

A Facile Synthesis of a Chiral Furan Diol from Glycals Catalyzed by Indium Trichloride[†]

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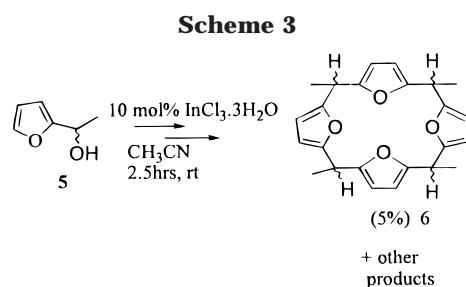
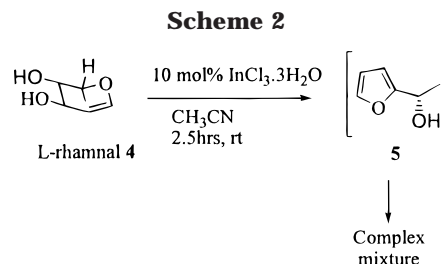
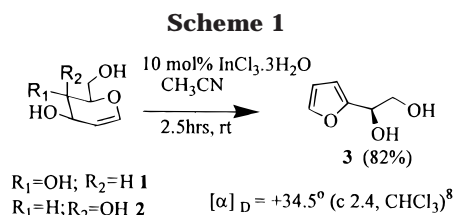
The furan ring system constitutes the basic framework of many natural products. Monosaccharides under acidic conditions lead to furans.¹ 2-(D-glycero-1,2-dihydroxyethyl)furan **3**, an optically active furan diol, is a potential chiral building block in organic synthesis. The transformation of D-glucal to **3** was first reported by Gonzalez *et al.*² using the toxic metal salt HgSO₄ in concentrated H₂SO₄. A recent report by Hayashi *et al.*³ on the use of relatively less toxic Sm(OTf)₃ or RuCl₂(PPh₃)₃ for the same transformation prompts us to communicate our own findings in this regard.

Of late, indium trichloride, which is a relatively strong Lewis acid, has been used as a catalyst for a wide variety of organic reactions, *viz.* Mukaiyama aldol reaction,⁴ imino Diels–Alder reaction,⁵ and Barbier reactions involving diastereoselective addition of allyltin to aldehydes or aldoses.⁶

As part of our ongoing program on the use of various Lewis acids in carbohydrate chemistry,⁷ we have found InCl₃·3H₂O to be a less expensive and equally efficient catalyst for the synthesis of **3** from unprotected D-glucal **1** and D-galactal **2** under mild conditions.

When 1 equiv of D-glucal **1** was treated with 0.1 equiv (10 mol %) of InCl₃·3H₂O in acetonitrile for 2.5 h at ambient temperature, chiral furan diol **3** was obtained in 82% yield. As expected, D-galactal **2** also underwent facile transformation to afford the same product, *viz.* **3** (Scheme 1).

Surprisingly, extension of the same reaction to L-rhamnal **4** did not provide the expected chiral furyl-methyl carbinol **5**, but led to a more complex mixture as revealed by HPLC analysis. The ¹H NMR spectrum and ¹³C NMR spectrum of this mixture clearly showed



absence of signals due to H-2 at δ 4.73 (t) and C-2 at δ 68.22, characteristic of **3**.⁹ Instead, it displayed signals at δ 1.53, 3.9–4.2, 5.8–6.01, 6.28, 7.31 in the ¹H NMR spectrum and at δ 18.05, 33.12, 104.86, 105.35, 110.06, 141.14, 155.28, 155.38, 156.73 in the ¹³C NMR spectrum. The multiplet at δ 3.9–4.2 in the ¹H NMR spectrum and the signal at δ 33.12 in the ¹³C NMR spectrum¹⁰ clearly reveals that this carbon is not attached to oxygen.¹¹ (Scheme 2).

It is likely that under the reaction conditions the carbinol **5**, if it all initially formed, would be unstable leading to spontaneous dehydration, followed by intermolecular alkylation and ultimately cyclization leading to complex mixture of products.

Indeed, when *rac*-**5**, prepared from the borohydride reduction of 2-acetylfuran, was treated with InCl₃·3H₂O in CH₃CN, it afforded the same complex mixture as obtained from the direct reaction of **4**.¹²

In summary, we have found that InCl₃·3H₂O is an efficient catalyst for the synthesis of 2-(D-glycero-1,2-

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[†] Dedicated to Prof. K. Nagarajan, Director, R&D, Recon Ltd. Bangalore, India, on the occasion of his 70th birthday.

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(8) Lit. $[\alpha]_D +36.4$ (c 1.2, CHCl₃); see ref 3.

(9) **Data for 2-(D-glycero-1,2-dihydroxyethyl)furan (3)**: $[\alpha]_D = +34.5^\circ$ (c 2.4, CHCl₃); IR (CHCl₃ cm⁻¹) 3600, 3424, 2928, 1600, 1494, 1468, 1376, 1145, 1088, 1068, 998, 937, 873, 825, 652, 595; ¹H NMR (200 MHz, CDCl₃, δ) 3.76 (d, 2H, *J* = 5.7 Hz), 4.73 (t, 1H, *J* = 5.54 Hz), 6.23–6.30 (m, 2H), 7.32–7.33 (m, 1H); ¹³C NMR (50 MHz, CDCl₃, δ) 64.83, 68.22, 106.78, 110.17, 142.07, 153.58; HRMS *m/z* calcd for C₆H₈O₃ 128.047 345, found 128.050 232 t2.

(10) The DEPT spectrum indicated CH at δ 33.12 and CH₃ at δ 18.05.

(11) We believe that one of the products could be the anhydro tetramer or the quaterene **6** based on literature reports,¹² or an oligomer (see Scheme 3).

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dihydroxyethyl)furan **3**, an optically active furandiol. The reaction proceeds at ambient temperature unlike the Sm-(OTf)₃⁻ or RuCl₂(PPh₃)₃-catalyzed reaction, which requires relatively higher temperature (80 °C). Besides, the workup is simple and amenable for scale-up, thereby providing an useful alternative to the reported methods.

Experimental Section

Typically, to D-glucal **1** (1 mmol) was added InCl₃·3H₂O (0.1 mmol; 10 mol %) in CH₃CN (1–3 mL) at ambient temperature and magnetically stirred. After completion (2.5 h, TLC), the reaction mixture was quenched with aqueous sodium hydrogen carbonate (10%, 25 mL), extracted with dichloromethane (3 × 25 mL), dried over anhydrous sodium sulfate, filtered, and

concentrated. The residue was purified by flash column chromatography on silica gel to obtain **3**.

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Supporting Information Available: Copies of ¹H and ¹³C NMR spectra for compounds **3** and **6**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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