T: 6-deoxy-6-amino-β-cyclodextrin[5] (0.5 g, 0.44 mmol) and triethylamine (60 µL, 0.44 mmol) were dissolved in dry DMF (10 mL) and cooled to 0°C. 1,3,5-benzenetricarbonyl trichloride (0.0355 g, 0.134 mmol) was added, and the reaction mixture was kept at 0°C for 1 h and then at RT for 12 h. The reaction product was precipitated with cold acetone (100 mL). The resulting solid was filtered and washed with cold acetone to remove the DMF. Finally the product was dissolved in water and purified through an Amicon 8050 ultrafiltration cell unit with a YM3 membrane ($M = 3000$) to give a white solid (0.279 g, 0.079 mmol, 59%). $R_f = 0.12$ (ethyl acetate/isopropyl alcohol/water/concentrated NH_4OH 2/3/4/0.3); m.p. 218–225°C (decomp); ^1H NMR (D_2O): $\delta = 8.23$ (s, 1H, Ar-H), 4.97–5.05(brs, 7H, H-1), 3.48–3.96 (m, 42H, H-2, H-3, H-4, H-5, H-6); ^{13}C and DEPT 135: $\delta = 171.5$ (CONH), 137.38 (substituted C_{Ar}), 131.77, (CH_{Ar}), 104.49 (C-1), 85.90 (C-4′), 83.72 (C-4), 75.69 (C-5), 74.68 (C-3), 74.22 (C-2), 62.92 (C-6), 43.57 (C-6′); positive-ion FAB-MS: m/z: 3559.0485 [M+1].

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Lithium Binaphtholates: Chiral Chains and Clusters**

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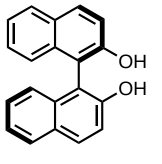

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Binaphthol (H_2binol) is chiral by virtue of restricted rotation about the C–C bond linking the two naphthyl units, and the absolute configuration of (R)-binaphthol (**1**) was first established unequivocally by X-ray diffraction in 1968.[1] The flexibility of the dihedral angle between the two naphthyl rings of this C_2-symmetric molecule allows coordination to a wide range of metal centers (examples are known from 45° to 110°), and H_2binol has been used as a chiral auxiliary in many metal-based enantioselective catalysts and reagents. Examples include the $Yb(OTf)_3$-catalyzed asymmetric Diels–Alder reaction,[2] the $TiCl_4$-derived catalyst for the asymmetric ene reaction,[3] and the chiral modification of $LiAlH_4$ for use in asymmetric reductions.[4] Multi-binaphthol species have attracted recent interest; particularly successful examples are Mikami's Ti–binaphtholate catalysts[5] and the heterometallic alkali metal/lanthanide binaphtholates synthesised by Shibasaki et al.[6] Examples of catalytically active multi-binaphthol Ti clusters have also been reported.[7, 8] In addition to these applications in asymmetric synthesis, binaphthol has also been of interest as a component of macrocycles for chiral recognition,[9, 10] and as a component of helical polymers with novel properties such as the emission of polarized light.[11]

In view of this widespread interest in binaphthol-containing species, it is surprising that no structural studies of the lithiated derivatives have been reported (inclusion compounds of *rac*-H_2binol with NaOH and KOH *have* been structurally characterized[12]). Lithiated H_2binol has been used in the preparation of many enantioselective catalysts and has also been investigated as a chiral auxiliary in its own right.[13] Our interest in lithium binaphtholates arose from our use of LiHbinol in the synthesis of anhydrous analogues of Shibasaki's heterometallic catalysts,[14] and herein we report on investigations of mono- and dilithiated derivatives of optically pure and racemic H_2binol. The previously overlooked structures of these compounds show unexpected diversity.

Lithiated H_2binol compounds [Li(*rac*-Hbinol)] (**2**), [Li{(R)-Hbinol}] (**3**), [Li_2(*rac*-binol)] (**4**), and [Li_2{(R)-binol}] (**5**) were prepared by reaction of H_2binol with stoichiometric quantities of nBuLi in THF at 0°C. All of these lithiated derivatives were precipitated as microcrystalline solids from THF solutions by the addition of petroleum ether, and we were able to grow X-ray-quality single crystals of **2**, **3**, and **4** by the slow diffusion of petroleum ether into the THF solutions at room temperature. Despite numerous attempts and using a range of precipitating solvents, good quality single crystals of **5** could not be obtained from THF solutions.

The monolithiated species **2** and **3** both crystallize as helical polymeric chains with $Hbinol^-$ units linked by $[Li(thf)_2]^+$ bridges, as shown for **2** in Figures 1 and 2. The chain structure of **3** is very similar, but less symmetrical, containing two inequivalent Li atoms. Short fragments of the chains of **2** and **3** are shown in Figures 3 and 4, respectively. The structure of **3** is necessarily composed of chains of a single enantiomer whereas that of **2** consists of arrays of R-configured polymer and S-configured polymer. The remaining O–H group has not been

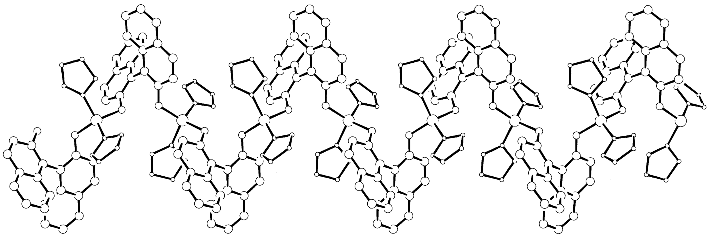

Figure 1. The [Li{(S)-Hbinol}] chain of [Li(*rac*-Hbinol)] (**2**).

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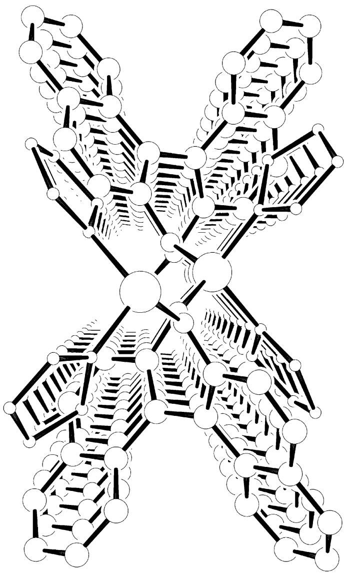

Figure 2. View along the [Li{(*S*)-Hbinol}] chain of [Li(*rac*-Hbinol)] (**2**) emphasizing the zigzag arrangement of Li atoms.

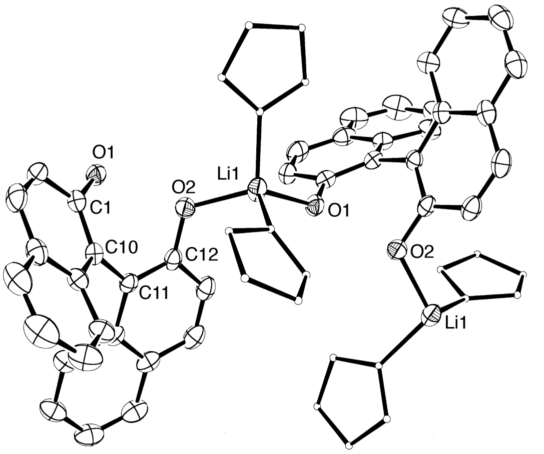

Figure 3. ORTEP plot of [Li(*rac*-Hbinol)] (**2**). Selected distances [Å] and angles [°]: Li1-O1 1.914(6), Li1-O2 1.942(6), O1 $\cdots$ O2(intramolecular) 2.4233(2), Li1 $\cdots$ Li1 5.6755(5); O1-Li1-O2 124.2(3), C1-C10-C11-C12 50.1(4).

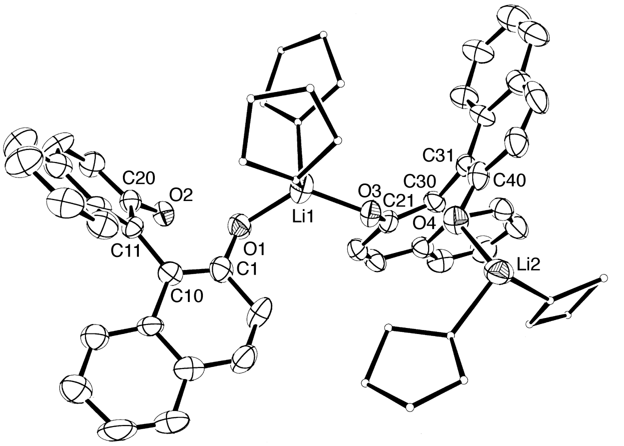

Figure 4. ORTEP plot of [Li{(*R*)-Hbinol}] (**3**). Selected distances [Å] and angles [°]: Li1-O1 1.920(15), Li1-O3 1.881(13), Li2-O4 1.929(14), Li2-O2 1.921(15), Li1 $\cdots$ Li2 5.6217(14), O1 $\cdots$ O3 3.3708(6); O1-Li1-O3 124.9(9), O2-Li2-O4 123.7(8), C1-C10-C11-C20 48.2(10), C21-C30-C31-C40 50.2(9).

located in the X-ray structure but it is reasonable to suppose that it occupies a bridging position between the O atoms of a single binol unit. This is clearly the case in THF where the ^{1}H NMR spectra of both **2** and **3** show a broad resonance arising from the phenolic OH which is shifted to very low field (11.1 ppm), a shift that is consistent with strong hydrogen bonding. The ^{1}H NMR spectra of **2** and **3** were indistinguishable; although the spectra were well-resolved, little useful structural information could be extracted. Between room temperature and $+50\,^{\circ}$C, there was essentially no change in the well-resolved spectra apart from an upfield shift of the OH resonance to 10 ppm; however, on lowering the temperature to $-50\,^{\circ}$C, considerable broadening was observed which would be consistent with the formation of an oligomeric structure similar to that observed in the solid state. The ^{13}C NMR spectra were also indistinguishable, and the ^{7}Li spectra showed a single resonance at $\delta = +2.70$ at temperatures between $+40$ and $-50\,^{\circ}$C.

It is useful to compare the crystal structures of **2** and **3** with those of (*R*)-H$_2$binol and *rac*-H$_2$binol, both of which crystallize as infinite H-bonded chains.[15, 16] (*R*)-H$_2$binol is made up of left-handed helical chains arranged along a 3_2 screw axis whereas the racemic compound crystallizes as arrays of 2_1-helical all-*R* chains and all-*S* chains. The H$_2$binol units are linked by hydrogen bonds which bridge intermolecular O–O distances of 2.961(4) Å for (*R*)-H$_2$binol and 2.852(3) Å for *rac*-H$_2$binol. The dihedral angles between the naphthyl groups of (*R*)- and *rac*-H$_2$binol are 101.65(5)° and 90.58(4)°, respectively, these are very much larger than those of **2** and **3**.

The dilithiated species [Li$_2$(*rac*-binol)] (**4**) exists in the solid state as the C_2-symmetric chiral cluster [Li$_6${(*R*)-binol}$_2${(*S*)-binol}(thf)$_8$] shown in Figures 5 and 6 and its *SSR* enantiomer (the unit cell contains two *RRS* clusters and two *SSR* clusters). Rings, stacked rings, and ladders are well known in lithium chemistry,[17] but the chiral central Li$_4$O$_4$ fragment of **4** is a novel structural motif which is best likened to a section of a spiral staircase. Li1, Li2, and Li4 have distorted tetrahedral geometry whereas Li3 is planar, as are the three-coordinate

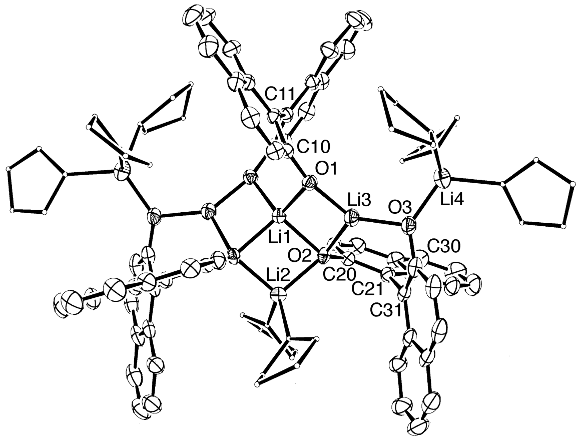

Figure 5. ORTEP plot of (*RRS*)-**4**. There is a C_2 axis along Li1-Li2. Selected distances [Å] and angles [°]: Li1-O1 1.902(9), Li1-O2 1.967(9), Li2-O2 1.945(10), Li3-O1 1.779(11), Li3-O2 1.923(10), Li3-O3 1.841(10), Li4-O3 1.842(12); O1-Li1-O1′ 105.2(7), O1-Li1-O2 94.83(16), O2-Li1-O2′ 97.7(6), O2-Li2-O2′ 99.3(7), O2-Li3-O1 100.6(4), O1-Li3-O3 143.4(6), O2-Li3-O3 115.6(6), C20-C21-C31-C30 -72.0(8), C10-C11-C11′-C10′ 64.1(7).

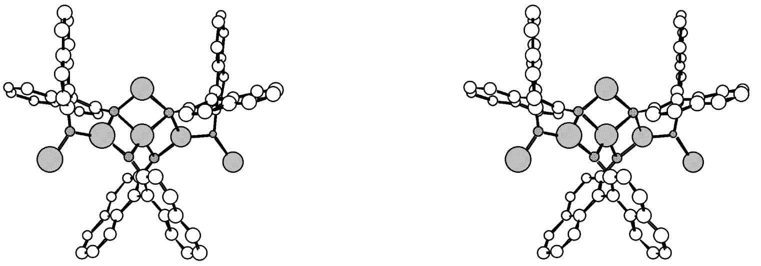

Figure 6. Stereoview of (*RRS*)-**4**. The thf ligands are omitted for clarity.

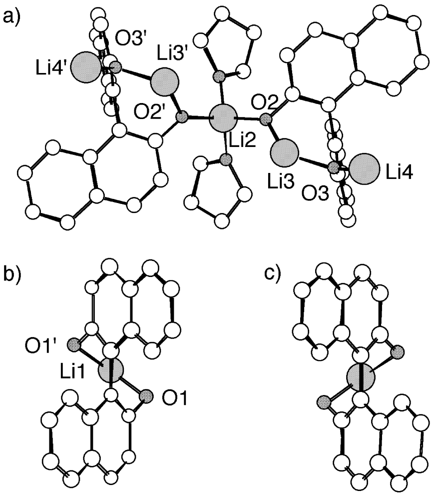

Figure 7. (*RRS*)-**4** separated into its component fragments: a) (*RR*)-$[Li_5(binol_2)]^+$ fragment, b) complementary $[Li\{(S)\text{-binol}\}]^-$ fragment, c) $[Li\{(R)\text{-binol}\}]^-$ fragment which cannot interact with fragment a).

O1 and O3 atoms. The remarkable self-assembly of the chiral cluster **4** cannot be explained by steric arguments. However, dissecting **4**, (Figure 7), into a) an *RR* fragment (a short section of an $[Li_2\{(R)\text{-binol}\}]$ chain), and b) an *S* fragment, illustrates clearly how the two $[Li_2\{(R)\text{-binol}\}]$ units of fragment a) cooperate to form a chiral template for recognition of fragment b). This fragment is perfectly aligned for interactions between O1′ and Li3′ and between O2′ and Li1, whereas these interactions are geometrically impossible for the enantiomeric fragment c). The low temperature solution structure of **4** is analogous to that found in the solid state: at 223 K the ^7Li NMR spectrum shows four resonances in the relative ratio 1:2:2:1, and 13 resonances are resolved in the aromatic region of the ^{13}C NMR spectrum. At 298 K the ^7Li spectrum shows only a single resonance although there is no apparent change in the ^{13}C NMR spectrum.

The previously overlooked structures of lithium binaphtholates have shown unexpected diversity. The well-known helical motif has manifested itself again in the monolithiated binaphthol derivatives, in this case with $[Li(thf)_2]^+$ acting as the intermolecular link, rather than hydrogen-bonding or covalent linkages. The novel chiral cluster, which self-assembles from $[Li_2(rac\text{-binol})]$, has provided a new structural motif in lithium alkoxide chemistry, and has also demonstrated that aggregates must always be considered when Li binaphtholates are used as reagents in solution.

Experimental Section

All the preparations described below were performed under strictly anaerobic conditions using standard Schlenk techniques. Solvents were distilled from sodium/benzophenone ketyl (non-deuterated) or CaH_2 (deuterated) and stored under N_2 over 4 Å molecular sieves prior to use. Samples for NMR spectroscopy were sealed under vacuum. ^1H and ^{13}C NMR spectra were recorded on a Gemini300 spectrometer. ^7Li NMR spectra were recorded on a Bruker WM250 spectrometer. Elemental analyses were performed in duplicate by Mr S. Apter of this Department.

Preparation of LiHbinol: A solution of *n*BuLi in hexanes (2.69 M, 1.22 cm³, 3.297 mmol) was added to a solution of H_2binol (*rac* or *R*, 0.944 g, 3.297 mmol) in THF (10 cm³) at 0 °C. The very pale yellow solution was allowed to warm to room temperature. Removal of the solvent in vacuo resulted in a white solid which was recrystallized from THF/petroleum ether. Li_2binol was prepared in an analogous manner using two equivalents of *n*BuLi.

Elemental analysis $[Li\{(R)\text{-Hbinol}\}(thf)_2]\cdot 1/4\,THF$ calcd (%) for $C_{29}H_{30}LiO_{4.25}$: C 76.64, H 6.87; found: C 73.04, H 6.53; $[Li(rac\text{-Hbinol})(thf)_2]$ calcd (%) for $C_{28}H_{29}LiO_4$: C 77.05, H 6.70; found: C 75.60, H 6.72; $[Li_2\{(R)\text{-binol}\}(thf)_n]$ calcd (%) for $C_{24}H_{20}Li_2O_3$: C 77.85, H 5.44; found: C 76.52, H 5.72; $[Li_6(rac\text{-binol})_3(thf)_8]\cdot 2\,THF$ calcd (%) for $C_{100}H_{116}Li_6O_{16}$: C 74.34, H 7.24; found: C 72.57, H 7.07.

^{13}C NMR (75 MHz, [D$_8$]THF, 25 °C, TMS), $[Li\{(R)\text{-Hbinol}\}]$: $\delta = 118.9$, 121.3, 123.7, 125.2, 127.1, 128.3, 128.4, 128.8, 136.1, 160.4; $[Li(rac\text{-Hbinol})]$: $\delta = 121.0$, 123.9, 125.0, 127.1, 128.3, 128.6, 136.2; $[Li_2\{(R)\text{-binol}\}]$: $\delta = 108.3$, 113.4, 118.9, 119.4, 123.7, 124.9, 126.1, 127.4, 135.8, 162–164(br); $[Li_2(rac\text{-binol})]$: $\delta = 108.8$, 118.6, 119.6, 123.8, 124.2, 126.3, 126.7, 127.4, 127.6, 127.8, 128.1, 137.1, 165.0. ^7Li NMR (217 MHz, [D$_8$]THF), $[Li_2\{(R)\text{-binol}\}]$ (298 K): $\delta = -2.4$; (223 K): $\delta = -2.35$, -3.01; $[Li_2(rac\text{-binol})]$ (298 K): $\delta = -2.4$; (223 K): $\delta = -0.92$ (1 Li), -2.34 (2 Li), -2.62 (2 Li), -3.36 (1 Li).

X-ray crystallography intensity data were collected using a STOE-IPDS image plate diffractometer ($Mo_{K\alpha}$, graphite monochromator) in the φ rotation scan mode. Data were collected at 213(2) K. The structures were solved by direct methods with the SHELXS97 package and refined using full-matrix least-squares on F^2 (SHELXL97).[18]

Crystal data for **2**: $C_{28}H_{28}LiO_4$, $M_r = 435.50$, monoclinic, space group $P2_1/c$, $a = 11.9330(17)$, $b = 10.8035(10)$, $c = 18.755(3)$ Å, $\beta = 100.093(17)$, $V = 2380.5(5)$ Å³, $Z = 4$, $\rho_{calcd} = 1.215\ g\,cm^{-3}$, $\mu\ (Mo_{K\alpha}) = 0.044\ mm^{-1}$, $F_{000} = 924$. A total of 3110 reflections were measured and used in the refinement. Refinement converged to $R = 0.0545$ for the 1719 reflections with $F > 2\sigma(F)$.

Crystal data for **3**: $C_{29}H_{30}LiO_{4.25}$, $M_r = 453.53$, monoclinic, space group $C2$, $a = 40.252(8)$, $b = 12.084(2)$, $c = 10.737(2)$ Å, $\beta = 105.47(3)$, $V = 5033.3(16)$ Å³, $Z = 4$, $\rho_{calcd} = 1.197\ g\,cm^{-3}$, $\mu\ (Mo_{K\alpha}) = 0.044\ mm^{-1}$, $F_{000} = 1928$. A total of 6332 reflections were measured and used in the refinement. Refinement converged to $R = 0.0958$ for the 4698 reflections with $F > 2\sigma(F)$.

Crystal data for **4**: $C_{100}H_{116}Li_6O_{16}$, $M_r = 1615.80$, monoclinic, space group $C2/c$, $a = 22.083(4)$, $b = 25.685(5)$, $c = 17.446(3)$ Å, $\beta = 113.76(3)$, $V = 9057(3)$ Å³, $Z = 4$, $\rho_{calcd} = 1.185\ g\,cm^{-3}$, $\mu\ (Mo_{K\alpha}) = 0.043\ mm^{-1}$, $F_{000} = 3448$. A total of 5471 reflections were measured and used in the refinement. Refinement converged to $R = 0.0758$ for the 2621 reflections with $F > 2\sigma(F)$.

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[18] Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-139116–139118. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

A Model for the Nonenzymatic BCD Cyclization of Squalene**

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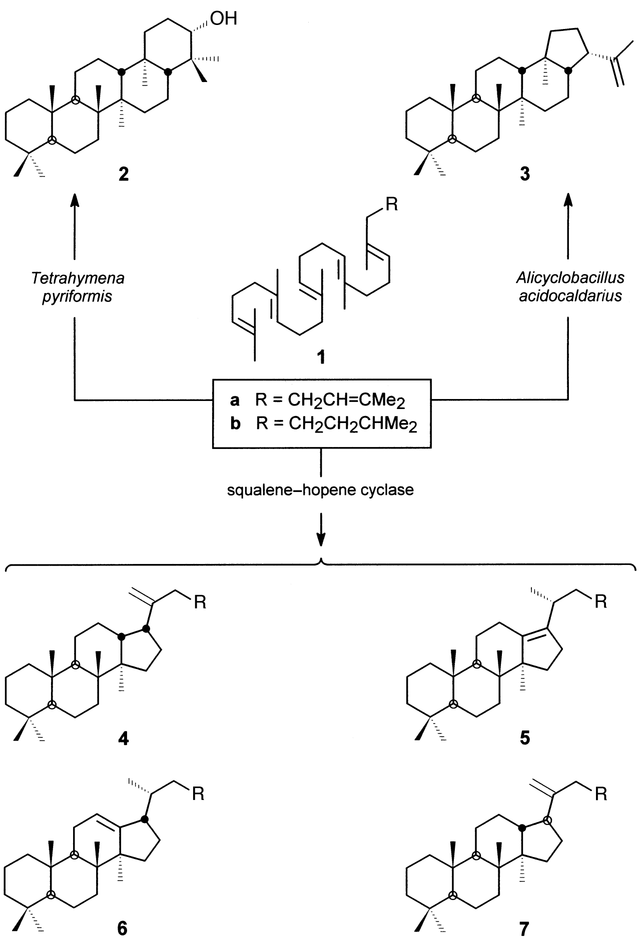
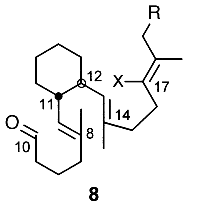
Marco Milanesio, and Davide Viterbo

The enzymatic polycyclization of squalene (**1a**) and 2,3-oxidosqualene (epoxysqualene) is a fascinating biogenetic process.[1] Whereas oxidosqualene cyclases produce sterols and plant triterpenes, the squalene cyclases (SC) of the protozoan *Tetrahymena pyriformis* and of the thermoacidophilic bacterium *Alicyclobacillus acidocaldarius* convert squalene (**1a**) into tetrahymanol (**2**) and hop-22(29)-ene (**3**, diploptene), respectively.[2, 3] Interestingly, a few years ago it was reported that squalene–hopene cyclase converts nonnatural 2,3-dihydrosqualene (**1b**) in high yield into a mixture of the tetracyclic triterpenes (20*R*)-dammar-13(17)-ene (**5b**) and (20*R*)-dammar-12-ene (**6b**) (Scheme 1).[4] More surprising even is the recent report about the isolation, next to the classical hopanoids, of the tetracyclic derivatives **4a**, **5a**, **6a**, and **7a**, each representing less than 2% relative to **3**, when the natural substrate squalene (**1a**) is treated with purified squalene–hopene cyclase.[5] This result raises the intriguing possibility that this enzyme has been "prepared" for performing the seemingly more complex transformation that bears analogy with the formation of lanosterol.[6] In this evolutionary context, however, one fundamental question remains unanswered: what is the nonenzymatic course of the poly-(tetra, penta)cyclization of squalene (and epoxysqualene)? Here we report on the results of the Lewis acid catalyzed cyclization of aldehydes **8a–c** that can provide an answer to the above question.



Scheme 1. Triterpenoids originating from cyclization of squalene (**1a**) and 2,3-dihydrosqualene (**1b**) catalyzed by bacterial squalene cyclases.



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a X = H ; R = $CH_2CH{=}CMe_2$
b X = H ; R = $CH_2CH_2CHMe_2$
c X = D ; R = $CH_2CH_2CHMe_2$

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