Pergamon

Tetrahedron: *Asymmetry* 13 (2002) 687–690

TETRAHEDRON: *ASYMMETRY*

Catalytic $FeCl_3$- or $Yb(OTf)_3$-mediated synthesis of substituted tetrahydrofurans and *C*-aryl glycosides from 1,4-diols†

G. V. M. Sharma,[a,*] K. Raman Kumar,[a] Punna Sreenivas,[a] Palakodety Radha Krishna[a] and Mukund S. Chorghade[b]

[a]*D 211, Discovery Laboratory, Organic Chemistry Division III, Indian Institute of Chemical Technology, Hyderabad 500 007, India*

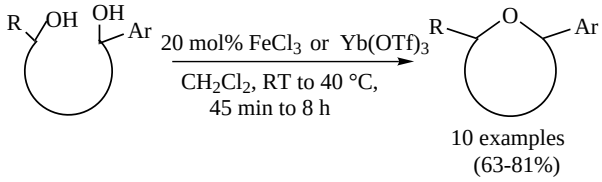
[b]*Chorghade Enterprises, 14 Carlson Circle, Natick, MA 01760-4205, USA*

Received 22 January 2002; accepted 11 April 2002

Abstract—A facile and mild protocol for the synthesis of substituted tetrahydrofurans, 2-deoxy *C*-aryl glycoside and *C*-aryl glycosides is described by use of 20 mol% $FeCl_3$ or $Yb(OTf)_3$ as acid catalysts. The benzylic carbocation generated undergoes intramolecular substitution by the oxygen nucleophile to result the tetrahydrofurans and *C*-aryl glycosides.

1. Introduction

The synthesis of substituted tetrahydrofurans,[1] *C*-aryl and 2-deoxy-*C*-aryl glycosides, structural features that are commonly encountered in a variety of natural products,[2–4] has attracted considerable attention due to their significant biological properties. Even though several acidic reagents[5–9] (mineral, Lewis and Bronsted) were reported for the intramolecular cyclo dehydration of 1,4-diols, most of these methods use the reagents in stoichiometric quantities, require elevated temperatures and longer reaction times to synthesize the tetrahydrofurans. Recent years have witnessed an upsurge in the synthesis of *C*-aryl glycosides[10–13] owing to the significant biological and pharmacological properties of some of these compounds. Taking advantage of facile carbocation formation in the presence of a variety of Lewis acids such as $FeCl_3$,[14] DIBAL-H[15] and $Yb(OTf)_3$,[16–19] we have recently reported methods in protection–deprotection chemistry. In continuation of our studies on the use of carbocation chemistry in organic synthesis, herein, we describe a facile $FeCl_3$-[20]or $Yb(OTf)_3$-mediated protocol for the conversion of 1,4-diols (Eq. (1)) into substituted tetrahydrofurans, 2-deoxy sugar and *C*-aryl glycosides.



(1)

2. Results and discussion

Initially (Table 1), on reaction with 20 mol% $FeCl_3$ in CH_2Cl_2 at room temperature, diol **1** underwent facile cyclisation in 45 min to afford the tetrahydrofuran **1a** as a racemic mixture (71%). Similarly 1,4-diol **2** under the above reaction conditions gave the corresponding tetrahydrofuran **2a** (77%) as a 2:1 (*trans*:*cis*) mixture. The C(5) proton signal for the *trans* isomer appeared at δ 4.98 as a triplet ($J=8.37$ Hz) while for the *cis* isomer, it resonated as a doublet by triplet ($J=2.32$, 7.44 Hz) at δ 4.84. The diol **3** afforded **3a** in 73% yield as a single isomer (*trans*), $[\alpha]_D=-43.3$ (*c* 1.7, $CHCl_3$), while the diol **4** gave 2-deoxy sugar **4a** in 81% yield (1:1). When diols **1**–**4** were treated with 20 mol% $Yb(OTf)_3$ in CH_2Cl_2 at room temperature the expected products **1a**–**4a** were formed. However, the reaction times were longer and the yields were lower than those from reactions with $FeCl_3$ (Table 1).

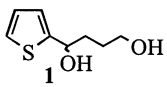
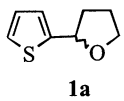
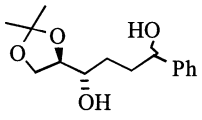
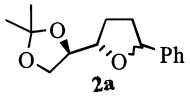
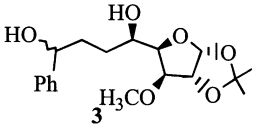
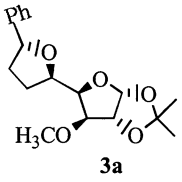
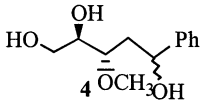
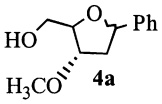
Having successfully prepared the tetrahydrofurans and 2-deoxysugar derivative, the protocol was then extended to the synthesis of *C*-aryl glycosides. Accord-

* Corresponding author. E-mail: esmvee@iict.ap.nic.in

† IICT Communication No. 4642.

0957-4166/02/$ - see front matter
PII: S0957-4166(02)00179-9

Table 1. 20 mol% $FeCl_3$- and $Yb(OTf)_3$-mediated cyclisation of 1,4-diols

S. No	Starting Material	Product	20 mol% $FeCl_3$		20 mol% $Yb(OTf)_3$	
			Time (min)	Yield in % (Ratio of Isomers)	Time (h)	Yield in % (Ratio of Isomers)
1.	 **1**	 **1a**	45	71 racemic	2.5	61 racemic
2.	 **2**	 **2a**	45	77 (2:1, *trans:cis*)	4.5	52 (2:1, *trans:cis*)
3.	 **3**	 **3a**	45	73 (100:0 *trans:cis*)	3	67 (100:0 *trans:cis*)
4.	 **4**	 **4a**	45	81 (1:1 *trans:cis*)	2	71 (1:1 *trans:cis*)

ingly, diol **5** (Table 2) on treatment with 20 mol% $FeCl_3$ gave the *C*-aryl glycoside **5a**, albeit in a very poor yield.

Our earlier experience with $Yb(OTf)_3$ prompted us to treat the diols **5** and **6** with 20 mol% $Yb(OTf)_3$ in dry CH_2Cl_2 at 40°C, to afford *C*-aryl glycosides **5a** (74%) and **6a** (71%), respectively as 3:2 (β:α) mixture of inseparable isomers. 1,4-Diols **7**, **8** and **9**, prepared from diacetone-D-mannose, when subjected to cyclization under the above reaction conditions, gave the *C*-aryl glycosides **7a** (72%), $[\alpha]_D = 19.4$ (*c* 1.2, $CHCl_3$), **8a** (68%), $[\alpha]_D = 12.4$ (*c* 1.2, $CHCl_3$) and **9a** (63%), $[\alpha]_D = -10.5$ (*c* 1.6, $CHCl_3$) respectively, as exclusive α-isomers. The C(1) proton signal for **7a** appeared at δ 5.0 as a doublet ($J = 8.6$ Hz), for **8a** at δ 5.28 as a singlet[21] and for **9a** the C(1)H resonated at δ 5.29 as a doublet ($J = 7.8$ Hz). Similarly, the 1,4-diol **10**, prepared from D-ribose, furnished the expected β-isomer **10a** in 68% yield as an exclusive product, ($[\alpha]_D = -17.7$ (*c* 0.9, $CHCl_3$).

The structures of compounds **7a** and **9a** as exclusive α-isomers were unambiguously confirmed from NOE studies (Fig. 1). In compound **7a**, C(1)H and C(2)H show NOE enhancements with the *ortho* protons of the phenyl ring, while **9a** shows an NOE enhancement for C(2)H with the lone *ortho* proton, thus confirming the assigned structures.

3. Conclusions

In summary, a facile and mild protocol for the synthesis of substituted tetrahydrofurans, 2-deoxy sugar and *C*-aryl glycosides is described using 20 mol% $FeCl_3$ or $Yb(OTf)_3$ as acid catalysts. This methodology would be of immense use for synthesizing chiral furans as well as *C*-aryl glycosides.

4. Experimental

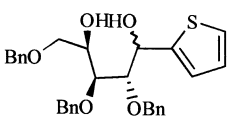
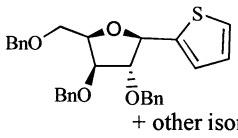
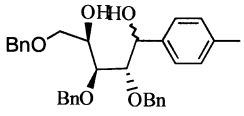
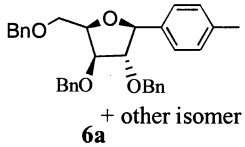
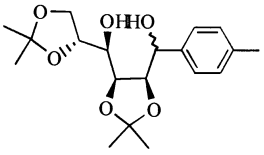
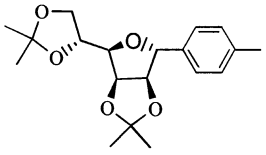
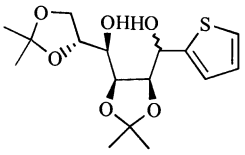
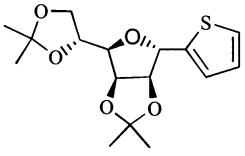
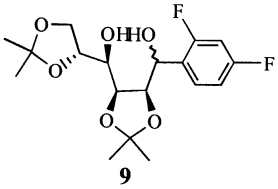
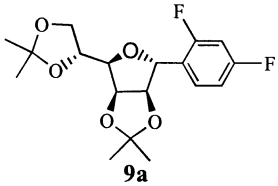
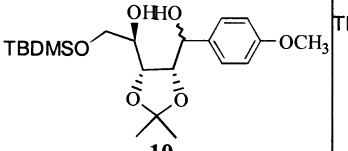
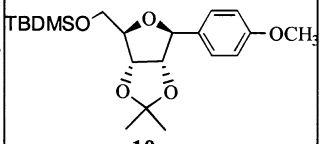
4.1. Typical experimental procedure

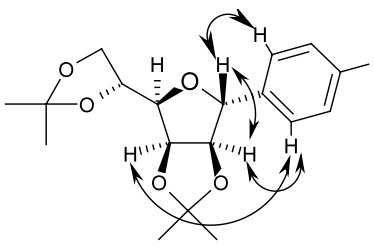
To a solution of diol **1** (0.2 g, 1.16 mmol) in CH_2Cl_2 (5 mL), anhydrous $FeCl_3$ (0.038 g, 0.23 mmol) was added and the mixture was stirred at room temperature for 45 min. After completion of the reaction (TLC analysis), it was diluted with CH_2Cl_2 (10 mL) and washed with saturated aq. $NaHCO_3$ solution (10 mL), water (10 mL), brine (10 mL) and dried (Na_2SO_4). Evaporation of solvent and purification by column chromatography (Si-gel, 5% EtOAc in hexane) gave **1a** in 71% yield as a syrup. A similar procedure was adopted for the $Yb(OTf)_3$ mediated synthesis of *C*-aryl glycosides.

4.2. Spectral data for selected compounds

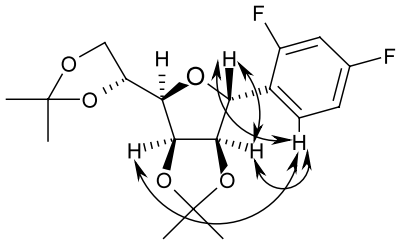
Compound 3a: ^1H NMR: (400 MHz, $CDCl_3$, TMS, δ in ppm): 1.30 (s, 3H, -CH_3), 1.50 (s, 3H, -CH_3), 1.79–1.9

Table 2. Conversion of 1,4-diols into *C*-aryl glycosides using 20 mol% $Yb(OTf)_3$

S.No.	Starting Material	Product	Time (h)	Yield(%)	Ratio of Isomers
1.	 **5**	 + other isomer **5a**	6	74	3:2 (β:α)
2.	 **6**	 + other isomer **6a**	4	71	3:2 (β:α)
3.	 **7**	 **7a**	6	72	exclusive (α)
4.	 **8**	 **8a**	5	68	exclusive (α)
5.	 **9**	 **9a**	8	63	exclusive (α)
6.	 **10**	 **10a**	5	68	exclusive (β)



7a



9a

Figure 1. NOE interactions in compounds **7a** and **9a**.

(m, 1H, H-6), 1.96–2.08 (m, 1H, H-6″), 2.18–2.26 (m, 1H, H-7), 2.32–2.42 (m, 1H, H-7′), 3.48 (s, 3H, -OCH_3), 3.79 (d, $J=10.2$ Hz, 1H, H-4), 4.00–4.06 (m, 1H, H-3), 4.38–4.46 (m, 1H, H-5), 4.52 (d, 1H, $J=10.2$ Hz, H-2), 4.98–5.04 (t, 1H, $J=11.28$ Hz, H-8), 5.86 (d, 1H, $J=10.2$ Hz, H-1), 7.18–7.34 (m, 5H, Ar-H); FAB-MS (m/z, %): 319 (M^+-1, 13.8), 147 (72.6), 91 (56.9), 81 (100), 77 (31.9).

Compound 4a: ^{1}H NMR: (400 MHz, $CDCl_3$, TMS, δ in ppm): 1.8–2.01 and 2.42–2.68 (2m, 2H, H-2.2[1]), 3.36 (s, 3H, -OCH_3), 3.4 (s, 3H, -OCH_3), 3.61–4.08 (m, 3H, H-4.5), 4.10–4.20 and 4.28–4.34 (2m, 1H, H-3), 5.00–5.05 and 5.10–5.18 (2m, 1H, H-1), 7.2–7.38 (m, 5H, Ar-H); EIMS (m/z, %): 208 (M^+, 63.4), 207 (M^+-1, 57.2), 177 (16.4), 124 (47.5), 77 (100).

Compound 5a: ^{1}H NMR: (400 MHz, $CDCl_3$, TMS, δ in ppm): 3.64–3.78 (m, 2H, H-5), 3.8–3.86 (m, 1H, H-4), 4.04–4.10 (m, 1H, H-3), 4.18–4.6 (m, 7H, benzylic CH_2, H-2), 5.04, 5.38 (2d, $J=11.0$ Hz, H-1, 1H (α:$\beta=2$:3), 6.88–7.32 (m, 15H, Ar-H); FAB-MS (m/z, %): 509 (M^++23, 9.7), 485 (M^+-1, 2.7), 281 (36.1) 181 (6.9), 91 (100).

Compound 8a: ^{1}H NMR: (400 MHz, $CDCl_3$, TMS, δ in ppm): 1.28 (s, 3H, -CH_3), 1.36 (s, 3H, -CH_3), 1.41 (s, 3H, -CH_3), 1.55 (s, 3H, -CH_3), 3.82–3.86 (m, 1H, H-4), 4.02–4.14 (m, 2H, H-6), 4.38–4.44 (m, 1H, H-5), 4.78–4.82 (m, 1H, H-3), 5.00 (d, 1H, $J=9.9$ Hz, H-2), 5.28 (s, 1H, H-1), 6.94–6.98 (m, 1H, Ar-H), 7.24–7.28 (m, 2H, Ar-H); FAB-MS (m/z, %): 349 (M^++23, 16.5), 327 (M^++1, 32), 311 (48) 303 (18) 143 (75).

Compound 10a: ^{1}H NMR: (200 MHz, $CDCl_3$, TMS, δ in ppm): 0.11 (s, 6H, -CH_3), 0.98 (s, 9H, -CH_3), 1.34 (s, 3H, -CH_3), 1.45 (s, 3H, -CH_3), 3.74-3.88 (m, 6H, -OCH_3, H-5, 6), 4.16–4.22 (m, 1H, H-4), 4.68–4.74 (m, 1H, H-3), 4.89 (d, 1H, $J=4.76$ Hz, H-2), 5.12 (d, 1H, $J=4.76$ Hz, H-1), 6.83 (d, $J=9.30$ Hz, 2H, Ar-H), 7.24 (d, 2H, $J=9.30$ Hz, Ar-H). FAB-MS (m/z, %): 393 (M^+-1, 4.6), 391 (M^+-3, 12.5), 359 (27.7), 279 (11.1), 121 (100).

Acknowledgements

K. Raman Kumar and P. Sreenivas acknowledge the financial support from the CSIR, New Delhi, India.

References

1. Harmange, J.-C.; Figadere, B. *Tetrahedron: Asymmetry* **1993**, *4*, 1711–1754.
2. *Polyether Antibiotics: Naturally Occurring Acid Ionophores*; Wetley, J. W., Ed.; Marcel Dekker: New York, 1982.
3. (a) Corney, C. J.; Weigel, L. O.; Chamerlin, A. R.; Lipshutz, B. *J. Am. Chem. Soc.* **1980**, *102*, 1439–1441; (b) Hanessian, S.; Lavalle, P. *Can. J. Chem.* **1981**, *59*, 870–877; (c) Keck, G. K.; Kachensky, D. F. *J. Org. Chem.* **1986**, *51*, 2487–2493; (d) Ramesh, S.; Kaila, N.; Goewal, G.; Frank, R. W. *J. Org. Chem.* **1990**, *55*, 5–7; (e) Binkley, R. W.; Koholic, D. J. *J. Org. Chem.* **1989**, *54*, 3577–3580.
4. Bycraft, B. W. *Dictionary of Antibiotics and Related Substances*; Chapman and Hall: London, 1988.
5. Larock, R. C. *Comprehensive Organic Transformations*, 2nd ed.; John Wiley and Sons, 1999; pp. 898–900.
6. Scott, L. T.; Naples, J. O. *Synthesis* **1973**, 209.
7. Olah, G. A.; Fung, A. P.; Malhotra, R. *Synthesis* **1981**, 474–476.
8. Molnar, A.; Felfoldi, K.; Bartok, M. *Tetrahedron* **1981**, *37*, 2149–2151.
9. Kim, S.; Chung, K. N.; Yang, S. *J. Org. Chem.* **1987**, *52*, 3917–3919.
10. (a) Hadfield, A. F.; Sartoslli, A. F. *Carbohydr. Res.* **1982**, *701*, 197–208; (b) Ciment, D. M.; Ferrier, R. J. *J. Chem. Soc.* **1980**, 441–445; (c) Grynkiewicz, G.; Priebe, W.; Zamojski, A. *Carbohydr. Res.* **1979**, *68*, 33–41.
11. (a) Hocksell, U.; Daves, G. D. *J. Prog. Med. Chem.* **1985**, *22*, 1–65; (b) Franz, G.; Gruen, M. *Plasta* **1983**, *47*, 131–140.
12. (a) Toshima, K.; Matsuo, G.; Nakata, M. *J. Chem. Soc., Chem. Commun.* **1994**, 199–200; (b) Allev, P.; Anastasia, M.; Ciuffreda, P.; Fiecchi, A.; Scala, A.; Bingham, S.; Muir, M.; Tyman, J. *J. Chem. Soc., Chem. Commun.* **1991**, 1319–1320; (c) Parker, K. A.; Coburn, C. A. *J. Am. Chem. Soc.* **1991**, *113*, 8516–8518; (d) Daves, G. D. J. *Acc. Chem. Res.* **1990**, *23*, 201–206; (e) Bellosta, V.; Czernecki, S. *J. Chem. Soc., Chem. Commun.* **1989**, 199–200; (f) Czeonecki, S.; Vilee, G. *J. Org. Chem.* **1989**, *54*, 610–612; (g) Casiraghi, G.; Cornia, M.; Colombo, L.; Rassu, G.; Favo, G. G.; Bericch, M. F.; Zetta, L. *Tetrahedron Lett.* **1988**, *29*, 5549–5552; (h) Schmidt, R. R.; Frick, W.; Haag-Zieno, B.; Apparao, S. *Tetrahedron Lett.* **1987**, *28*, 4045–4048; (i) Bellosta, V.; Czernecki, S. *Carbohydr. Res.* **1987**, *171*, 279–288.
13. (a) Kometani, T.; Konda, H.; Fujimori, Y. *Synthesis* **1988**, 1005–1007; (b) Matsumoto, T.; Katsuki, M.; Suzuki, K. *Tetrahedron Lett.* **1988**, *29*, 6935–6938; (c) Mastumoto, T.; Katsuki, M.; Juna, H.; Suzuki, K. *Tetrahedron Lett.* **1989**, *30*, 6185–6188; (d) Matsumoto, T.; Hosoga, T.; Suzuki, K. *Tetrahedron Lett.* **1990**, *31*, 4629–4632; (e) Matsumoto, T.; Hosoya, T.; Suzuki, K. *Synlett* **1991**, 709–711.
14. Sharma, G. V. M.; Mahalingam, A. K.; Nagarajan, M.; Ilangovan, A.; Radha Krishna, P. *Synlett* **1999**, 1200–1202.
15. Sharma, G. V. M.; Ilangovan, A.; Sreenivas, P.; Mahalingam, A. K. *Synlett* **2000**, 615–618.
16. Sharma, G. V. M.; Ilangovan, A.; Mahalingam, A. K. *J. Org. Chem.* **1998**, *63*, 9103–9104.
17. Sharma, G. V. M.; Ilangovan, A. *Synlett* **1999**, 1963–1965.
18. Sharma, G. V. M.; Mahalingam, A. K. *J. Org. Chem.* **1999**, *64*, 8943–8944.
19. Sharma, G. V. M.; Rajendra Prasad, T.; Mahalingam, A. K. *Tetrahedron Lett.* **2001**, *42*, 759–761.
20. Barrett, I. C.; Langille, J. D.; Kerr, M. A. *J. Org. Chem.* **2000**, *65*, 6268–6269.
21. Radha Krishna, P.; Lavanya, B.; Ilangovan, A.; Sharma, G. V. M. *Tetrahedron: Asymmetry* **2000**, *11*, 4463–4472.