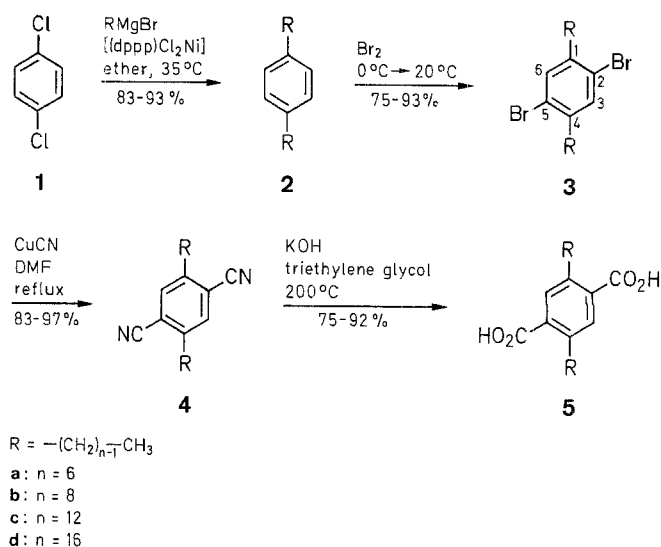


The dialkylbenzenes **2** were obtained in analogy to a literature procedure for 1,2-di-*n*-butylbenzene.⁵ Thus, the *n*-alkylmagnesium bromides were coupled with **1** under nickel-catalysis, giving the respective compounds **2** in high yields (Table 1). In agreement with published results,⁶ we observed that (dppp)Cl₂Ni [dppp = 1,3-bis(diphenylphosphino)propane as a bidentate ligand] was the most effective catalyst in these coupling reactions.⁷ The purity of the products **2** with respect to positional scrambling of the alkyl substituents attached to the benzene ring, or isomerization of these primary substituents to secondary ones was checked by high field NMR (Tables 1, 2) and (for *n* = 6) by GC/MS. No evidence for such processes was obtained,⁸ if they occur we estimate an upper limit for such side reactions to be 0.5%.



A High-Yield Route to 2,5-Di-*n*-alkyl-1,4-benzenedicarboxylic Acids

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A simple and inexpensive method for preparing the previously unknown 2,5-di-*n*-alkylterephthalic acids **5a-d** in high yields is presented. The length of the alkyl chains can be varied easily (*n* = 6, 8, 12, 16).

Terephthalic acid (1,4-benzenedicarboxylic acid) is utilized industrially as a monomer for the production of polyesters and polyamides. Recently, it has gained importance as building block in liquid crystal chemistry,¹ where it has been shown that the solubility and processability of such conformationally rigid species can be greatly enhanced by attaching flexible side chains.² We are interested in developing efficient and, in regard to the length of the chain, general syntheses of compounds substituted with flexible chains which are suitable as monomers in polymerization reactions.

We report a straightforward four-step synthesis of 2,5-di-*n*-alkylterephthalic acids **5a-d** (*n* = 6, 8, 12, 16) proceeding in an overall yield of up to 75% based on 1,4-dichlorobenzene (**1**). Except for the known 1,4-di-*n*-alkylbenzenes **2a-d**,³ for which we present a simple and very efficient synthesis, all the compounds reported are new.⁴

In the next step compounds **2a-d** were brominated, either as neat liquids (**2a, b**) or in concentrated dichloromethane solution (for **2c, d**) under rigorous exclusion of light. Analogous to the case of *p*-xylene,¹⁰ the isolated materials **3a-d** were exclusively brominated at the opposite carbons C-2 and C-5. This was verified by investigating compound **3c**, as an representative example, by HPLC and high field ¹H-NMR. The HPLC trace of **3c** showed only one peak (60:40 acetonitrile/dichloromethane retention time: 4.40 min), and its ¹H-NMR spectrum one singlet at $\delta = 7.35$, respectively. Hence, exclusively one product was formed. The ¹³C-satellites of the aromatic singlet in the proton spectrum of **3c** proved to be a well resolved doublet ($^1J_{13\text{C,H}} = 164$ Hz; width at half height 1.4 Hz) without any further splitting, a feature only consistent with **3c** being the 2,5-dibromo compound.^{11,12}

The von Braun cyanation of haloaromatic compounds with copper(I) cyanide is a well established method for preparing aromatic nitriles.¹³ Under the von Braun conditions the dibromides **3** gave the dinitriles **4** in a clean, high-yield process. In the purification step, the last traces of copper salt impurities were removed by extracting the material with acetone, followed by a filtration through silica gel. Finally, the dinitriles **4a-d** were hydrolyzed to the corresponding terephthalic acids **5a-d** under forcing conditions.¹⁴ The acids **5b-d** showed all sharp clearing points, although differential scanning calorimetry experiments showed several endotherms below the melting points presumably to be associated with various phase transitions.

Table 1. Compounds 2-5 Prepared

Product	Yield (%)	mp (°C) and/or bp (°C)/mbar	Molecular Formula ^a	IR (KBr) ν (cm ⁻¹)	MS (70 eV) <i>m/z</i> (rel.int., %)	¹³ C-NMR (CDCl ₃ /TMS) ^o
2a	87	134/0.13	C ₁₈ H ₃₀ (246.4)	—	246 (M ⁺ , 27); 175 (100)	14.10 (q); 22.71, 29.16, 31.87, 35.70 (5t), 128.28 (d); 140.08 (s)
2b	93	192/0.13	C ₂₂ H ₃₈ (302.6)	—	302 (M ⁺ , 66); 203 (85); 105 (100)	14.11 (q); 22.73, 29.34, 29.47, 29.58, 31.63, 35.66 (7t); 128.26 (d); 140.08 (s)
2c	87	42.5 253/0.13	C ₃₀ H ₅₄ (414.8)	—	414 (M ⁺ , 45); 105 (100)	14.10 (q); 22.73, 29.40, 29.45, 29.59, 29.66, 29.70, 29.73, 31.61, 31.98, 35.63 (10t); 128.25 (d); 140.09 (s)
2d	83	60 309/0.13	C ₃₈ H ₇₀ (527.0)	—	527 (M ⁺ , 100); 105 (32)	14.11 (q); 22.74; 29.41, 29.45, 29.59, 29.66, 29.75, 31.60, 31.99, 35.63 (9t); 128.24 (d); 140.09 (s)
3a	90	33.2	C ₁₈ H ₂₈ Br ₂ (404.2)	—	406 (M ⁺ , 64); 404 (M ⁺ , 100); 402 (M ⁺ , 54)	14.06 (q); 22.60, 29.34, 29.80, 31.64, 35.56 (5t); 123.11 (s); 133.76 (d); 141.35 (s)
3b	93	40.0	C ₂₂ H ₃₆ Br ₂ (460.3)	—	462 (M ⁺ , 14); 460 (M ⁺ , 28); 458 (M ⁺ , 15)	14.05 (q); 22.65, 29.21, 29.34, 29.37, 29.80, 31.87, 35.53 (7t); 123.08 (s); 133.74 (d); 141.33 (s)
3c	90	58.3	C ₃₀ H ₅₂ Br ₂ (572.6)	—	574 (M ⁺ , 1); 572 (M ⁺ , 3); 570 (M ⁺ , 1)	14.12 (q); 22.72, 29.37, 29.44, 29.58, 29.68, 29.70, 29.83, 31.96, 35.55 (9t); 123.13 (s); 133.76 (d); 141.38 (s)
3d	75	62.0	C ₃₈ H ₆₈ Br ₂ (684.8)	—	686 (M ⁺ , 23); 684 (M ⁺ , 4); 682 (M ⁺ , 3)	14.11 (q); 22.71, 29.38, 29.43, 29.58, 29.73, 29.83, 31.96, 35.56 (8t); 123.12 (s); 133.79 (d); 141.39 (s)
4a	96	53.5	C ₂₀ H ₂₈ N ₂ (296.5)	2220	296 (M ⁺ , 7); 227 (18)	14.00 (q); 22.51, 28.83, 30.56, 31.48, 33.91 (5t); 116.65, 116.72 (2s); 133.40 (d); 144.84 (s)
4b	94	64	C ₂₄ H ₃₆ N ₂ (352.6)	2220	352 (M ⁺ , 12); 281 (83); 254 (26)	14.06 (q); 22.64, 29.17, 29.26, 30.59, 31.82, 33.90 (6t); 116.65, 116.72, 133.39 (d); 144.84 (s)
4c	97	78	C ₃₂ H ₅₂ N ₂ (464.8)	2220	464 (M ⁺ , 12); 337 (20); 310 (3)	14.09 (q); 22.71, 29.18, 29.31, 29.36, 29.49, 29.65, 30.60, 31.95, 33.92 (9t); 116.65, 116.72 (2s); 133.38 (d); 144.84 (s)
4d	83	87	C ₄₀ H ₆₈ N ₂ (577.0)	2220	576 (M ⁺ , 2)	14.09 (q); 22.71, 29.19, 29.31, 29.38, 29.50, 29.63, 29.69, 29.72, 30.59, 31.96, 33.92 (11t); 116.66, 116.72 (2s); 133.33 (d)
5a	85	230	C ₂₀ H ₃₀ O ₄ (334.5)	1695	334 (M ⁺ , 47); 263 (69)	13.80 (q); 21.92, 28.52, 30.91, 31.08, 32.76 (5t); 131.86 (d); 133.14, 140.27, 168.41 (3s)
5b	92	220	C ₂₄ H ₃₈ O ₄ (390.6)	1690	390 (M ⁺ , 86); 291 (60)	13.81 (q); 22.00, 28.55, 28.70, 28.90, 31.13, 31.19, 32.81 (7t); 131.93 (d); 133.10, 140.31, 168.38 (3s)
5c	90	190	C ₃₂ H ₅₄ O ₄ (502.8)	1690	502 (M ⁺ , 49)	13.80 (q); 22.01, 28.64, 28.74, 28.88, 28.94, 31.10, 31.23, 32.82 (8t); 131.94 (d); 133.04, 140.30, 168.33 (3s)
5d	75	177	C ₄₀ H ₇₀ O ₄ (615.0)	1685	614 (M ⁺ , 50); 570 (53)	13.58 (q); 21.98, 28.63, 28.83, 28.95, 28.98, 31.09, 33.04 (7t); 131.99 (d); 132.62, 140.46, 168.53 (3s)

^a Satisfactory microanalyses obtained: C ± 0.22, H ± 0.18, Br ± 0.21, N ± 0.32, except for **4d** (N - 0.49) and **5d** (C - 0.72).

^b Compounds **5a-5d** were measured in DMSO-*d*₆.

Table 2. ¹H-NMR (CDCl₃/TMS) data for compounds 2-5.^a

Product	δ^b
2	0.88 (t); 1.30 (m); 1.59 (m); 2.55 (t); 7.07 (s)
3	0.88 (t); 1.37 (m); 1.57 (m); 2.63 (t); 7.35 (s)
4	0.89 (t); 1.34 (m); 1.67 (m); 2.83 (t); 7.56 (s)
5	0.82 (t); 1.21 (m); 1.49 (m); 2.85 (t); 7.60 (s) ^c

^a The given chemical shifts are average values of the respective homologues **a-d**. The maximum deviation is 0.04 ppm. The integrations match the structural requirements.

^b The ω -methyl and the α -methylene hydrogens show ³J_{H,H}-values of 7 Hz, and 8 Hz, respectively, throughout for all compounds.

^c Measured in DMSO-*d*₆.

From an inspection of the figures given in Table 1, the lowest yields of isolated materials in each step were obtained where $n = 16$. We assume that this fact reflects the generally more tedious purification of the compounds with very long alkyl chains.

All reagents were purchased from Fluka Chemical Co. and used without further purification. (dppp)Cl₂Ni was prepared according to the literature procedure.¹⁵ All solvents were dried under standard conditions. All reactions, except the bromination of the alkylbenzenes **2a-d**, were carried out under N₂. Melting points were recorded on a Reichert Thermovar melting point microscope and are uncorrected, the figures given refer to the transition into the isotropic phase. Mass spectra were obtained using a Varian MAT CH 7A spectrometer with EI ionization. GC/MS were recorded using a Hewlett Packard 5790 GC with a 25 m methyl silicone capillary column directly coupled to a VG analytical 7070 E mass spectrometer and VG-250 data system. We thank Dr. M. Jones (Durham) for these measurements. IR spectra were obtained using a Perkin-Elmer 1430 spectrometer. ¹H- (Table 2) and ¹³C-NMR spectra were obtained on a Bruker AC 300 spectrometer (300 MHz). The HPLC measurement was carried out using a Spectra Physics SP 8700 Solvent Delivery System with a RP-18 Lichrosorb column (10 μ , 25 cm).

1,4-Di-*n*-alkylbenzene 2; General Procedure:

The *n*-alkylmagnesium bromide ($n = 6, 8, 12, 16$; 2.0 mol, 2.5 equiv) is added dropwise, over 15 min, to an ice-cooled and stirred mixture of 1,4-dichlorobenzene (118 g, 0.80 mol) and (dppp)Cl₂Ni (500 mg, 0.9 mmol) in dry ether (600 mL). The cooling bath is removed and the ether begins to boil after an induction period of about 30 min. The mixture is then refluxed for 1 d, cooled to 0°C and carefully quenched

with water (50 mL), followed by 2 N HCl (500 mL). After separation of the layers, the aqueous layer is extracted with ether (2 × 200 mL), the combined organic layer is then washed with H₂O (100 mL) and dried (MgSO₄). The solvent is removed *in vacuo* and the crude product **2** is distilled through a Vigreux column (20 cm) under the conditions given in Table 1.

2,5-Dibromo-1,4-di-*n*-alkylbenzenes **3**; General Procedure:

Method A (for liquids; **2a, b**): Bromine (54.6 g, 0.34 mol, 2.05 equiv.) is added dropwise, over 30 min, to a stirred and ice-cooled solution of the 1,4-di-*n*-alkylbenzene **2a** or **2b** (0.16 mol) and iodine (0.2 g, 1.6 mmol), under rigorous exclusion of light. After 1 d at room temperature, 20% aq. KOH solution (100 mL) is added and the mixture is shaken under slight warming until the color disappears. The mixture is then cooled to room temperature, the aqueous solution is decanted, and the remaining residue is recrystallized from EtOH (2 × 400 mL).

Method B (for solids; **2c, d**): Bromine (27.6 g, 170 mmol, 2.05 equiv.) is added quickly to a stirred solution of the 1,4-di-*n*-alkylbenzene **2c** or **2d** (80 mmol) and iodine (0.1 g, 0.8 mmol) in dichloromethane (**2c**: 100 mL; **2d**: 300 mL) at room temperature, and stirred under rigorous exclusion of light. 20% Aq. KOH solution (100 mL) is added until the color of the solution disappears. The solvent is removed under reduced pressure and the precipitate is washed with EtOH (2 × 200 mL) on a Büchner funnel. The crude material is recrystallized from EtOH (3 × 1500 mL).

2,5-Dicyano-1,4-di-*n*-alkylbenzenes **4**; General Procedure:

The 2,5-dibromo-1,4-di-*n*-alkylbenzene **3** (30 mmol) and CuCN (8.1 g, 90 mmol, 3 equiv.) is refluxed in DMF (100 mL) for 2 d. The mixture is poured into a solution of NH₃ (15 weight %) in water (500 mL) out of which a solid precipitates. This is then washed with another portion of the NH₃ solution (500 mL), followed by H₂O (500 mL). The solid is dried in a desiccator over P₄O₁₀ for 1 d at 0.13/mbar. Finally, the material is hot extracted with acetone in a Soxhlet apparatus (250 mL, 5 h) giving a yellow solution. After evaporation of the solvent the residue is dissolved in CHCl₃ (200 mL), and the resulting solution is filtered through silica gel. The pure compound **4** is obtained by removal of the solvent under reduced pressure and recrystallization from EtOH (**4a, b**: 500 mL; **4c, d**: 2 × 2 L).

2,5-Di-*n*-alkyl-1,4-benzenedicarboxylic Acids **5**; General Procedure:

A stirred mixture of 2,5-dicyano-1,4-di-*n*-alkylbenzene **4** (30 mmol), KOH (20.2 g, 120 mmol, 4 equiv.), and triethylene glycol (300 mL) is heated to 200°C until the evolution of ammonia ceases (2–5 d). The resulting mixture is poured into 50% aq. H₂SO₄ (600 mL) and the precipitate formed is filtered under suction, washed with H₂O (300 mL), dried in a desiccator over P₄O₁₀ at 0.13 mbar and is recrystallized from acetone (**5a, b**: 600 mL; **5c, d**: 2 × 1.8 L) at –20°C.

GC/MS. Only one sharp fraction showed a mass spectrum with M⁺ at *m/z* = 246. The fragmentation pattern was exactly the one expected for a straight chain dialkylbenzene. No typical fragments of branched chain compounds were observed.⁹

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- (7) We also tested the catalytical activity of (a) dichloro(2,2'-bipyridyl)nickel, (b) dichlorobis(triphenylphosphine)nickel, and (c) dichloro(bis-1,2-diphenylphosphinoethane)nickel under identical conditions and isolated **2a** in yields of (a) less than 5%, (b) about 10%, and (c) about 70%.
- (8) No signals from any isomer of **2** could be observed in the ¹H- and ¹³C-NMR spectra of isolated material. To find out whether an isomeric species had been removed during work-up, a representative part of a crude reaction mixture of **2a** was analyzed by