Monatsh Chem (2009) 140:79–81
DOI 10.1007/s00706-008-0010-9

ORIGINAL PAPER

One-step regioselective green synthesis of 2,3-mannoepoxy-β-cyclodextrin under aqueous conditions

Zhi-zhong Wang · Wei Jiao · Guang-yun He · Run-hua Lu

Received: 30 May 2008 / Accepted: 2 June 2008 / Published online: 9 August 2008

Abstract A simple method for the straightforward regioselective synthesis of 2,3-mannoepoxy-β-cyclodextrin, which is a valuable precursor for further functionalization of β-cyclodextrin, is achieved under aqueous conditions without any organic solvents at a moderate yield.

Keywords Cyclodextrins · 2,3-Mannoepoxy-β-cyclodextrin · Regioselective synthesis · Sulfonylimidazole

Introduction

Cyclodextrins (CDs) are well-known cyclic oligosaccharides consisting of six or more α-1,4-linked D-glucopyranose units, which possess the secondary C-2 and C-3 hydroxyls on their more open face and the primary C-6 hydroxyls on the other face. Cyclodextrins have been widely used as artificial enzymes, sensors, drug delivery systems, and chiral reagents [1–6] owing to their hydrophobic and optically active interior. Since the more open secondary hydroxyl side of CDs is stated to be catalytically very important [7, 8], modifications of this face are believed to produce valuable derivatives for catalysis, enzyme mimic, chiral discrimination, etc.

The most commonly used method for selective functionalization of the secondary face of β-CD (**1**) is shown in Scheme 1 (steps I, II, and IV), which takes the mono-2-tosyl-β-cyclodextrin (**2**) as the key intermediate, and whose synthesis is still difficult [9–11]. In recent years, research has focused on improving the preparation of mono-2-tosyl-β-cyclodextrin, and several successful strategies have been developed [12–20]. In fact, 2,3-mannoepoxy-β-cyclodextrin (**3**) is also a key intermediate, and its synthesis has not excited considerable attention. Herein, we report a one-step regioselective synthesis of 2,3-mannoepoxy-β-cyclodextrin under aqueous conditions without any organic solvents (step III in Scheme 1).

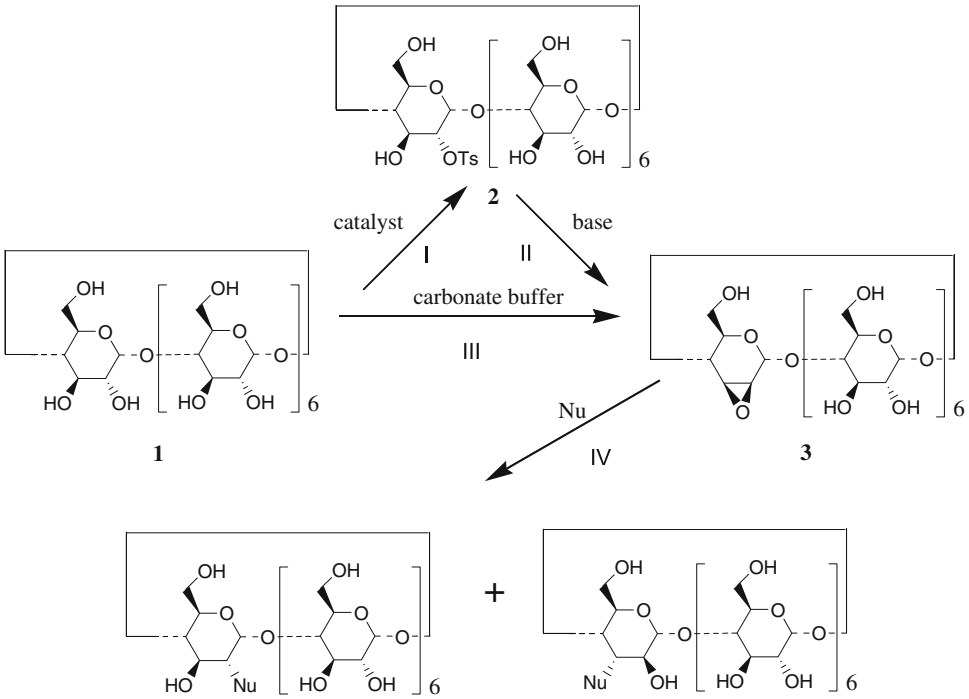
Z. Wang · W. Jiao · G. He · R. Lu (✉)
Chengdu Institute of Biology, Chinese Academy of Sciences, 610041 Chengdu, China
e-mail: lurh@cib.ac.cn

Results and discussion

In our previous work [21], we developed a convenient and economic method for monosulfonylation of β-CD at the 2-position by using the combination of *N*-tosylimidazole and carbonate buffer (pH 9.9) in DMF, and found that carbonate buffer can efficiently promote the reaction; moreover the reaction is highly regioselective at the 2-position. Therefore, we tried to do the experiment environmentally friendly in carbonate buffer solution without any organic solvents. Surprisingly, it was found that cyclodextrin epoxide that was not a tosylate of β-cyclodextrin was formed under the experimental conditions. The ^{1}H NMR spectrum (in D_2O) of the epoxide showed a one-proton doublet at δ 3.4 ppm (J = 3.2 Hz) and an unsplit one-proton signal at 5.2 ppm, in addition to normal cyclodextrin signals. Its ^{13}C NMR spectrum (in DMSO-d_6) demonstrated the presence of the epoxide carbons at δ 49.1 and 54.0 ppm, and its ESI-MS spectrum contained the molecular ion at m/z 1139 ($[M+Na]^+$). These facts indicated that the epoxide was 2,3-mannoepoxy-β-cyclodextrin, which was identical with that reported in references [22–24].

The optimized conditions for the synthesis of 2,3-mannoepoxy-β-cyclodextrin are β-CD/*N*-tosylimidazole = 1/2

Scheme 1



(mol/mol), β-CD/carbonate buffer = 1/20 (g/cm^3) at 60 °C for 2 h and 80 °C for another 1 h. The ESI-MS spectrum demonstrated the decrease in 2,3-mannoepoxy-β-cyclodextrin under higher temperature and longer reaction times.

In conclusion, 2,3-mannoepoxy-β-cyclodextrin is directly synthesized in one step in a carbonate buffer solution at a moderate yield. The process reported here is an economic and green synthesis method.

Experimental

NMR spectra were recorded on Bruker AM-600 (^{1}H 600 MHz and ^{13}C 150 MHz) in D_2O and DMSO-d_6 solutions with TMS as standard. The ESI-MS experiments were performed using a ThermoQuest Finnigan LCQ^{DECA} system equipped with an ESI source (ThermoQuest LC/MS Division, San Jose, CA, USA). *N*-Tosylimidazole was prepared according to the method described in [25]. Carbonate buffer (0.2 M; pH 9.9) was prepared by mixing equal volumes of 0.2 M sodium carbonate and 0.2 M sodium bicarbonate. All other chemicals were of commercial grade without further purification.

General experimental procedure

A mixture of 1.50 g β-CD (1.32 mmol) and 0.58 g (2.62 mmol) *N*-tosylimidazole in 30 cm^3 of 0.2 M carbonate buffer (pH 9.9) was stirred at 60 °C for 2 h, and continued at 80 °C for another 1 h. Then the mixture was neutralized with 0.1 M HCl, evaporated in vacuo to a volume of ca. 20 cm^3, and 140 cm^3 of acetone were added to precipitate cyclodextrin derivatives. The collected solid was washed with 400 cm^3 acetone–water (4:1, *v*:*v*) twice and filtered. The two filtrates were combined, and evaporated to dryness in vacuo giving crude product **3** at a 15% yield. It was further purified on a RP-18 column to give 150 mg pure **3** (10%). ESI-MS: m/z = 1139 ([M+Na]$^+$); ^{1}H NMR (600 MHz, D_2O): δ = 3.44 (d, J = 3.2 Hz, 1H), 3.47–3.73 (m, 15H), 3.75–4.03 (m, 26H), 4.95–5.08 (m, 6H), 5.22 (s, 1H) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 49.1, 54.0, 60.2, 60.3, 60.4, 60.7, 61.0, 70.1, 70.6, 71.8, 72.5, 72.6, 72.8, 72.9, 73.3, 73.5, 73.8, 80.3, 81.3, 81.7, 81.9, 82.1, 82.2, 97.5, 102.0, 102.1, 102.3, 102.4 ppm.

Acknowledgments Financial support from the Chinese Natural Science Foundation (No. 20772120) is gratefully acknowledged.

References

1. Breslow R (1994) Pure Appl Chem 66:1573
2. Breslow R (1995) Acc Chem Res 28:146
3. Breslow R, Dong SD (1998) Chem Rev 98:1997
4. Stainer CA, Alderman SJ, Claridge TD, Anderson HL (2002) Angew Chem Int Ed 41:1769
5. Hedges AR (1998) Chem Rev 98:2035
6. Uekama K, Hirayama F, Irie T (1998) Chem Rev 98:2045

7. D'Souza VT, Bender ML (1987) Acc Chem Res 20:146
8. Vanetten RL, Sebastian JF, Clowes GA, Bender ML (1967) J Am Chem Soc 89:3242
9. Dienst EV, Snellink BHM, Piekartz IV, Grote Gansey MHB, Venema F, Feiters MC, Nolte RJM, Engbersen JFJ, Reinhoudt DN (1995) J Org Chem 60:6537
10. Yuan DQ, Tahara T, Chen WH, Okabe Y, Yang C, Yagi Y, Nogami Y, Fukudome M, Fujita K (2003) J Org Chem 68:9456
11. Khan AR, Forgo P, Stine KJ, D'Souza VT (1998) Chem Rev 98:1977
12. Ueno A, Breslow R (1982) Tetrahedron Lett 23:3451
13. Rong D, D'Souza VT (1990) Tetrahedron Lett 31:4275
14. Law H, Baussanne I, Garc Fernandez JM, Defaye J (2003) Carbohydr Res 338:451
15. Teranishi K, Watanabe K, Hisamatsu M, Yamada T (1998) J Carbohydr Chem 17:489
16. Teranishi K (2000) Chem Commun 14:1255
17. Teranishi K (2000) Tetrahedron Lett 41:7085
18. Teranishi K (2001) Tetrahedron Lett 42:5477
19. Yu H, Teramoto A, Fukudome M, Xie RG, Yuan DQ, Fujita K (2006) Tetrahedron Lett 47:8837
20. Strerath M, Meng M, Kubik S (2007) Synthesis: 348
21. Wang ZZ, He GY, Lu RH (2008) Monatsh Chem (in press)
22. Breslow R, Czarnik AW (1983) J Am Chem Soc 105:1390
23. Breslow R, Czarnik AW, Lauer M, Leppkes R, Winkler J, Zimmerman S (1986) J Am Chem Soc 108:1969
24. Fujita K, Tahara T, Nagamura S, Imoto T, Kogas T (1987) J Org Chem 52:636
25. Hicks DR, Fraser Reid B (1974) Synthesis: 203