Synthesis of Highly Symmetrical Triptycene Tetra- and Hexacarboxylates

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Abstract: Two alternative procedures, both starting from easily accessible tetramethylanthracenes and employing the Diels–Alder addition as the key reaction step(s), have been examined in the synthesis of the title compounds.

Key words: carboxylic acids, Diels–Alder reactions, oxidations, triptycenes, arynes

We are interested in the synthesis of high-symmetry aromatic oligocarboxylic acids and their supramolecular self-assembly.1 As a part of this long-standing program, we have focused our attention on the triptycene analogues of phthalic and terephthalic acids, which, owing to the unique geometry of the triptycene skeleton, are expected to find versatile application in molecular tectonics and possibly also in molecular electronics.2 In this paper, we wish to report two alternative procedures for synthesis of the target acids, both starting from easily accessible tetramethylanthracenes and exploiting the Diels–Alder addition as the key reaction step(s).

In the first procedure (Scheme 1), tetramethylanthracenes 1 and 4 undergo Diels–Alder reaction with an aryne3 gen-

Scheme 1  Reagents and conditions: (a) anthranilic acid or 3,6-dimethylanthranilic acid, isoamyl nitrite, 1,2-dichloroethane, THF, reflux, 7 h; (b) KMnO₄, pyridine, H₂O, reflux, 24 h; then aq 3 M HCl; (c) anthranilic acid or 4,5-dimethylanthranilic acid, isoamyl nitrite, 1,2-dichloroethane, THF (diglyme), reflux (95 °C), 7 h; (d) KMnO₄, pyridine, H₂O, reflux, 24 h; then aq 3 M HCl.

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In this way the target phthalic acid analogues obtained in high purity and very satisfactory yields. Starting from the isomeric, ortho-substituted anthracene 1, the Diels–Alder addition reaction with the complementary arynes was found to be complicated by the formation of the respective positional naphthobenzobarrelene isomers 6a,b,c,d,e,f dimensioning the reaction yields and rendering separation of the products 5,6,7,8,9a,b,c,d,e,f difficult (see experimental section).

To circumvent this complication, we turned our attention to a stepwise formation of the third aromatic ring in the triptycene skeleton 7,8 (Scheme 2) in place of the aryne addition 4, or 2,3-dimethylanthracene 8, the synthesis proceeded in six consecutive reaction steps: (a) Diels–Alder reaction with 1,4-dichlorobut-2-ene, (b) subsequent double dehydrochlorination, (c) Diels–Alder addition of the resulting exo-diene to dimethyl acetylenedicarboxylates and (d) subsequent aromatization, followed by (e) hydrolysis of the diester moiety, and (f) KMnO₄-mediated oxidation of the methyl substituents.

In this way the target phthalic acid analogues 7a,b were obtained in high purity and very satisfactory yields.

Melting points were determined on a Kofler apparatus and are uncorrected. NMR spectra were measured on Bruker Avance 400 (1H at 400 MHz and 13C at 100.6 MHz) and Bruker Avance 500 (1H at 500 MHz and 13C at 125.8 MHz) spectrometers. Chemical shifts (in ppm, δ scale) were referenced to TMS as an internal standard; coupling constants (J) are given in Hz. The assignments of protons and carbons were determined by analysis of correlated heteronuclear 1H, 13C HSQC and 1H, 13C HMBC spectra. Mass spectra were recorded on a ZAB-EQ (VG-Analytical) instrument using EI or FAB ionization techniques. ESI MS was performed on an LCQ Classic (Thermo Finnigan) mass spectrometer with quadrupole ion trap detection.

1,4,5,8-Tetramethylanthracene (1),9 2,3,6,7-tetramethylanthracene (4),10 2,3-dimethylanthracene (8),10 3,6-dimethylanilic acid11 and 4,5-dimethylanilic acid12 were prepared according to literature procedures.

**Scheme 2** Reagents and conditions: (a) 1,4-dichlorobut-2-ene, 190 °C, 48 h; (b) t-BuOK, DMSO, THF, r.t., 66 h; (c) dimethyl acetylenedicarboxylate, 1,2-dichloroethane, reflux, 19 h; (d) DDQ, toluene, r.t., 72 h; (e) aq 1 M KOH, MeOH, reflux, 10 h, then aq 3 M HCl; (f) KMnO₄, aq 0.5 M KOH, 80 °C, 40 h, then aq 3 M HCl.
1H NMR (400 MHz, CDCl₃); δ = 7.46 (s, 6 H, H-2,3,6,7,14,15), 7.52 (s, 4 H, H-1,4,5,8,13,16), 7.77 (s, 2 H, H-9,10), 13.44 (br s, 4 H, CO₂H).

13C NMR (125.8 MHz, DMSO-d₆): δ = 51.3 (CH₂), 124.3 (CH-14,15), 124.7 (CH-13,16), 125.6 (CH-13,14), 131.6 (C-2,3,6,7,14,15), 144.1 (C-9,10,11,12,13,16), 147.0 (C-4a,8a,9a,10a,11a,12a), 168.2 (C=O).

MS (FAB): m/z (%) = 519 (12, [M + Na]+), 497 (13), 453 (18), 409 (21), 365 (25), 321 (24), 277 (19).

Anal. Calcld for C₂₆H₂₆O₈·H₂O·C: 58.22; H, 3.01. Found: C, 58.53; H, 3.16.

Triptycene-1,4,5,8,13,16-hexacharboxylic Acid (3b)
Prepared as described for 3a using 2b (1.35 g, 4.00 mmol) as the starting material; white powder, yield: 650 mg (94%); mp ≥360 °C.

1H NMR (400 MHz, DMSO-d₆); δ = 7.46 (s, 6 H, H-1,4,5,8,13,16), 7.77 (s, 2 H, H-9,10), 13.44 (br s, 4 H, CO₂H).

13C NMR (125.8 MHz, DMSO-d₆); δ = 51.8 (CH₂), 124.7 (CH-14,15), 125.8 (CH-13,14), 131.6 (C-2,3,6,7,14,15), 144.0 (C-9,10,11,12), 147.0 (C-4a,8a,9a,10a,11a,12a), 168.2 (C=O).

MS (FAB): m/z (%) = 541 (8, [M + Na]+), 497 (13), 453 (18), 409 (21), 365 (25), 321 (24), 277 (19).

Anal. Calcld for C₂₆H₂₆O₈·H₂O·C: 58.22; H, 3.01. Found: C, 58.53; H, 3.16.

Triptycene-1,4,5,8,13,16-tetracharboxylic Acid (7a)
Prepared analogously as 2a using 5b (470 mg, 1.19 mmol) as the starting material. Analytical sample was recrystallized from acetonitrile-H₂O; white powder; yield: 165 mg (44%); mp ≥360 °C.

1H NMR (400 MHz, DMSO-d₆); δ = 7.46 (s, 6 H, H-1,4,5,8,13,16), 7.77 (s, 2 H, H-9,10), 13.44 (br s, 4 H, CO₂H).

13C NMR (125.8 MHz, DMSO-d₆); δ = 51.3 (CH₂), 124.3 (CH-14,15), 124.7 (CH-13,16), 125.8 (CH-13,14), 131.6 (C-2,3,6,7,14,15), 144.1 (C-9,10,11,12,13,16), 147.0 (C-4a,8a,9a,10a,11a,12a), 168.2 (C=O).

MS (FAB): m/z (%) = 519 (12, [M + Na]+), 497 (13), 453 (18), 409 (21), 365 (25), 321 (24), 277 (19).

Anal. Calcld for C₂₆H₂₆O₈·H₂O·C: 58.22; H, 3.01. Found: C, 58.53; H, 3.16.

Triptycene-1,4,5,8,13,16,17-hexacharboxylic Acid (7b)
Prepared analogously as 2a using 5b (470 mg, 1.19 mmol) as the starting material; white powder, yield: 165 mg (44%); mp ≥360 °C.

1H NMR (400 MHz, DMSO-d₆); δ = 7.46 (s, 6 H, H-1,4,5,8,13,16), 7.77 (s, 2 H, H-9,10), 13.44 (br s, 4 H, CO₂H).

13C NMR (125.8 MHz, DMSO-d₆); δ = 51.3 (CH₂), 124.3 (CH-14,15), 124.7 (CH-13,16), 125.8 (CH-13,14), 131.6 (C-2,3,6,7,14,15), 144.1 (C-9,10,11,12,13,16), 147.0 (C-4a,8a,9a,10a,11a,12a), 168.2 (C=O).

MS (FAB): m/z (%) = 519 (12, [M + Na]+), 497 (13), 453 (18), 409 (21), 365 (25), 321 (24), 277 (19).

Anal. Calcld for C₂₆H₂₆O₈·H₂O·C: 58.22; H, 3.01. Found: C, 58.53; H, 3.16.
1H NMR (400 MHz, CDCl3); δ = 1.68–1.77 (m, 2 H, H-11,12), 2.21 (s, 6 H, CH3), 2.95 and 3.01 (2 dd, J gem = 10.8 Hz, J vic = 9.3 Hz, 2 × 1 H, bCH3), 3.29 and 3.32 (2 dd, J gem = 10.8 Hz, J vic = 4.3 Hz, 2 × 1 H, aCH3), 4.34 and 4.35 (2 d, 2 × 1 H, H-9,10), 7.08–7.15 (m, 4 H, H-1,4,5,8), 7.25–7.30 (m, 2 H, H-6,7).

13C NMR (100.6 MHz, CDCl3); δ = 19.6 (CH3), 45.7, 45.8 (CH-9,10), 47.7, 47.8 (CH3Cl), 47.9, 48.0 (CH-11,12), 123.7 (CH-1 or CH-4), 125.2, 125.4 (CH-6,7), 126.1, 126.4 (CH-5,8), 126.8 (CH-1 or CH-4), 134.1, 134.4 (C-2,3), 137.2, 139.9 (C-4a,9a), 140.1, 142.8 (C-8a,10a).

MS (EI, 70 eV): m/z (%) = 259 (16, [M + H]+), 229 (12), 206 (14).

**11a**

1H NMR (500 MHz, CDCl3); δ = 2.15 (s, 6 H, CH3), 3.84 (s, 6 H, CO2CH3), 5.41 (s, 2 H, H-9,10), 6.97–7.02 (m, 2 H, H-14,15), 7.18 (s, 2 H, H-5,8), 7.33–7.38 (m, 2 H, H-13,16), 7.69 (s, 2 H, H-1,4).

13C NMR (125.8 MHz, CDCl3); δ = 19.5 (CH3), 52.5 (OCH3), 53.3 (CO2H), 123.7 (CH-13,16), 123.8 (CH-1,4), 125.3 (CH-5,8), 125.5 (CH-14,15), 129.1 (C-2,3), 133.5 (C-6,7), 141.5 (C-8a,10a), 144.2 (C-11,12), 149.0 (C-4a,9a), 168.0 (CO=O).

**11b**

1H NMR (500 MHz, CDCl3); δ = 2.14 (s, 12 H, CH3), 3.83 (s, 6 H, CO2CH3), 5.34 (s, 2 H, H-9,10), 7.15 (s, 4 H, H-5,8,13,16), 7.66 (s, 2 H, H-1,4).

13C NMR (100.6 MHz, CDCl3); δ = 19.5 (CH3), 52.5 (OCH3), 52.9 (CH), 123.7 (CH), 125.2 (CH), 129.0 (C), 133.4 (C), 141.8 (C), 149.3 (C), 168.1 (CO=O).

MS (FAB): m/z (%) = 427 (20, [M + H]+), 395 (31).
Triptycene-2,3,6,7-tetracarboxylic Acid (7a)

To a solution of 12a (100 mg, 270 μmol) in aq 0.5M KOH (5 mL) was added KMnO₄ (510 mg, 3.24 mmol) and the mixture was stirred at 80 °C for 40 h. After cooling to r.t., the excess KMnO₄ was destroyed by aq formaldehyde (37%) and the precipitated MnO₂ was filtered off and washed with boiling H₂O (3 × 5 mL). The filtrate was concentrated on a rotary evaporator to approximately one half of its original volume and then acidified to pH 1 with aq 3 M HCl. The precipitated product was collected by filtration; yield: 85.0 mg (73%). The product was in all respects identical to that prepared by oxidation of tetramethyltriptycene 5a (see above).

Triptycene-2,3,6,7,14,15-hexacarboxylic Acid (7b)

Prepared in a manner similar to that for 7a, using 12b (200 mg, 500 μmol) as the starting material; yield: 155 mg (60%). The product was in all respects identical to that prepared by oxidation of hexamethyltriptycene 5b (see above).

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References


(4) 6a: 'H NMR (400 MHz, CDCl₃): δ = 1.84 (s, 6 H), 2.35 (s, 6 H), 4.77 (s, 2 H), 6.98 (m, 2 H), 7.29 (m, 2 H), 7.42 (s, 2 H), 7.50 (s, 2 H), 7.60 (s, 2 H). 6b: 'H NMR (400 MHz, CDCl₃): δ = 1.83 (s, 6 H), 2.16 (s, 6 H), 2.34 (s, 6 H), 4.70 (s, 2 H), 7.10 (s, 2 H), 7.40 (s, 2 H), 7.46 (s, 2 H).

(5) Similar problems with regioselectivity are common in arylene addition to anthracenes, cf. ref 6. Steric hindrance to arylene approach due to methyls may account well for the different outcomes obtained with anthracenes 1 and 4 in Scheme 1.


