A High-Yield Route to 1,2-Dihydrocyclobutabenzene-3,6-dicarboxylic Acid

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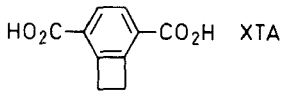
A simple five-step method for preparing the previously unknown 1,2-dihydrocyclobutabenzene-3,6-dicarboxylic acid (XTA) in high yield is presented. All intermediates were crystalline compounds which allowed the preparation to be scaled up without complication. The title compound is of interest as a crosslinkable derivative of the widely used monomer, terephthalic acid (TA).

Terephthalic acid (TA) is widely used as a monomer in the production of high-performance aromatic polymers such as poly{(benzo[1,2-*d*;4,5-*d'*]bisoxazole-2,6-diyl)-1,4-phenylene} (PBO),[1] poly{(benzo[1,2-*d*;4,5-*d'*]bisthiazole-2,6-diyl)-1,4-phenylene} (PBT),[2] poly(*p*-phenylene terephthalamide) (PPTA or Kevlar®),[3] and poly(ethylene terephthalate (PET). Here we describe the design and synthesis of a derivative of TA that can undergo a thermally induced-crosslinking reaction. This derivative, XTA, should be suitable as a comonomer with TA, thus potentially transforming conventional rigid-rod polymers into structoset materials.[4] We feel that the ability to crosslink fibers of rigid-rod polymers may help to overcome the poor compressive strengths of these materials.



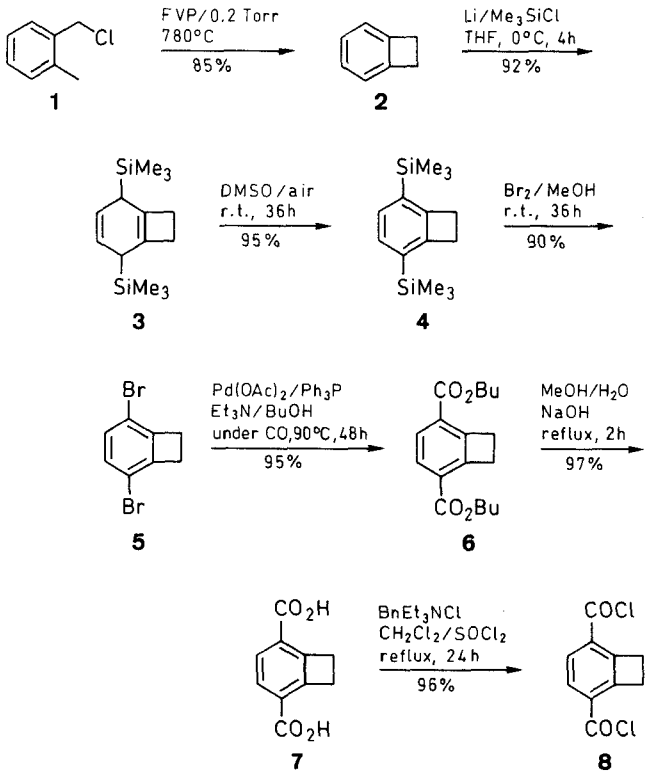
XTA

The XTA comonomer was designed with several criteria in mind. First, incorporation of this comonomer into polymer backbones should not dramatically alter present methods employed for polymer synthesis or processing. This means that crosslinking should not occur at an appreciable rate below 200 °C. Moreover, since fiber processing of rigid-rod polymers involves spinning of lyotropic nematic solutions, the comonomer should not severely distort the polymer's axial ratio so as not to reduce the stability of the ordered fluid phase. Perhaps the most ideal processing scheme is one in which crosslinking is thermally-triggered during the post-spinning heat treatment step (i.e. > 300 °C). Crosslinking should occur without evolution of volatile byproducts and should involve minimal molecular reorganization so as not to severely disrupt chain packing in the solid fiber. The crosslinking chemistry should involve a highly reactive intermediate in order to maximize crosslinking conversion. Finally, the reactive comonomer should be easily synthesized.

We believe that XTA will satisfy many of these requirements. XTA is a compact comonomer which should maintain the high axial ratio of rigid-rod polymers. The crosslinking reaction can be thermally triggered resulting in ring opening of cyclobutabenzene (BCB) to form the highly reactive *o*-quinodimethane intermediate at temperatures above 250 °C. The *o*-quinodimethane intermediate[5] is sufficiently reactive to homopolymerize through an addition reaction or by Diels–Alder dimerization.[6] In either case, crosslinking should take place with little or no mass loss as the cyclobutene ring unfurls. The extent of crosslinking in a polymeric material containing XTA might easily be controlled by changing the molar ratio of XTA to TA in the polymerization reaction.

To explore the thermal behavior of XTA derivatives, we have synthesized two model compounds relevant to PPTA **(9)** and PBO **(10)**. The synthesis of these model compounds closely follows known polymerization conditions (Scheme 2). In each case, differential scanning calorimetry (DSC) experiments reveal a reversible melting followed by an irreversible chemical reaction (Table 3). This reaction, presumably the opening of the cyclobutane ring,[9] proceeds appreciably above 300 °C.

Previous use of the BCB functionality in polymer chemistry has been limited to structoterminal prepolymers (endcapping of oligomers with BCB).[6-8] These approaches suffer from limited processability and the ability to vary crosslink density. We believe that the BCB unit will make an excellent structopendant crosslinking group which all require difunctionalization of the aromatic ring. In all of the structoterminal prepolymers, mentioned above, the aromatic BCB ring was simply monofunctionalized at the 4 position (the product accessible through electrophilic aromatic substitution). In our synthesis



Scheme 1

Table 1. 1,2-Dihydrocyclobutabenzene Derivatives **2–8** Prepared

Product	Scale (mmol)	Yield (%)	Molecular Formula	MS (70 eV)
2	606	85	C_8H_8 (104.1)	105 (12.3), 104 (100), 103 (75.3)
3	459	92	$C_{14}H_{26}Si_2$ (250.5)	–
4	440	95	$C_{14}H_{24}Si_2$ (248.5)	248 (100), 249 (26.8), 250 (9.1)
5	363	90	$C_8H_6Br_2$ (261.9)[a,b]	264 (48.0), 262 (100), 260 (51.5)
6	144	95	$C_{16}H_{24}O_4$ (280.4)[a]	280 (100), 281 (17.9), 282 (2.4)
7	130	97	$C_{10}H_8O_4$ (192.2)[a,b]	192 (100), 193 (12.4), 194 (1.7)
8	120	96	$C_{10}H_6Cl_2O_2$ (229.1)[a,b]	228 (100), 229 (13.3), 230 (63.9)

[a] Satisfactory HRMS obtained: $m/z \pm 0.0010$.
[b] Satisfactory microanalyses obtained: C ±0.20, H ±0.26.

Table 2. NMR Spectroscopic Data of 1,2-Dihydrocyclobutabenzene Derivatives **5–8**

Compound	^{1}H NMR in $CDCl_3$, δ	^{13}C NMR in $CDCl_3$, δ
5	0.90 (t, 6H), 1.40 (m, 4H), 1.65 (quint, 4H), 3.38 (s, 4H), 4.21 (t, 4H), 7.72 (s, 2H)	13.8, 20.0, 31.0, 31.5, 64.5, 127.5, 128.0, 148.8, 165.5
6	3.10 (s, 4H), 7.17 (s, 2H)	38.8, 114.5, 131.3, 146.9
7[a]	3.35 (s, 4H), 7.68 (s, 2H), 13.0 (br, 2H)	31.2, 127.9, 128.8, 148.5, 166.1
8	3.55 (s, 4H), 7.82 (s, 2H)	32.5, 129.0, 132.7, 150.9, 165.1

[a] ^{1}H NMR and ^{13}C NMR, DMSO-d_6.

Table 3. NMR and DSC data of 1,2-Dihydrocyclobutabenzene Derivatives **9, 10**

Compound	Molecular Formula[a]	^{1}H NMR in DMSO-d_6, δ	T_m[b] (°C)	T_r[c] (°C)
9	$C_{21}H_{18}N_2O_2$ (330.1)	3.50 (s, 4H), 7.10 (t, 2H), 7.35 (t, 4H), 7.73 (d, 4H), 7.82 (s, 2H), 10.03 (s, 2H)	314	335
10	$C_{22}H_{14}N_2O_2$ (338.4)	3.71 (s, 4H), 7.40 (m, 4H), 7.61 (m, 2H), 7.81 (m, 2H), 8.20 (s, 2H)	303	349

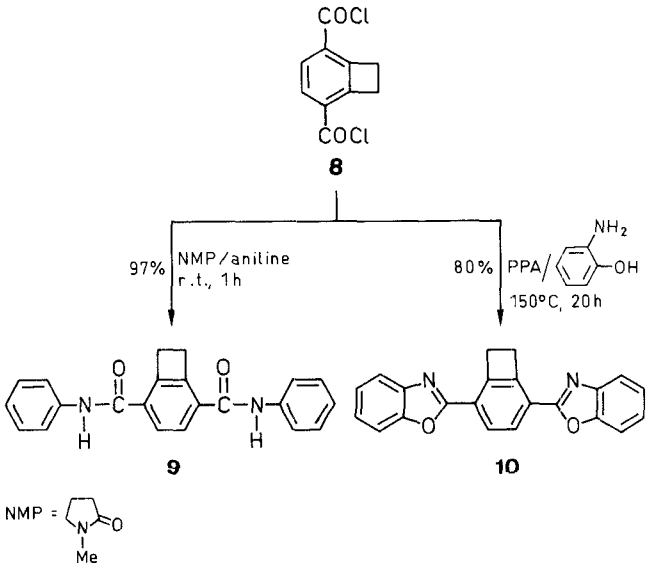
[a] Satisfactory HRMS obtained: $m/z \pm 0.0004$.
[b] T_m – Reversible melting transition (heating rate = 20 °C/min).
[c] T_r – Onset of irreversible chemical reaction.

described below, we have regioselectively introduced functionality at positions 3 and 6 by reductive silylation of BCB as first described by Kundig et al.[10]

The five-step synthesis of XTA from BCB is shown in Scheme 1. The preparation gives pure XTA in an overall yield of 70% based on BCB. The synthesis of BCB in one step from α-chloro-*o*-xylene by flash vacuum pyrolysis (FVP) is known,[11] although we describe an improved preparative scale procedure. The pyrolized product typically contained a mixture of BCB and starting material in a ratio of 7:1.[12] The unreacted starting material was easily removed by conversion to the corresponding benzyl alcohol with excess powdered potassium hydroxide (KOH) in dimethyl sulfoxide (DMSO) followed by distillation.

Reductive silylation of BCB was performed as described by Kundig et al.[10] Rearomatization of the resulting dihydrobenzene proceeded erratically as originally described and became especially troublesome on larger scales. The original procedure simply involved bubbling air through a rapidly stirred toluene solution. We explored the use of oxidation reagents such as 2,3-dichloro-5,6-dicyano-1,4-benzoquinone and tetrachloro-1,4-benzoquinone. Although moderately successful, these reagents were difficult to remove, were required in large molar excess to be effective, and were expensive for large scale preparations. We then discovered that aromatization of **3** proceeded smoothly and conveniently simply by changing the solvent from toluene, as originally described, to DMSO. Under these conditions, crystals of **4** precipitate from solution and the reaction was complete in 24–36 hours.

Bromodesilylation[13] proceeded smoothly and in high yield to give exclusively the crystalline 3,6-dibromocyclobutabenzene, **5**. At this point, several different routes were attempted to convert **5** to the corresponding diacid. Dimetalation and subsequent carboxylation proved difficult. For example, metalation of **5** using more than 2 equivalents of *tert*-butyllithium in diethyl ether at −78 °C gave largely the monoacid after the addition of carbon dioxide. Grignard chemistry was also attempted and gave the diacid in about 80% yield. However, substantial monocarboxylic acid was again obtained and this by-product was difficult to remove. Palladium-carbonylation of **5** in the presence of 1-butanol was found to give excellent yield of the diacid **6** with no trace of monoester at the end of the reaction. 1-Butanol was used as solvent in the reaction because of the higher solubility of CO in



Scheme 2

this alcohol, relative to ethanol or methanol.[14] The palladium-carbonylation procedure proved to be amenable to 100 mmol scale.

Following saponification, the diacid was converted to the diacid chloride for subsequent use in polycondensation reactions. The diacid chloride was best prepared using thionyl chloride and a phase transfer reagent such as benzyltriethylammonium chloride, to help overcome the insolubility of the diacid in organic solvents.[15] The crude diacid chloride was then sublimed and subsequently recrystallized to give pure **8** for use in polymer syntheses. Model compounds **9** and **10** were prepared as shown in Scheme 2.

Unless otherwise noted, all starting materials were obtained from commercial suppliers and used without further purification. Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are uncorrected. Dry Et_3N was obtained by vacuum transfer from CaH_2. Dry THF and pentane were obtained by vacuum transfer from sodium and benzophenone. The ^1H and ^{13}C NMR spectra were recorded on a Bruker AM-300 in the indicated solvents using residual solvent protons as internal standard. Analytical thin layer chromatography (TLC) was performed on Kieselgel F-254 Pre-Coated TLC plates. Silica for flash chromatography is silica gel 60 (230–400 mesh) from EM Science. Mass spectra (MS) and high resolution mass spectra (HRMS) were recorded on a Finnigan 4021 mass spectrometer and a VG 70-S mass spectrometer, respectively, either by FAB or EI (70 eV). Differential Scanning Calorimetry was run on a Perkin-Elmer DSC 7. Gas chromatography (GC) was performed on an HP-5890 Series II gas chromatographer equipped with a 25 m × 0.2 mm × 0.33 mm HP-1 silicone column. Elemental analyses were performed on a Perkin-Elmer 2400 CHN Elemental Analyzer.

1,2-Dihydrocyclobutabenzene (BCB) (2):
The starting material **1** (10 g, 71.1 mmol) was degassed to 1 Torr and the reaction was run by slow passage of α-xylene through a horizontal quartz tube containing no packing at 780 °C.[16] A Kugelrohr bulb was placed at the oven outlet in liquid N_2 to collect the organic products followed by a second, more efficient trap to collect the HCl gas. This trap system utilized the large difference in volatility of BCB and HCl to separate these species and thus simplify product workup. The reacton was run successfully over the pressure range of 0.2–0.5 Torr and required 30 min for 10 g of starting material. The crude product was taken up in 15% aq NaOH (200 mL) and extracted into pentane (3 × 200 mL). The entire procedure was repeated ten times.[17] The combined organic layers were washed with sat. aq NaCl and analyzed by GC to be 88% BCB, 12% starting material, and < 1% side reactions (styrene, ethylbenzene). Upon removing solvent, the oil is taken up in DMSO (1 L) with rapid stirring. Excess powdered KOH (20 g) was added[18] to convert **1** to α-hydroxy-*o*-xylene. This conversion was monitored by GC and complete within 4 h. The resulting solution was extracted into H_2O (1 L), adjusted to pH 7, and washed with petroleum ether (3 × 750 mL). The combined organic layers were dried (Na_2SO_4) and the solvent was removed. The resulting brown solution was distilled (65–68 °C at 20 Torr) to yield BCB (**2**; 63 g, yield: 85%) as a colorless liquid.

3,6-Bis(trimethylsilyl)1,2-dihydrocyclobutabenzene (4):
3,6-Bis(trimethylsilyl)-1,2,3,6-tetrahydrocyclobutabenzene (**3**): A dry, magnetically stirred, 500 mL Schlenk flask was charged with a mixture of 57.2 g of Li dispersion (5% Na content) in mineral oil and placed under an Ar atmosphere. Dry pentane was added via vacuum transfer under rapid stirring to solvate the mineral oil. The pentane/mineral oil solution was removed via filtration under Ar. Pentane washing was repeated several times to ensure efficient removal of the mineral oil.[19] The remaining mass of Li metal (14.1 g, 2.03 mol) was determined and the flask was cooled to 0 °C and charged with dry THF (500 mL) via cannula transfer. In one portion, Me_3SiCl (187.2 mL, 1.48 mol) was added. BCB (**2**; 52 g, 500 mmol) was then added dropwise over a period of an hour via syringe to the rapidly stirring solution. The reaction continued for 4 h and was monitored by GC until complete. Upon completion the mixture was cooled to 0 °C and *i*-PrOH (100 mL) was added dropwise to carefully quench excess Li. The resulting solution was partitioned into H_2O (1 L) and washed with petroleum ether (3 × 750 mL). The combined organic layers were dried (Na_2SO_4) and removal of solvent yielded a brown oil **3** (114.9 g, yield: 92%) that was a mixture of cis and trans isomers.

3,6-Bis(trimethylsilyl)-1,2-dihydrocyclobutabenzene (**4**): The oil was placed in a 1 L three-neck flask, taken up in DMSO (750 mL), and bubbled with O_2 while rapidly stirring the solution. Aromatization was complete in 24–36 h as determined by GC. The resulting solution was taken up in H_2O (1 L) and washed with petroleum ether (3 × 750 mL). The combined organic layers were dried (Na_2SO_4) and upon removal of solvent gave crystals of **4** (109.2 g; yield: 88% based on BCB).

3,6-Dibromo-1,2-Dihydrocyclobutabenzene (5):
To a solution of **4** (100 g, 402 mmol) in MeOH (2 L) was slowly added a solution of Br_2 (192.79 g, 1206 mmol) in MeOH (1 L). The addition takes place over 24 h and the reaction was monitored by GC until complete (36 h). The resulting solution was partitioned into H_2O (1 L) and washed with petroleum ether (3 × 1 L). The combined organic layers were dried (Na_2SO_4). The solvent was removed to yield a yellow solid. The crude product was run through a short plug of silica gel in petroleum ether. Et_2O (90:10). Removal of eluent solvent yielded white crystals of **5** (95 g, yield: 90%).

Dibutyl 1,2-Dihdrocyclobutabenzene-3,6-dicarboxylate (6):
A dry, magnetically stirred, 500 mL Schlenk flask was charged with **5** (30 g, 108 mmol), $Pd(OAc)_2$ (400 mg, 1.77 mmol), and Ph_3P (2.80 g, 10.6 mmol). This vessel was evacuated to 0.02 Torr and refilled with CO. This procedure was repeated four times. A solution of dry Et_3N (80 mL) and dry BuOH (100 mL) was added via syringe. The resulting solution was degassed several times under rapid stirring to remove all gasses dissolved in the solvents and refilled with CO. The vessel was placed under a slight positive pressure of CO and heated to 80 °C under very rapid stirring. The reaction required 48 h and was monitored by GC until complete. The crude mixture was partitioned into H_2O (1 L) and washed with petroleum ether (3 × 750 mL). The combined organic layers were dried (Na_2SO_4). The crude product was run through a short plug of silica gel with petroleum ether/Et_2O (90:10) to remove catalyst. Removal of eluent solvent left a light yellow oil of **6** (40.60 g, yield: 95%).

1,2-Dihydrocyclobutabenzene-3,6-dicarboxylic Acid (7):
A solution of **6** (40 g, 142 mmol) and powdered NaOH (8 g, 200 mmol) was taken up in MeOH (600 mL) with H_2O (40 mL) and refluxed for 2 h. H_2O (1 L) was added to dissolve excess sodium salts and filtered. The mixture was then cooled to 0 °C and acidified to pH 7. The product precipitated out of solution. Filtration of the precipitated product and subsequent washing with acetone (300 mL) yielded[7] (XTA) (26.5 g, yield: 97%) as a white powder.

1,2-Dihydrocyclobutabenzene-3,6-dicarbonyl Dichloride (8):
To a dry, magnetically stirred, 1 L three-neck flask was added **7** (25.0 g, 130 mmol), $BnEt_3NCl$ (65.0 mg, 0.29 mmol), and dry CH_2Cl_2 (600 mL). The mixture was brought to reflux and $SOCl_2$ (25.3 mL, 345 mmol) was added in one portion. The reaction requires 24 h and was monitored by GC until complete. The mixture was filtered hot and solvent was removed to yield dark yellow crystals which were sublimed (0.05 Torr, 80 °C) to yield light yellow crystals. Recrystallization from dry Et_2O yielded white crystals of **8** (28.6 g, yield: 96%).

1,2-Dihydro-*N,N'*-diphenylcyclobutabenzene-3,6-dicarboxamide (9):
A 100 mL, magnetically stirred, round-bottom flask was charged with aniline (1.63 g, 17.2 mmol) and 1-methylpyrrolidinone (5 mL). Under stirring, **8** (1.0 g, 4.4 mmol) was added and a yellow solution resulted. The reaction was complete within 1 h and the solution was filtered yielding yellow crystals. The solid was washed with H_2O (50 mL) and acetone (50 mL) to yield white crystals **9** (1.45 g, yield: 97%).

3,6-Bis(benzoxazol-2-yl)-1,2-dihydrocyclobutabenzene (10):
A 250 mL-three-neck flask equipped with a mechanical stirrer and a N_2 inlet was charged with **8** (1.0 g, 4.4 mmol), degassed polyphosphoric acid (PPA, 50 mL), and 2-aminophenol (1.9 g, 17.4 mmol). The reaction was heated to 90 °C with stirring and degassed to remove HCl. The reaction was then heated to 150 °C for 20 h.[20] The resulting solution was partitioned into H_2O (500 mL), brought to neutral conditions via addition of NaOH solution, and filtered to collect the solid. Recrystallization of the material from DMSO yielded fluffy, pale yellow crystals **10** (1.19 g, yield: 80%).

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(12) Trace (< 1%) amounts of styrene and ethylbenzene present as side-products.
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(16) We found that best results were obtained by not packing the quartz tube thus minimizing residence time. The temperature in the tube and pressure were carefully modified as reported to optimize yields.
(17) This scale of FVP run (10 g of **1**) proved optimal, larger scale runs provided increasing percentages of **1**.
(18) In this step it is crucial that the KOH be powered very fine to aid solvation. A minimum of four equivalents of KOH is used.
(19) The Li used in the Birch reduction came in a mineral oil dispersion with a 5% Na content. Multiple washings of the dispersion with dry pentane effectively removed the mineral oil leaving only the Li. As the scale was increased however, effective removal of the mineral oil became increasingly difficult. A small amount of remaining mineral oil proved not to be a problem. Neither the Birch reduction nor the aromatization was effected by a small amount of mineral oil. The mineral oil also proved difficult to remove from the aromatized product **4**. However, this was not a problem either. The mineral oil could be carried on to the bromination step and brominated along with **4**. The mineral oil, once brominated, will not move on silica gel in 1:10 Et_2O petroleum ether and was easily separated by filtering the mixture through a short plug of silica gel.
(20) The reaction was complete within 8 h but allowed to continue for comparison to polymerization conditions. See: Choe, E.W.; Kim, S.N. *Macromolecules* **1981**, *14*, 920, for polymerization conditions.