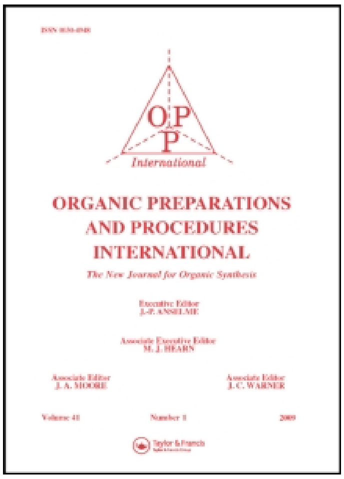

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6,6-*bis*(CARBOXY-2-OXABUTYL)-4,8-DIOXAUNDECANE-I,II-DICARBOXYLIC ACID

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6,6-*bis*(CARBOXY-2-OXABUTYL)-4,8-DIOXAUNDECANE-1,11-DICARBOXYLIC ACID

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(10/11/95)

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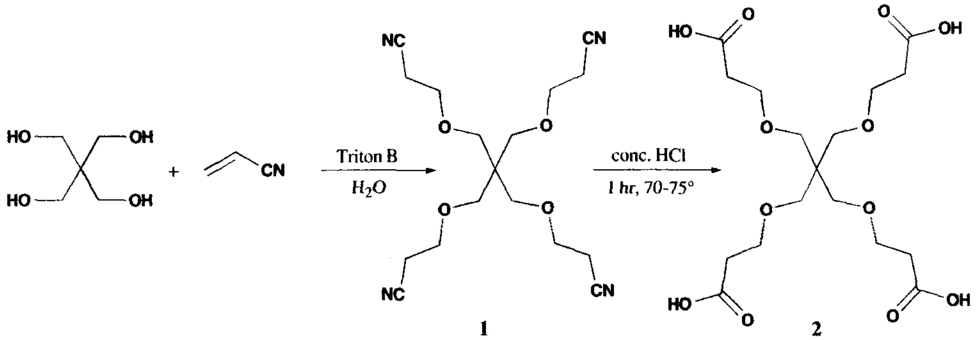
One of the prominent tetrafunctional *C*-cores[1] for the construction of dendritic macromolecules is 6,6-*bis*(carboxy-2-oxabutyl)-4,8-dioxaundecane-1,11-dicarboxylic acid. Thus far, the most highly branched, aliphatic polyfunctional cascade polymers have been synthesized utilizing this simple tetraacid core, because alternative four-directional cores [*e. g.*, adamantane-tetracarboxylic acid[2] and *tetrakis*(carboxyethyl)methane[3]], are available only by cumbersome multiple step procedures. The inexpensive reagents, pentaerythritol and acrylonitrile, have been used[4-7] to construct the tetranitrile **1**, the ideal precursor for the tetracarboxylic acid **2**; however, the original preparation, as well as subsequent slight improvements, generally provided a highly impure product, in which the isolated compound was described as an oil. Some progress in small scale preparation of **1** was achieved but tedious chromatographic separation[8] from its principal by-product, 4-oxa-1,7-dicyanoheptane and an array of dark-colored side-products was a notable deterrent.

Since these methods were not amenable to large scale preparations, development of a rational, feasible synthesis and a highly efficient work-up procedure for both **1** and **2** was desired. The use of water as the reaction medium (and a moderator of an otherwise *very exothermic* reaction) combined with Triton-B, as base catalyst, provided a highly efficient combination to afford nearly colorless **1**. The bulk of the by-product, 4-oxa-1,7-dicyanopentane, was removed by simple distillation and final purification was readily achieved by recrystallization of **1** from water; residual traces of 4-oxa-1,7-dicyanopentane were water soluble.[9,10] The single crystal structure of **1** was confirmed by X-ray analysis.[11]



Previously, tetranitrile **1** was converted[12,13] into the tetramethyl ester using conventional methods; subsequent alkaline hydrolysis provided the desired **2** in unspecified yield and purity. In general, only small scale preparations of **2** have been mentioned in the literature and no large scale method for purification has been furnished. Since the pure, crystalline tetranitrile **1** is free of contaminants, simple hydrolysis with concentrated HCl, followed by ether extraction from the aqueous phase provided nearly pure material, which was recrystallized from acetonitrile to furnish pure, crystalline tetraacid **2**.

EXPERIMENTAL SECTION

All starting materials were purchased from Aldrich Chemical Co. Melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Bruker AC 250 MHz spectrometer.

5,5-*bis*(4-Cyano-2-oxabutyl)-1,9-dicyano-3,7-dioxanonane (1).- (*Caution: Acrylonitrile is highly toxic, its use should be confined to a well ventilated hood.*) A 3-liter flask was equipped with a mechanical stirrer and charged with water (1 L), pentaerythritol (136 g, 1 mol), benzyltrimethylammonium hydroxide (30 mL, Triton-B; 40% in H_2O), and acrylonitrile (370 g, 462 mL, 7 mol). Rapid stirring was commenced and maintained for a period of 8 hrs. Undissolved crystals of pentaerythritol slowly dissolved as the reaction proceeded. The product separated as a heavy oil and formed a suspension in the bottom of the flask. The reaction mixture was transferred into a 5-liter separatory funnel and conc. HCl (15 mL) was added. The lower oily layer was separated, dissolved in toluene (1.5 L) and washed with water (2 250 mL). Toluene and traces of water were removed *in vacuo* affording a colorless oil, which was distilled *in vacuo* to yield 55-60.5 g (75-77%) of 4-oxa-1,7-dicyanoheptane as a colorless oil, bp. 110-120°/0.1 mm. ^1H NMR ($CDCl_3$): (2.78 (t, J = 5.9 Hz, 4H, CH_2CN), 3.67 (t, J = 5.8 Hz, 4H, CH_2O), ^{13}C NMR (DMSO-d_6): δ 18.0 (CH_2CN), 65.07 (CH_2O), 118.92 (CN).

The residual light oil was poured into a 500 mL beaker and allowed to solidify affording 325-335 g (93-96%) of colorless crystals, which were dissolved in a boiling water-ethanol mixture (9:1; 3250-3350 mL) and allowed to cool slowly to 25° with mechanical stirring. At 30-35°, crystallization may be induced by adding a crystal of the tetranitrile. Crystallization without stirring resulted in the formation of large lumps of crystals with occluded water. After cooling in an ice bath, the crystals were collected and dried *in vacuo* over P_2O_5 to yield 261-286 g (75-77%) of white needles, mp. 44-46°. ^1H NMR (DMSO-d_6): (2.83 (t, J = 5.8 Hz, 8H, CH_2CN), 3.67 (s, 8H, CH_2O), 3.95 (t, J = 5.8 Hz, 8H, OCH_2), ^{13}C NMR (DMSO-d_6): δ 17.59 (CH_2CN), 45.24 (^4C), 65.67 (OCH_2), 68.54 (CH_2O), 119.14 (CN).

6,6-*bis*(4-Carboxy-2-oxabutyl)-4,8-dioxaundecane-1,11-dicarboxylic Acid (2).- A 1-liter 3-necked round bottom flask, equipped with a stirrer and thermometer was charged with 6,6-*bis*(4-cyano-2-oxabutyl)-4,8-dioxaundecane-1,11-dinitrile (104 g, 300 mmol) and conc. HCl (450 mL). The stirred suspension was heated[14] at 70-75° for 1 hr; crystals of **1** slowly dissolved and ammonium chloride began to participitate at about 50-55°. Then the solution was diluted twice with water (450 mL) and concentrated *in vacuo* to give an oily semicrystalline residue, which was dissolved in water (260 mL) and continuously extracted with diethyl ether for 8 hrs. Acid **1** is not very soluble in ether and thus separated as an oil, affording an immiscible suspension. The ether was removed *in vacuo* yielding a colorless oil, from which the residual water was also removed *in vacuo* over 3-8 hrs. The resultant solid (110-112 g) was recrystallized from acetonitrile (180-185 mL) to give 99-100 g (87-89%) of the pure tetracarboxylic acid **2** as white crystals, mp. 104-106°, lit.[8] mp. 94-96°. IR (nujol): 3450-2500 (CO_2H), 1701 (CO_2H) cm^{-1}, ^1H NMR (DMSO-d_6): δ 2.84 (t, J = 6 Hz, 8H, CH_2CO_2H), 3.67 (s, 8H, CH_2O), 3.96 (t, J = 6 Hz, 8H, CH_2O), ^{13}C NMR (DMSO-d_6): δ 36.01 (CH_2CO_2H), 45.43 (^4C), 67.09 (OCH_2), 173.16 (CO_2H).

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REFERENCES

1. G. R. Newkome and X. Lin, *Macromolecules*, **24**, 1443 (1991).
2. G. R. Newkome, A. Nayak, R. K. Behera, C. N. Moorefield and G. R. Baker, *J. Org. Chem.*, **57**, 358 (1992).
3. G. R. Newkome, S. Arai, F. R. Fronczek, C. N. Moorefield, X. Lin and C. D. Weis, *ibid.*, **58**, 898 (1993).
4. H. A. Bruson and T. W. Riener, *J. Am. Chem. Soc.*, **65**, 23 (1943).
5. H. A. Bruson (The Resinous Products and Chemical Corp.), *US Patent*, 2,401,607 (**1941**); *Chem. Abstr.*, **40**, 5450 (1941).
6. H. A. Bruson (The Resinous Products and Chemical Corp.), *US Patent*, 2,437,905 (**1941**); *Chem. Abstr.*, **42**, 4195 (1942).
7. H. Meerwein in *"Methoden der Organische Chemie (Houben-Weyl)"*, Vol. VI/3, p. 23, E. Mueller, Ed., Georg Thieme Verlag, Stuttgart, 1965.
8. G. R. Newkome and X. Lin, *Macromolecules*, **24**, 1443 (1991).
9. C. J. Schmidle and R. C. Mansfield, *Ind. Eng. Chem.*, **44**, 1338 (1952).
10. I. G. Farben, *Germ. Patent*, 731,708 (**1940**); *Chem. Abstr.*, **38**, 555^5 (1944).
11. G. R. Newkome, C. D. Weis, X. Lin and F. R. Fronczek, *Acta Cryst.*, **C49**, 998 (1993).
12. G. R. Newkome, C. N. Moorefield and K. J. Theriot, *J. Org. Chem.*, **53**, 5552 (1988).
13. F. Sorm and G. Beranek, *Collect. Czech. Chem. Commun.*, **19**, 298 (1954).
14. The reaction may became slightly exothermic; the temperature, however, should not exceed 80-85°, since higher temperatures enhanced the formation of oily by-products which hampered considerably crystallization of the acid.

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