35–53; (b) Satake, M.; Ofuji, K.; Naoki, H.; James, K. J.; Furey, A.; McMohan, T.; Silke, J.; Yasumoto, T. *J. Am. Chem. Soc.* **1998**, *120*, 9967–9968; (c) Sanglier, J. J.; Quesniaux, V.; Fehr, T.; Hofmann, H.; Mahnke, M.; Memmert, K.; Schuler, W.; Zenke, G.; Gschwind, L.; Mauer, C.; Schlling, W. *J. Antibiot.* **1999**, *52*, 466–473; (d) Chatgilialoglu, C.; Gimisis, T.; Spada, G. P. *Chem. Eur. J.* **1999**, *5*, 2866–2876.
18. (a) Moi, S.; Inchinose, R.; Goto, K.; Sugai, S. *Tetrahedron* **1991**, *47*, 2111–2120; (b) Sano, H.; Sugai, S. *Tetrahedron* **1995**, *51*, 4635–4646; (c) Hanessian, S.; Sanceau, J. Y.; Chemla, P. *Tetrahedron* **1995**, *51*, 6669–6678.
19. (a) Bichard, C. J. F.; Mitchell, E. P.; Wormald, M. R.; Watson, K. A.; Johnson, L. N.; Zographos, S. E.; Koutra, D. D.; Oikonomakos, N. G.; Fleet, G. W. J. *Tetrahedron Lett.* **1995**, *36*, 2145–2148; (b) de la Fuente, C.; Krülle, T. M.; Watson, K. A.; Gregoriou, M.; Johnson, L. N.; Tsitsanou, K. E.; Zographos, S. E.; Oikonomakos, N. G.; Fleet, G. W. J. *Synlett* **1997**, 485–487; (c) Martin, A.; Perez-Martin, I.; Suarez, E. *Org. Lett.* **2005**, *7*, 2027–2030.
20. (a) Czifrak, K.; Szilagyi, P.; Somsak, L. *Tetrahedron: Asymmetry* **2005**, *16*, 127–141; (b) Czifrak, K.; Kovacs, L.; Kover, K. E.; Somsak, L. *Carbohydr. Res.* **2005**, *340*, 2328–2334; (c) Somsak, L.; Czifrak, K.; Veres, E. *Tetrahedron Lett.* **2004**, *45*, 9095–9097; (d) Dondoni, A.; Scherrmann, M. C.; Marra, A.; Delepine, J. L. *J. Org. Chem.* **1994**, *59*, 7517–7520.
21. Gopal Reddy, B.; Madhusudanan, K. P.; Vankar, Y. D. *J. Org. Chem.* **2004**, *69*, 2630–2633.
22. (a) Suzuki, T.; Suzuki, S. T.; Yamada, I.; Kaoshi, Y.; Yamada, K.; Chida, N. *J. Org. Chem.* **2002**, *67*, 2874–2880; (b) Aravind, A.; Sankar, M. G.; Varghese, B.; Baskaran, S. *J. Org. Chem.* **2009**, *74*, 2858–2861.