SHORT PAPER

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Synthesis and inclusion properties of novel host compounds derived from abietic acid[†]

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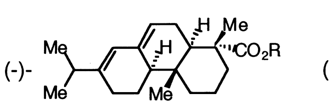
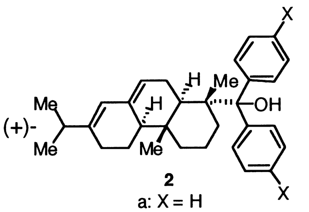
The novel host compounds, (7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,4b,5,6,10,10a-decahydro-phenanthren-1-yl)-diphenyl-methanol **(2a)** and its *p*-chlorophenyl- **(2b)** and *p*-methoxyphenyl- **(2c)** derivatives, have been synthesised by the Grignard reaction of abietic acid ethyl ester with the corresponding ArMgBr. The host compounds **(2a–2c)** include various organic compounds by hydrogen bonding between the host and guest compounds.

Keywords: abietic host compounds, inclusion complex

The design of new lattice inclusion systems has been of interest in recent years due to their potential applications in separation, synthetic and material sciences.[1] We have designed optically active host compounds from (+)-tartaric acid.[2] Optical resolution and enantioselective transformation of the guest compounds have been studied by inclusion complexation with the host compounds.[3] Here, we report the inclusion properties, molecular recognition and X-ray crystal structure of novel chiral host compounds (**2a–2c**) derived from (-)-abietic acid (**1a**), which is readily available by the isomerisation of rosin.[4]



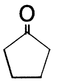
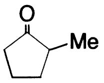
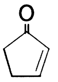
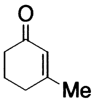
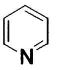
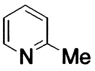
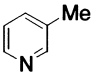
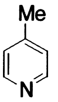
1
a: R = H
b: R = Et



2
a: X = H
b: X = OMe
c: X = Cl

Treatment of (-)-abietic acid ethyl ester (**1b**) with PhMgBr in THF gave crude crystals of (7-isopropyl-1,4a-dimethyl-1,2,3,4,4a,4b,5,6,10,10a-decahydro-phenanthren-1-yl)-diphenyl-methanol (**2a**). Recrystallisation of the crude crystals from isopropanol gave pure crystals of **2a** in 79% yield. Compounds, **2b** and **2c** were prepared by treatment of **1b** with the corresponding Grignard reagents in 53 and 48% yield, respectively. These new host compounds (**2a–2c**) formed inclusion crystals with various organic compounds such as ketones, DMSO, DMF and pyridine derivatives with 1:1 stoichiometry. In particular, host **2a** showed high inclusion ability. (Table 1)

Table 1 Host-guest ratios of inclusion complexes of **2a**, **2b** and **2c**[a]

Guest	2a	2b	2c
Acetone	1:1	—[b]	—
DMF	1:1	1:1	1:1
DMSO	1:1	—	—
	1:1	1:1	1:1
 (3)	1:1	—	—
	1:1 (4)	—	—
	1:1	—	—
	1:1	1:1	1:1
	1:1	1:1	1:1
	1:1	1:1	—
	1:1	1:1	—

[a]The ratios were determined by TG and ^{1}H NMR spectroscopy.
[b]No complexation occurred.

It was noticeable that the host molecule **2a** showed selective inclusion complexation of 2-methylcyclopentanone (**3**) from a mixture with the 3-methyl isomer. For example, when **2a** was recrystallised from a 1:1 mixture of 2-methyl- and 3-methylcyclopentanone, a 1:1 inclusion crystal of **2a** and 2-methylcyclopentanone (**3**) was obtained as colourless prisms, which upon heating gives **3** of 100% purity in 52% yield. In the inclusion complexation of **2a** with 2-methylcyclopentanone (**3**), the partial optical resolution of (±)-**3** also occurred. For example, when **2a** was recrystallised from neat **3**, a 1:1 inclusion crystal (**4**) of **2a** and (-)-**3** was obtained as colourless prisms, which upon heating gives (-)-**3** of 9.1 % ee.

The crystal structure of the inclusion complex (**4**) of **2a** and cyclopentenone was analysed by X-ray diffraction methods in order to elucidate the mode of molecular assembly modes. Figure 1 shows the crystal structure of **4** projected along the

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[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

c-axis, bound between *z*=0.5 and 1.0 for clarity. The host molecules with their long molecular axes lie nearly parallel to the *b*-axis at almost equal elevation from the projected plane. If it is assumed that these molecules form a layer structure, the crystal structure may be described as consisting of such layers stacked along the *c*-axis. The guest molecules are contained in cavities formed in each layer, which are connected to the host molecules by hydrogen bonds between O (1) and O (2), 2.798 (4) Å.

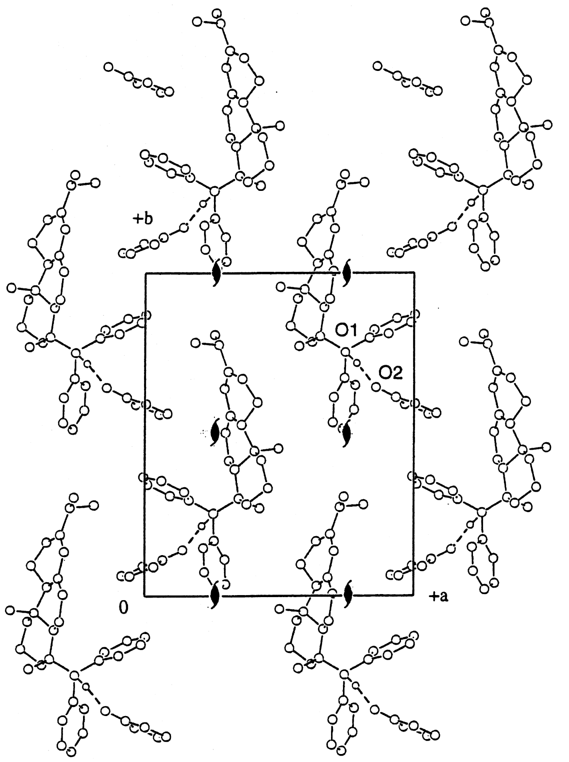

Fig. 1 *C*-axis projection of the crystal structure of **4**. Two-fold screw axes parallel to the *c*-axis are represented only. Intermolecular contacts shorter than 3.6 Å are as follows: O (2) – C (16) = 3.529 (6) and O (2) – C (15) = 3.547 (6) Å between layers; C (24) – C (35) = 3.555 (7) Å in the layer.

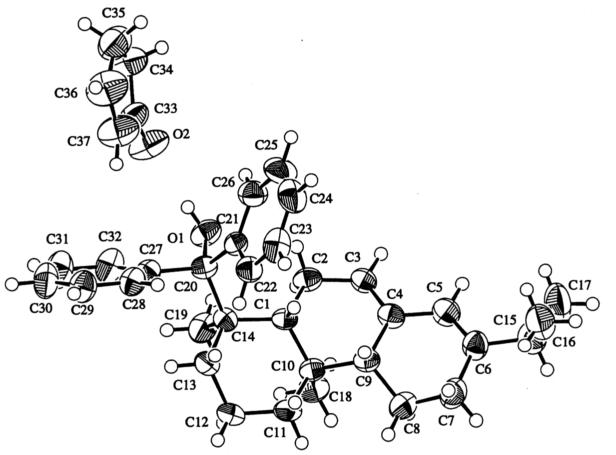

Fig. 2 Perspective plot of the inclusion crystal **(4)** showing the atom-numbering scheme.

Experimental

Synthesis of **2a:** A mixture of **1b** (25 g, 0.075 mol) and PhMgBr prepared from bromobenzene (94.2 g, 0.6 mol) and Mg (14.6 g, 0.6 mol) in dry THF was heated under reflux for 15 h. The reaction mixture was decomposed with dil. HCl and the organic layer was extracted with toluene. Evaporation of the solvent gave (+)-**2a** as colourless prisms after recrystallisation from isopropanol in 79 % yield (26 g, m.p. 167–169°C, $[\alpha]_D$ +66.0°(*c* 1.0, toluene)). **2a:** IR (Nujol) ν/cm^{-1}: 3573 (OH). ^{1}HNMR (300 MHz, $CDCl_3$), δ 7.81 (d, *J* = 6 Hz, 2H, Ph), 7.52 (d, *J* = 6 Hz, 2H, Ph), 7.32–7.15 (m, 6H, Ph), 5.66 (s, 1 H, CH), 5.17 (brs, 1H, CH), 2.46 (s, 1H, OH), 2.2–1.5 (m, CH_2, 15H), 1.28 (s, 3H, CH_3) , 0.98 (d, *J* = 6 Hz, 3H, CH_3), 0.84 (s, 3H, CH_3). Anal. calc. for $C_{32}H_{40}O$, C, 87.22; H, 9.15. Found; C, 87.22; H, 9.08.

Synthesis of **2b:** A mixture of **1b** (10 g, 0.03 mol) and *p*-$MeOC_6H_4MgBr$ prepared from bromoanisol (28 g, 0.15 mol) and Mg (3.6 g, 0.15 mol) in dry THF was heated under reflux for 15 h. The reaction mixture was decomposed with dil. HCl and the organic layer was extracted with toluene. Evaporation of the solvent gave (+)-**2b** as colourless prisms after recrystallisation from MeOH in 53% yield (7.96 g, m.p. 183–186°C, $[\alpha]_D$ +97.3°(*c* 1.0, toluene)). **2b:** IR (Nujol) ν/cm^{-1}: 3502 (OH). ^{1}HNMR (300 MHz, $CDCl_3$), δ 7.71 (d, *J* = 6 Hz, 2H, Ar), 7.41 (d, *J* = 6 Hz, 2H, Ar), 6.83 (d, *J* = 6 Hz, 2H, Ar), 6.76 (d, *J* = 6 Hz, 2H, Ar), 5.67 (s, 1 H, CH), 5.19 (brs, 1H, CH), 3.80 (s, 3H, OCH_3), 3.76 (s, 3H, OCH_3), 2.34 (s, 1H, OH), 2.2–1.5 (m, CH_2, 15H), 1.25 (s, 3H, CH_3) , 0.98 (d, *J* = 6 Hz, 3H, CH_3), 0.83 (s, 3H, CH_3). Anal. calc. for $C_{34}H_{44}O_3$, C, 81.56; H, 8.86. Found; C, 81.54; H, 9.20.

Synthesis of **2c:** A mixture of **1b** (10 g, 0.03 mol) and *p*-ClC_6H_4MgBr prepared from *p*-chlorobromobenzene (28.7 g, 0.15 mol) and Mg (3.6 g, 0.15 mol) in dry THF was heated under reflux for 15 h. The reaction mixture was decomposed with dil. HCl and the organic layer was extracted with toluene. Evaporation of the solvent gave (+)-**2c** as colourless prisms after recrystallisation from MeOH in 48 % yield (7.34 g, m.p. 161–163°C, $[\alpha]_D$ +91.5°(*c* 1.0, toluene)). **2c**: IR (Nujol) ν/cm^{-1}: 3569 (OH). ^{1}HNMR (300 MHz, CDC13), δ 7.74 (d, *J* = 6 Hz, 2H, Ar), 7.41 (d, *J* = 6 Hz, 2H, Ar), 7.28 (d, *J* = 6 Hz, 2H, Ar), 7.20 (d, *J* = 6 Hz, 2H, Ar), 5.67 (s, 1 H, CH), 5.16 (brs, 1H, CH), 2.45 (s, 1H, OH), 2.2-1.5 (m, CH_2, 15H), 1.24 (s, 3H, CH_3), 0.99 (d, *J* = 6 Hz, 3H, CH_3), 0.84 (s, 3H, CH_3). Anal. calc. for $C_{32}H_{38}Cl_2O$, C, 75.43; H, 7.52. Found; C, 75.66; H, 7.44.

Preparation of inclusion complex: The host–guest inclusion compounds were prepared by recrystallisation of host compounds **(2a–2c)** from the neat guest solution and the host-guest ratios were determined by TG and ^{1}H-NMR spectra. TG and ^{1}H-NMR spectra were recorded on a SHIMADZU DT-30 thermal analyzer and JEOL LAMBDA-300 instrument, respectively. For example, mass change corresponding to the loss of guest molecules occurred upon heating the inclusion complex in TG. The host-guest ratios were easily determined by calculating the mass change in TG. The data are summarised in Table 1.

Separation of 2-methyl- and 3-methylcyclopentanone by inclusion crystallization with **2a**: When **2a** (1.5 g, 3.4 mmol) was recrystallised from a 1:1 mixture of 2-methyl- and 3-methylcyclopentanone (1.0 g, 10.2 mmol), a 1:1 inclusion crystal of **2a** and 2-methylcyclopentanone was obtained as colourless prisms (1.52 g, 64% yield), which upon heating *in vacuo* gave pure 2-methylcyclopentanone. The purity was determined by GC.

Optical resolution of 2-methylcyclopentanone by inclusion crystallisation with **2a**: When **2a** (2 g, 4.5 mmol) was recrystallised from (±)-2-methylcyclopentanone (**3**, 3.0 g, 30.6 mmol), a 1:1 inclusion crystal of **2a** and **3** was obtained as colourless prisms (1.52 g, 64% yield, m.p. 74–76°C), which upon heating *in vacuo* gave (-)-**3** {0.18 g, $[\alpha]_D$ –10.1° (*c* 0.85, MeOH), 9.1% ee}. The optical purity was determined by comparison with the reported $[\alpha]_D$ value (–110.5° (*c* 1.19, MeOH))^5.

X-ray crystallography: $C_{37}H_{46}O_2$, *M* = 522.77, colourless prisms 0.30 × 0.25 × 0.10 mm, orthorhombic, $P2_12_12_1$, *a* = 14.418(1), *b* = 17.149(2), *c* = 12.396(1) Å, V = 3064.9(5) Å^3, *Z* = 4, Dc = 1.133 g/cm$_3$, μ(Mo-Kα)=0.68 cm^{-1}, *F*(000) = 1136.00, *T* = 296 K, Final *R* =0.066, *Rw* = 0.068 for 353 variables and 3026 reflections with $I>2\sigma(I)$. The structures were solved by direct methods (SIR97)6 and refined by full matrix least-squares on F^2. CCDC 155684.

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