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CYCLIC ANHYDRIDES FORMED FROM 1,12-DIMETHYLBENZO[*c*]PHENANTHRENE-5,8-DICARBOXYLIC ACID AND 1,3-BENZENEDICARBOXYLIC ACIDS[#]

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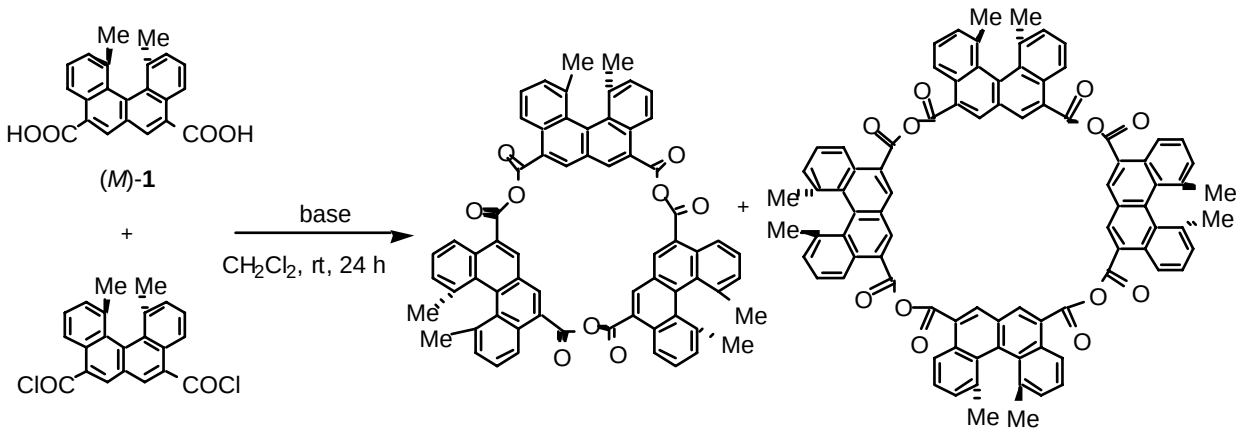
Abstract– Optically active 1,12-dimethylbenzo[*c*]phenanthrene-5,8-dicarboxylic acid and 1,3-benzenedicarboxylic acids were converted to cyclic anhydrides with trimeric and/or tetrameric structure.

Cyclic anhydrides are a group of compounds possessing many carbonyl groups in the ring structure, and potentially can exhibit interesting properties like crown ethers or calixarenes. They, however, have been ignored because of the lack of efficient synthetic method; such anhydrides were considered to be too unstable to handle. During our studies on the synthesis of macrocyclic amides possessing a novel helicene unit, 1,12-dimethylbenzo[*c*]phenanthrenedicarboxylate (**1**),[1,2] it was found that cyclic anhydrides were readily obtained from **1** in good yields (Scheme 1).



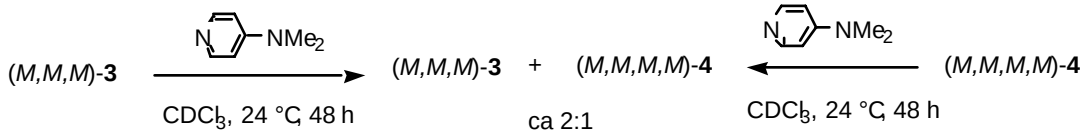
	(*M,M,M*)-**3**	(*M,M,M,M*)-**4**
base: K_2CO_3	14%	56%
base: pyridine	27%	22%

Scheme 1.

Treatment of the optically active diacid ((*M*)-**1**) with the corresponding acid chloride ((*M*)-**2**) in the presence of K_2CO_3 in CH_2Cl_2 at room temperature for 24 h gave a mixture of cyclic anhydrides (Scheme 1). They were relatively stable, and could be separated by recycling gel permeation

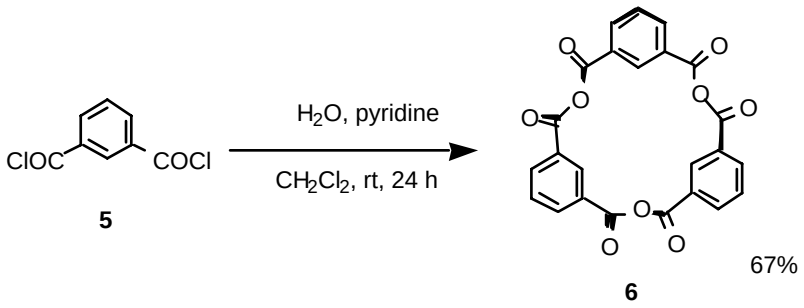
[#] This paper is dedicated to Professor T. Mukaiyama.

chromatography (GPC) giving cyclic trimer ((*M*,*M*,*M*)-**3**) and tetramer ((*M*,*M*,*M*,*M*)-**4**) in the yield of 14% and 56%, respectively. When pyridine was used for the base, the yields of the cyclic anhydride changed to 27% and 22%, respectively. Although trace amounts of the higher oligomers were also formed as indicated by the GPC spectrum, the trimer and the tetramer were the major products. The NMR spectra of (*M*,*M*,*M*)-**3** and (*M*,*M*,*M*,*M*)-**4** were similar, and showed only one set of the benzo[*c*]phenanthrene protons and carbons. IR absorptions at *ca*. 1774 and 1724 cm^{-1} clearly indicated the presence of anhydride moiety. Since MS spectroscopy was not effective for the determination of the molecular weight, vapor phase osmometry (VPO) was employed. (*M*,*M*,*M*)-**3**, and not (*M*,*M*,*M*,*M*)-**4**, appeared to aggregate in organic solvents such as $CDCl_3$, since the NMR spectra exhibited concentration dependences. The anhydrides are under equilibrium; when either (*M*,*M*,*M*)-3 or (*M*,*M*,*M*,*M*)-**4** was treated with 4-(*N*,*N*-dimethylamino)pyridine in $CDCl_3$, *ca*. 2:1 mixture of (*M*,*M*,*M*)-**3** and (*M*,*M*,*M*,*M*)-**4** was obtained in the total yield of *ca*. 75% (Scheme 2).



Scheme 2.

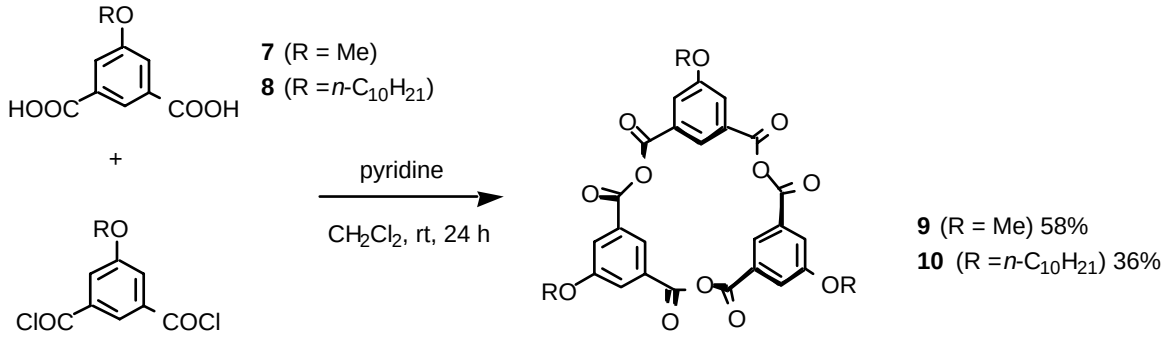
Since the benzo[*c*]phenanthrene nuclei can be regarded as a chiral equivalent of *m*-phenyleneunit,[2] 1,3-benzenedicarboxylic acid was also expected to give cyclic anhydrides. Treatment of the acid chloride (**5**) with water and pyridine at room temperature for 24 h gave cyclic trimer (**6**) in 67% yield (Scheme 3). Here, carboxylic acids were generated *in situ* by the hydrolysis of **5**. Use of K_2CO_3 gave low yield of **6** presumably because of lower solubility of the intermediates, oligomeric acyclic anhydrides. Such cyclic anhydride of 1,3-benzenedicarboxylic acid has not been known, although its polymer was reported.[3] Functionalized trimeric anhydrides (**9**) and (**10**) were also synthesized from the corresponding dicarboxylic acids (**7**)[4] and (**8**),[5] respectively (Scheme 4).



Scheme 3

EXPERIMENTAL

(*M*)-1,12-Dimethylbenzo[*c*]phenanthrene-5,8-dicarboxylic acid anhydrides ((*M*,*M*,*M*)-3 and (*M*,*M*,*M*,*M*)-4). Base: K_2CO_3. A mixture of (*M*)-**1** (170 mg, 0.50 mmol) and $SOCl_2$ (15 mL, 41 mmol) was heated at reflux for 24 h. After cooled to rt the solvent was evaporated under a reduced pressure, and dry CH_2Cl_2 (200 mL), K_2CO_3 (2.7 g, 20 mmol), and (*M*)-**1** (170 mg, 0.50 mmol) were added. After vigorous stirring for 24 h at rt, the mixture was filtered, and concentrated *in vacuo*. The residue was chromatographed by recycling GPC ($CHCl_3$, Japan Analytical Industry JAI-



Scheme 4.

GEL 1H-2H), giving (*M,M,M*)-**2** (46 mg, 14%) and (*M,M,M,M*)-**3** (180 mg, 56%). **Base: pyridine.** A mixture of (*M*)-**1** (47 mg, 0.14 mmol) and $SOCl_2$ (3 mL, 41 mmol) was refluxed for 3 h. After cooled to rt the solvent was evaporated under a reduced pressure, and dry CH_2Cl_2 (50 mL), pyridine (0.3 mL), and (*M*)-**1** (44 mg, 0.13 mmol) were added. After vigorous stirring for 24 h at rt, the reaction was quenched with saturated aqueous $KHSO_4$. The organic materials were extracted with $CHCl_3$ twice. The combined organic layers were washed with water and brine, dried over $MgSO_4$,and concentrated *in vacuo*. The residue was chromatographed by recycling GPC ($CHCl_3$) giving(*M,M,M*)-**3** (24 mg, 27%) and (*M,M,M,M*)-**4** (20 mg, 22%). (*M,M,M*)-**3**: mp >300 ˚C (toluene). $[\alpha]_D^{23}$ -890° (c 0.55, $CHCl_3$). UV-VIS ($CHCl_3$) λ_{max} (ε) 314 nm ($1.2x10^5$). CD ($CHCl_3$, 11 μM) λ_{max} (Δε) 379 (-75), 356 (-58), 338 (-92), 312 (+139), 284 nm (-52). Anal. Calcd for $C_{66}H_{42}O_9$: C, 80.97; H, 4.32. Found: C, 80.48; H, 4.26. VPO ($CHCl_3$, benzil). Calcd for $C_{66}H_{42}O_9$: 979. Found: 890. IR (KBr) 1774, 1724 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$, 11 μM) δ 1.79 (18H, s), 7.45 (6H, d, *J*= 7.2 Hz), 7.70 (6H, dd, *J*= 7.2, 8.8 Hz), 9.03 (6H, d, *J*= 8.8 Hz), 9.05 (6H, s). ^{13}C-NMR (100 MHz, $CDCl_3$, 11 μM) δ 23.4, 123.0, 125.1, 127.7, 128.9, 129.7, 130.7, 130.7, 131.3, 133.6, 136.9, 162.4. (*M,M,M,M*)-**4:** mp >300 ˚C (toluene). $[\alpha]_D^{25}$ -590° (c 0.62, $CHCl_3$). UV-VIS ($CHCl_3$) λ_{max} (ε) 319 nm ($1.6x10^5$). CD ($CHCl_3$, 9 μM) λ_{max} (Δε) 385 (-92), 323 (+108), 291 nm (-22). Anal. Calcd for $C_{88}H_{56}O_{12}$: C, 80.97; H, 4.32. Found: C, 80.27; H, 4.67. VPO ($CHCl_3$, benzil). Calcd for $C_{88}H_{56}O_{12}$: 1305. Found: 1310. IR (KBr) 1775, 1718 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.86 (24H, s), 7.47 (8H, d, *J*= 6.8 Hz), 7.74 (8H, dd, *J*= 6.8, 8.8 Hz), 8.78 (8H, s), 9.14 (8H, d, *J*= 8.8 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 23.4, 123.0, 124.2, 128.0, 129.1, 129.7, 131.0, 131.1, 132.5, 134.4, 137.0, 162.0.

Equilibration Experiment. Under an argon atmosphere in a NMR tube, *N,N*-(dimethylamino)-pyridine (0.070 mg, 0.5 μmol) in $CDCl_3$ (0.1 mL) was added to a solution of (*M,M,M*)-**3** (1.2 mg, 1.2 μmol) or (*M,M,M,M*)-**4** (1.2 mg, 0.9 μmol) in $CDCl_3$ (0.9 mL). The reaction was monitored by ^{1}H-NMR at 24 °C for 48 h, when the reaction reached to equilibration containing (*M,M,M*)-**3** (49%) and (*M,M,M,M*)-**4** (25%), or (*M,M,M*)-**3** (50%) and (*M,M,M,M*)-**4** (28%), respectively. The yields of the products were determined by ^{1}H-NMR using internal standard (CH_2Br_2).

1,3-Benzenedicarboxylic Acid Anhydride (6). Under an argon atmosphere, to a solution of **5** (41 mg, 0.20 mmol) and pyridine (1 mL) in dry CH_2Cl_2 (200 mL) was added water (3.6 μL, 0.20 mmol). After being vigorously stirred for 24 h at rt, the mixture was washed with saturated aqueous $KHSO_4$, water, and brine. The organic layer was dried over $MgSO_4$, and concentrated *in vacuo*. The residue was chromatographed by recycling GPC ($CHCl_3$) giving **6** (20 mg, 67%). mp >300 ˚C ($CHCl_3$-hexane). Anal. Calcd for $C_{24}H_{12}O_9$: C, 64.87; H, 2.72. Found: C, 64.64; H, 2.83. VPO

($CHCl_3$, benzil). Calcd for $C_{24}H_{12}O_9$: 444. Found: 460. IR ($CHCl_3$) 1790, 1719 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.79 (3H, t, *J* = 8.0 Hz), 8.53 (6H, dd, *J* = 1.6, 8.0 Hz), 8.86 (3H, t, *J* = 1.6 Hz). ^{13}C-NMR (100MHz, $CDCl_3$) δ 128.9, 129.6, 130.2, 137.0, 159.8.

5-Methoxy-1,3-benzenedicarboxylic Acid Anhydride (9). Under an argon atmosphere, a mixture of **7**[4] (160 mg, 0.82 mmol) and $SOCl_2$ (3 mL, 41 mmol) was heated at reflux for 10 h. After cooled to rt the solvent was evaporated under a reduced pressure, and dry CH_2Cl_2 (200 mL), K_2CO_3 (2.3 g, 16 mmol), and **7** (160 mg, 0.82 mmol) were added successively. After being vigorously stirred for 24 h at rt, the mixture was filtered, and concentrated *in vacuo*. The residue was chromatographed by recycling GPC giving **9** (167 mg, 58%). mp >300 °C (CH_2Cl_2-hexane). Anal. Calcd for $C_{27}H_{18}O_{12}$: C, 60.68; H, 3.39. Found: C, 60.65; H, 3.57. VPO ($CHCl_3$, benzil). Calcd for $C_{27}H_{18}O_{12}$: 534. Found: 550. IR ($CHCl_3$) 1795, 1733 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 3.97 (9H, s), 7.99 (6H, d, *J*=1.2 Hz), 8.42 (3H, t, *J*=1.2 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 56.1, 121.1, 122.2, 130.9, 159.8, 160.4.

5-Decyloxy-1,3-benzenedicarboxylic acid anhydride (10). Under an argon atmosphere, a mixture of **8**[5] (80 mg, 0.25 mmol) and $SOCl_2$ (3 mL, 41 mmol) was refluxed for 3 h. After cooled to rt the solvent was evaporated under a reduced pressure, and dry CH_2Cl_2 (50 mL), pyridine (0.1 mL), and **8** (73 mg, 0.23 mmol) were added. After being vigorously stirred for 24 h at rt, the reaction was quenched with saturated aqueous $KHSO_4$. Organic materials were extracted with $CHCl_3$ twice. The combined organic layer was washed with water and brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was chromatographed by recycling GPC giving **10** (52 mg, 36%) as a colorless oil. Anal. Calcd for $C_{54}H_{72}O_{12}$: C, 71.03; H, 7.95. Found: C, 71.03; H, 7.75. VPO ($CHCl_3$, benzil). Calcd for $C_{54}H_{72}O_{12}$: 912. Found: 940. IR ($CHCl_3$) 1795, 1732 cm^{-1}. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.89 (9H, t, *J*=6.8 Hz), 1.20-1.45 (36H, m), 1.50 (6H, br quin, *J*=7.2 Hz), 1.85 (6H, quin, *J*=6.8 Hz), 4.10 (6H, t, *J*=6.8 Hz), 7.95 (6H, d, *J*=1.6 Hz), 8.38 (3H, t, *J*=1.6 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 14.2, 22.8, 26.0, 29.1, 29.4, 29.4, 29.6, 29.6, 32.0, 69.1, 120.9, 122.6, 130.8, 159.8, 159.9.

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