ORGANIC
LETTERS

2006
Vol. 8, No. 6
1061−1064

Crystal or Low Molecular Mass Organogel Based on Sugar-Derived Chiral Pyrano[2,3-*b*]naphtho[1,2-*e*]pyrans

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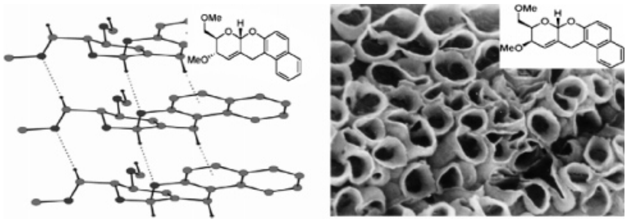
Received December 7, 2005

ABSTRACT



2-*C*-Acetoxymethyl glycal derivatives reacted with β-naphthol in the presence of InCl$_3$ (30 mol %) to give chiral pyrano[2,3-*b*]naphtho[1,2-*e*]pyrans in good to excellent yields via stereoselective Ferrier rearrangement–tandem cyclization. The major glucose-derived product exhibited crystal packing with C–H···O and C–H···π (arene) interactions and the major galactose-derived product, a low molecular mass organogelator (LMOG), formed a rare type of micro tubular gel assembly in *n*-hexane.

Because of various possible applications[1] such as membrane materials in separation technology, in catalysis or drug delivery, low molecular mass organogelators (LMOG)[2] have recently gained much attention. Such molecules can gelatinize in a variety of organic solvents, forming interesting assembled structures, which are characterized by the corresponding SEM or TEM pictures. Driving forces of molecular aggregation such as H-bonding, π-stacking, etc. are responsible for the assembly of such molecules in the gel or crystal.[3,4] In continuation of our systematic scanning of the efficacy of In(III)-based organic reactions,[5] we report herein InCl$_3$-catalyzed stereoselective synthesis (via Ferrier rearrangement−tandem cyclization of 2-*C*-acetoxymethylglycals[6]) of D-glucose- and D-galactose-derived chiral fused pyrano[2,3-*b*]naphtho[1,2-*e*]pyrans (Scheme 1). Such molecules exhibit crystal structures that show different types of

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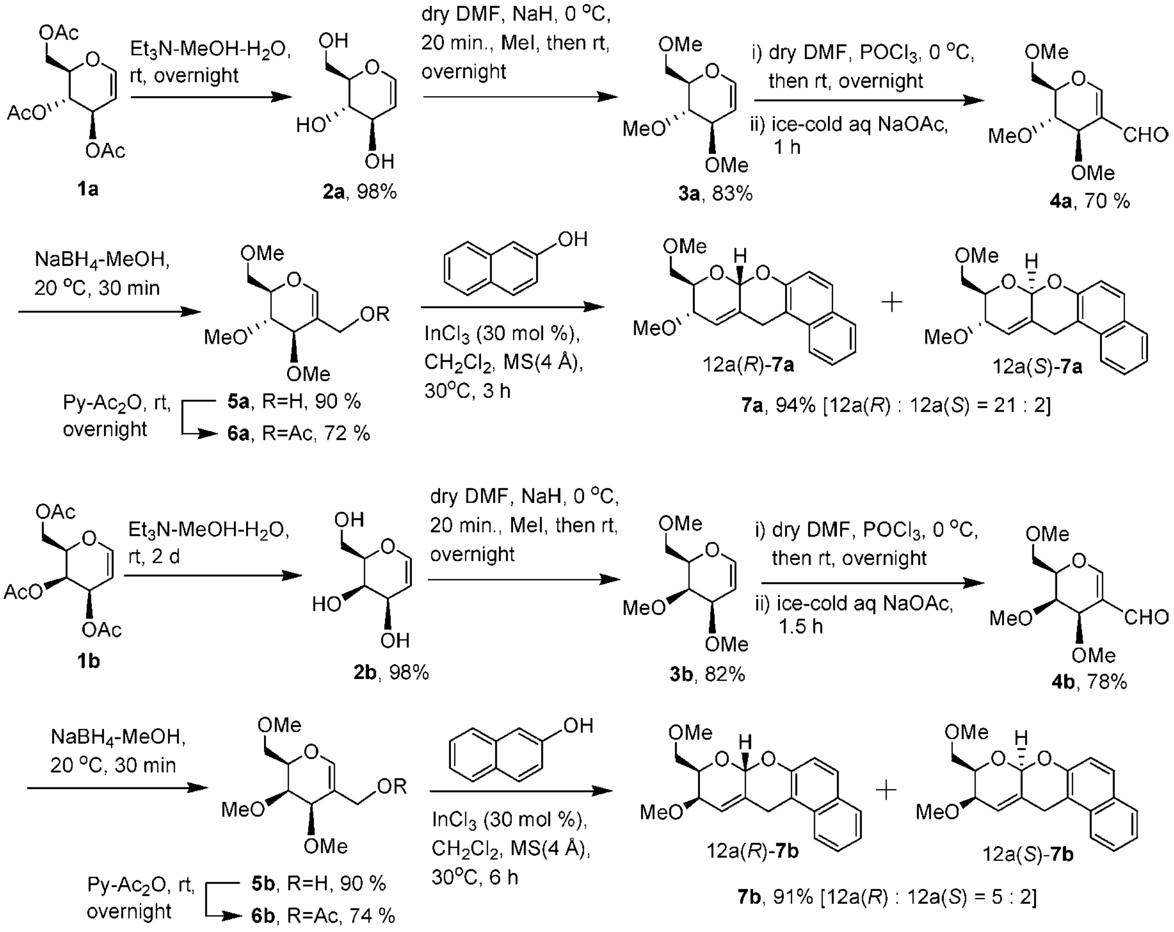
10.1021/ol052963e CCC: $33.50

Scheme 1. Synthesis of Sugar-Derived Chiral Pyrano[2,3-*b*]naphtho[1,2-*e*]pyrans



C−H···O and C−H···π (arene) interactions and constitute a new class of organogel. Analogous fused tetrahydro[2,3-*b*][1]benzopyrans are found in various naturally occurring bioactive molecules.[7] Balasubramanian et al.[8] first reported the synthesis of sugar-based chiral pyrano[2,3-*b*][1]benzopyrans via the $BF_3{\cdot}OEt_2$-mediated reaction of 2-*C*-acetoxymethylglycal derivatives with different phenols, and to the best of our knowledge, only one example of a related pyranonaphthopyran has been cited in the literature.[6]

The synthesis of the title compounds from per-*O*-acetylglucal or galactal is depicted in Scheme 1.

Tri-*O*-acetylglycals (**1a**,**b**) were converted to the corresponding 2-*C*-acetoxymethylglycals (**6a**,**b**) in five steps by the literature procedure.[5g,6] Compounds **1a** and **1b** on deacetylation followed by methylation furnished the corresponding tri-*O*-methylglycals (**3a,b**), which were then formylated under Vielsmeyer conditions; reduction and subsequent acetylation of the resulting 2-*C*-formyl-3,4,6-tri-*O*-methylglycals (**4a**,**b**) finally afforded the respective 2-*C*-acetoxymethyl-3,4,6-tri-*O*-methylglycals (**6a**,**b**). Compound **6a** on treatment with β-naphthol in the presence of 30 mol % of $InCl_3$ in dichloromethane at ambient temperature furnished, via Ferrier rearrangement followed by tandem cyclization−elimination, the corresponding pyrano[2,3-*b*]naphtho[1,2-*e*]pyrans (**7a**) in 94% yield and excellent diastereoselectivity in favor of (2*R*,3*S*,12a*R*)-2,3,5,12a-tetrahydro-2-methoxymethyl-3-methoxypyrano[2,3-*b*]naphtho[1,2-*e*]pyran [12a(*R*)/12a(*S*)= 21:2]. The reaction of the galactal-based Ferrier system (**6b)** with β-naphthol also proceeded efficiently, resulting in the corresponding pyrano[2,3-*b*]naphtho[1,2-*e*]pyrans (**7b**) in excellent yield (91%) with moderate stereoselectivity (5:2) in favor of the 12a(*R*)-isomer. All products were characterized by IR, NMR (^1H and ^{13}C), mass, and C,H,N analysis. Stereochemistry of 12a(*R*)- and 12a(*S*)-**7a** was established from the corresponding NOESY correlations. C_2-H and C_{12a}-H showed a NOE correlation in 12a(*S*)-**7a** but not in 12a(*R*)-**7a**, thus revealing the relative *cis* disposition of these two hydrogens in 12a(*S*)-**7a** and *trans* disposition in 12a(*R*)-**7a**. Final confirmation of the structure of

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12a(*R*)-**7a** was obtained by the single-crystal X-ray diffraction analysis.[9,10] The ORTEP diagram of a single crystal of 12a(*R*)-**7a** is shown in Figure 1. The crystal packing of 12a-

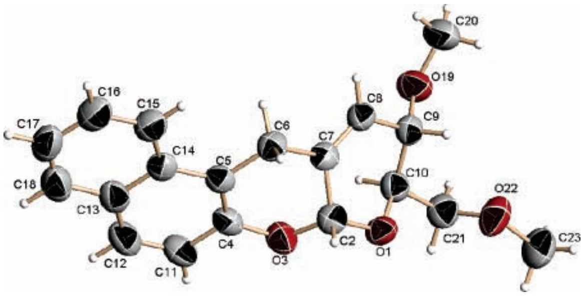

Figure 1. ORTEP structure of 12a(*R*)-**7a** (ellipsoids are drawn at 50% probability).

(*R*)-**7a** exhibits different types of intermolecular C−H···O and C−H···π (arene) hydrogen bonds. When viewed down the *a*-axis (Figure 2a), the molecules are stacked as single and running parallel to the *b*-axis. Intermolecular C−H···O hydrogen bonds [C20···O22 3.573 (3) Å, C20−H20C···O22 145.8(2)°] link each molecule of the single layer to two successive molecules of the adjacent double layer. Between the molecules of the double layer there exist C−H···O hydrogen bonds [C2···O3 3.639(3) Å, C2−H2···O3 157.9(2)°; C21···O22 3.506(3) Å, C21−H21B···O22 135.0(3)°] and C−H···π (arene) interaction [C6···C9 (C4, C5, C11−C14) 3.755(3) Å], thus forming a cluster of three molecules (Figure 2b).

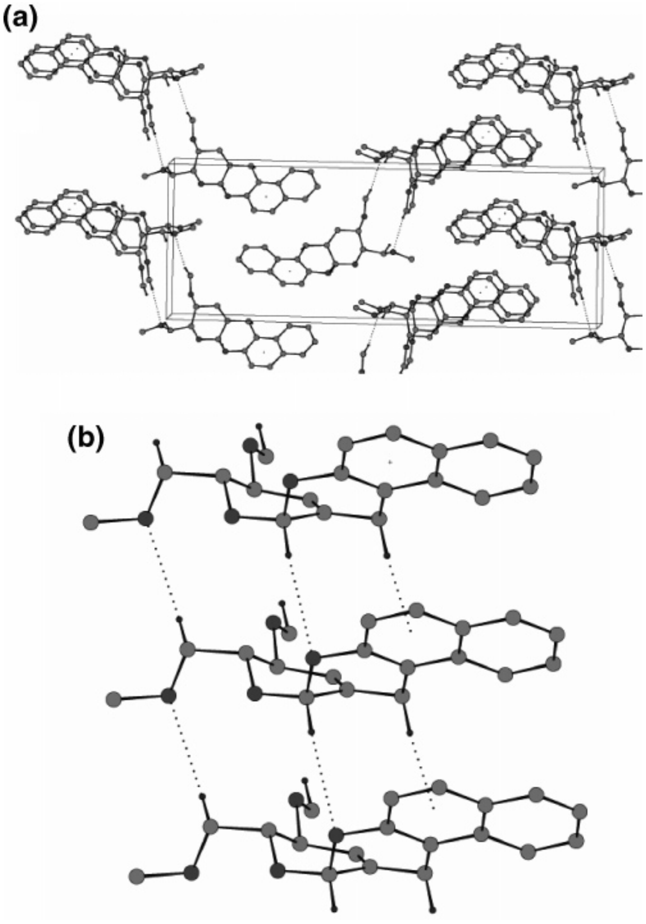

Figure 2. (a) Crystal packing down *a*-axis. (b) Crystal packing showing C−H···O and C−H···π (arene) interactions.

Compound 12a(*R*)-**7b** was a good organogelator in different organic solvents such as *n*-hexane, petroleum ether, ethanol, and methanol. To obtain visual insights into the morphology of the gel in different solvents SEM experiments were performed. The SEM pictures (Figure 3) of the organogel in nonpolar *n*-hexane (1.08×10^{-1}M) show the formation of micro tubular assembly. The driving force of aggregation of gelator molecules in the gel is probably due to related intermolecular H-bonding (C−H···O and/or C−H·

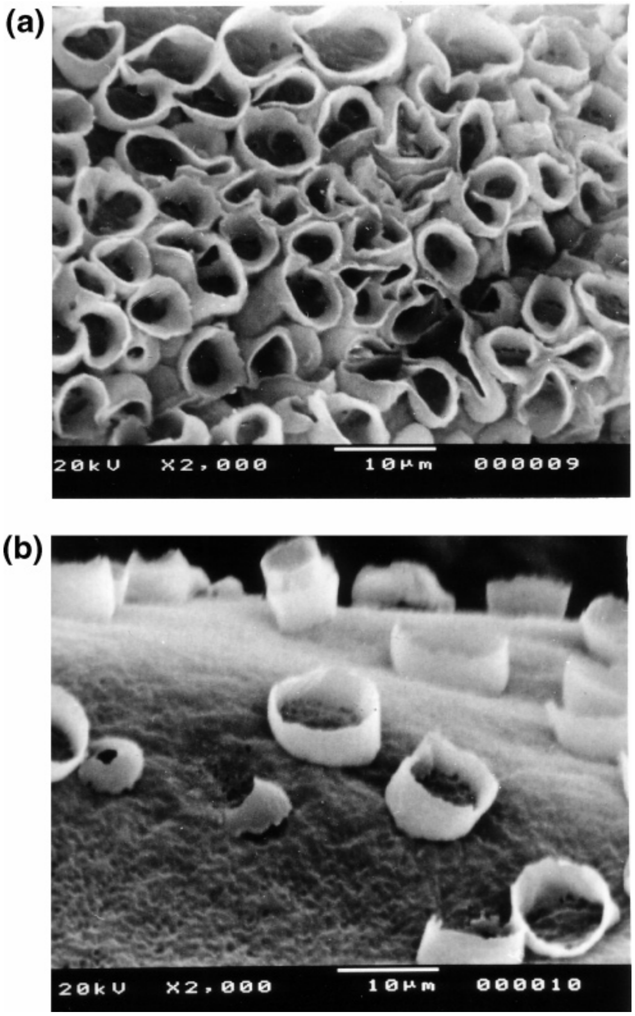

Figure 3. (a) SEM pictures of 12a(*R*)-**7b**−*n*-hexane gel (top view). (b) SEM pictures of 12a(*R*)-**7b**−*n*-hexane gel (tilted view).

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$\cdot\cdot\pi$) as also observed in the crystal packing of the corresponding epimer 12a-(*R*)-**7a** and/or π-stacking. To determine the concentration dependence of gelation ability T_{gel} was determined at various concentrations in *n*-hexane (Figure 4).

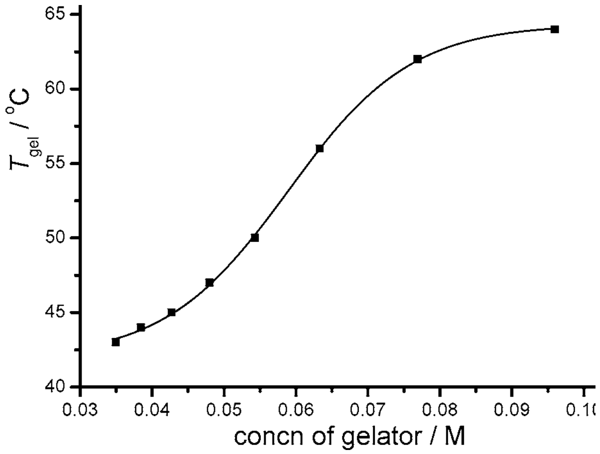

Figure 4. Concentration dependence of the T_{gel} of 12a(*R*)-**7b** in *n*-hexane.

In conclusion, $InCl_3$ turned out to be an efficient moisture-compatible Lewis acid catalyst for successful synthesis of D-glucose- and D-galactose-derived chiral pyrano[2,3-*b*]-naphtho[1,2-*e*]pyrans, with interesting respective crystal structure or gel assembly. We are closely examining in depth physical properties to establish the driving forces of gel assembly and find possible applications of the organogelator. Although our entry to this new class of organogel was serendipitous (like many others), further judicial variations of the aromatic part and the protecting groups are being continued to create new molecules of this type with differing properties.

Acknowledgment. Financial assistance from CSIR (Scheme Nos. 01/1672/00/EMR-II and 01/1951/04/EMR-II) to R.G. and from UGC, India, to A.C. (in the form of senior research fellowships) are gratefully acknowledged. R.G. thanks Professor Alok K. Mukherjee, Department of Physics, Jadavpur University, for his valuable suggestions on the crystal packing interactions.

Supporting Information Available: Experimental procedures and full spectroscopic data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) Single crystals of the complex were grown by slow evaporation of the solution in aqueous methanol. Colorless needle of approximate size 0.47 × 0.09 × 0.08 mm was used for data collection for the θ range = 1.95−25.0°, completeness to θ of 25.0° is 99.8%. $C_{19}H_{20}O_4$, $M = 312.35$, orthorhombic, $a = 4.5846(5)$ Å, $b = 11.1492(13)$ Å, $c = 30.445(4)$ Å, $V = 1556.2(3)$ Å^3, $T = 295(2)$ K, space group $P2_12_12_1$, $Z = 4$, μ(Mo Kα) = 0.093 mm^{-1}, 7939 reflections measured, 2748 unique [$I > 2\sigma(I)$], $R = 0.0453$, w$R_2 = 0.0958$.