

# Convenient Small-Scale Preparation of *p*-Carborane by Pyrolysis of *o*-Carborane

Paul I. Dron, Walter E. Klein, and Josef Michl

Department of Chemistry and Biochemistry, University of Colorado, Boulder, CO 80309-0215, USA

Reprint requests to J. M.; E-mail: [michl@eefus.colorado.edu](mailto:michl@eefus.colorado.edu)

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*Dedicated to Prof. Jörg Fleischhauer on the occasion of his 75th birthday.*

A convenient procedure for the preparation of *p*-carborane by pyrolysis of *o*-carborane on a scale of 300–350 mg of > 99.5% pure product per day is described.

**Key words:** *p*-Carborane; Pyrolysis.

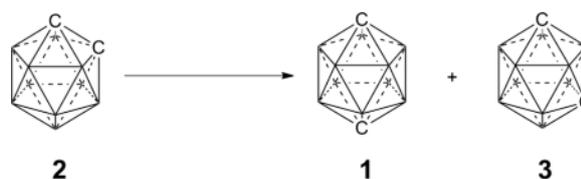
## 1. Introduction

1,12-Dicarba-*closo*-dodecaborane (**1**) [1], usually referred to simply as *p*-carborane, is one of the relatively few building blocks suitable for the construction of straight and rigid molecular rods [2] and thus finds applications in nanoscience. The bonds directed from antipodal positions on the icosahedral cage of **1** are antiparallel, the two carbon positions are easily functionalized, and the cage is not only a fairly good electrical insulator but also very resistant to damage by heat or irradiation. In addition to its use as a synthon in the design and synthesis of rigid-rod molecules for nanoarchitecture [3–5], of molecular rotors [6], of nanomachines for the conversion of energy into controlled motion on a surface and transport of nano-loads [7], of liquid crystals [8], of nonlinear optical materials [9, 10], and of spacers in photoactive metal-polypyridine dyads [11, 12], it has seen medical applications, both in the design of potential candidates for boron neutron capture therapy in the treatment of cancer and rheumatoid arthritis [13] and as a hydrophobic core structure for anti-androgens active toward LNCaP human prostate cancer cells with mutated androgen receptors [14].

The only serious obstacle to efforts to exploit the unique structure **1** is its poor synthetic accessibility. The original method for the preparation of **1** [1] (Scheme 1) involved a batch thermal rearrangement of the easily available *o*-carborane (**2**) in a stainless steel autoclave at 615 °C for 17 h. High pressures (200–300 psi) were usually developed in the chamber during

the heating, and an extended cooling time was required before the container was safe to open. The product was a mixture of **1** with *m*-carborane (**3**) and the yield of isolated **1** was only 6.5%. Subsequently, a safer procedure was developed [15] that took advantage of the volatility of carboranes. A stream of **2**, with or without an inert carrier gas, was heated to 650–700 °C under atmospheric pressure, with a reactant residence time of ~0.5 min. This procedure also resulted in a mixture of **1** and **3**, and according to an infrared analysis **1** was present in the mixture in a maximum yield of 22%.

Both preparative procedures suffer from extensive side reactions that result in copious amounts of black solids deposited on reactor walls. They need to be cleaned before the next reaction is run, and this requires laborious effort and considerable time. No wonder, then, that the pyrolytic preparation of **1** has long had a bad reputation as a time-consuming messy procedure that affords low yields and is best avoided. At times, it was possible to circumvent the problem since **1** was available commercially, albeit at a considerable cost. Lately, however, its commercial availability has been spotty at best.



Scheme 1. Thermal rearrangement of *o*-carborane,  $C_2B_{10}H_{12}$ .

Although a wide range of mechanistic pathways for the thermal rearrangement of **2** has been proposed, no definitive answer has been reached. Initial studies of derivatives of **2** in which substituents were used as vertex labels led the authors to propose a cooperative diamond–square–diamond (DSD) mechanism [16] in which the isomerization of **2** to **3** proceeds through a cuboctahedral intermediate. However, using this mechanism alone does not convert **2** to **1**, and others were formulated for the purpose. They involved a rotation of the two halves of the icosahedron (pentagonal pyramids) in opposite directions [17], a rotation of the triangular faces in the icosahedron surface [18], an extended triangle rotation (ETR) [19], cross-polyhedral binding [20], single-edge cleavage [21], and isomerization via an anti-cuboctahedron [22].

Other experimental studies used unsubstituted **2** with  $^{10}\text{B}$  labeled vertices [23] and tried to explain the isomerization through 12-vertex *nido*- $\text{C}_2\text{B}_{10}$  intermediates. Recent computations suggest that mechanisms involving a cage opening or combinations of any of the previously proposed mechanistic pathways are possible [24] and the issue remains unsettled.

We required a small-scale but reliable supply of **1** for our work on molecular rotors [25] and have decided to find out whether the pyrolytic conversion of **2** into **1** could be made friendlier. Presently, we report a variation of the literature procedure that is quite convenient and has proven itself suitable for a steady production of 300–350 mg of pure **1** per day. The key to progress was brief daily chemical in-situ cleaning of the walls of the pyrolytic apparatus that did not require a disassembly.

## 2. Results

### 2.1. Apparatus

The high-temperature apparatus we designed (Fig. 1) is standard, with a quartz thermolysis tube (25 mm in diameter) placed in a thermolysis oven. The U-shaped form of the tube is accidental and was dictated by the geometry of the furnace that was at our disposal. The front end is attached through glass fittings to a sublimation chamber made of a 250 ml three-neck round flask. A heating mantle delivers the heat for the vaporization of the starting material and also preheats the carrier gas. The outlet of the pyrolysis U-tube is connected through glass fittings to a double

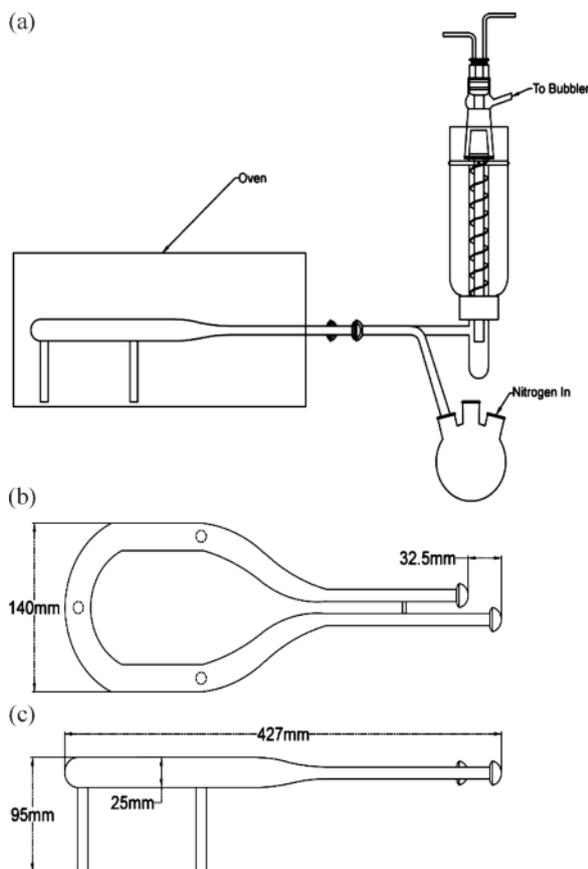


Fig. 1. Pyrolysis apparatus (a) and top (b) and side (c) views of the pyrolysis U-tube.

cooled receiver. The double wall of the condensation chamber allows exterior cooling when packed with dry ice. The inner water cooled heat exchanger has a coil shape to slow down the vapor flow. The top of the condensation chamber is connected to a bubbler filled with pentane in order to trap any product vapors that might otherwise escape.

The glass connectors at both ends of the thermolysis U-tube are maintained at constant temperature with heating tape. The temperature of the connectors and of the sublimation chamber is monitored by external thermocouples. Inside the thermolysis oven, the temperature is monitored by an internal thermocouple.

### 2.2. Operation

Immediately after all the parts of the apparatus are connected and the thermocouples, the heating tape, and

the coolants are in place, nitrogen carrier gas is connected and the system is purged for 45 min at room temperature with a flow of 100 ml/min in order to eliminate all traces of oxidants. After 45 min, the vaporization chamber is charged with **2** (~1.3 g) and the system is purged for another 15 min, after which the oven heat is turned up. When the temperature in the oven reaches 775 °C the vaporization chamber and the glass connections are heated to 200 °C and maintained at constant temperature. The pyrolysis is run under these conditions for 1 h.

After 1 h all heating is turned off and the nitrogen flow is discontinued. The water cooled heat exchanger is removed and the top of the condensation chamber is closed with a rubber septum. The heat exchanger is washed immediately with pentane and the resulting solution is kept in a closed vessel. The dry ice surrounding the condensation chamber is discarded and the chamber is washed immediately with pentane. Any brown residue still present after pentane wash is easily cleaned with acetone but it does not contain any **1**. All pentane fractions are combined and concentrated to about 5–10 ml on a rotary evaporator, using 450 mm mercury pressure and a cooling bath at 8–10 °C. Under these conditions pentane evaporates but carboranes do not. About half of the mass of the starting **2** is recovered as crude reaction product. Its proton nuclear magnetic resonance spectrum shows that it contains about one part of **1**, two parts of **3**, and no starting material.

### 2.3. Product Purification

The crude product is purified by column chromatography on basic alumina with pentane as the mobile phase. Small fractions (3–5 ml) are collected from the column and immediately checked using an HP 6850 Gas chromatograph. Setting the inlet temperature at 180 °C, the column temperature at 140 °C, and the flame ionization detector (FID) temperature at 250 °C, only two fractions are detected. The peak eluted first contains **1** (retention time 2.84 min) and the second peak contains **3** (retention time 3.2 min).

After column chromatography most of the product **1** is isolated pure. However, only a small portion of the pure side product **3** is isolated and most of it remains contaminated with traces of **1**. Running a second thermal isomerization on this mixture does not modify the ratio between **1** and **3**, but running a second

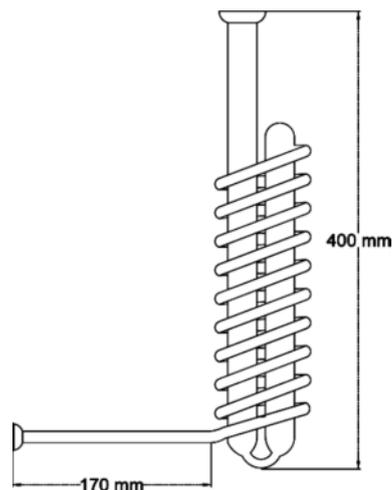


Fig. 2. Schematic drawing of the bubbler used in the cleaning procedure.

column chromatography allows additional pure **1** to be isolated, while the side product **3** still remains contaminated with small amounts of **1**. The fractions containing pure **1** are concentrated on a rotary evaporator at 8–10 °C under 450 mm mercury pressure to yield a total of 340 mg (27% yield from 1280 mg of **2**) of at least 99.5% pure white **1** with spectral characteristics identical to the authentic material [1, 26].

### 2.4. Resetting the Apparatus

When the isomerization reaction is finished, the vaporization chamber and the condensation chamber are disconnected. With the thermolysis U-tube still in the oven, a chlorine supply is attached to its inlet and a dedicated bubbler (Fig. 2) filled with 30% aqueous potassium hydroxide solution is connected to the outlet. The oven is reheated and when the temperature reaches 900 °C a small flow of chlorine (~60 ml/min) is passed through the system for 10 min. The heating is then stopped and the chlorine supply discontinued. The entire system is allowed to cool for several hours, after which the isomerization/cleaning cycle can be resumed.

## 3. Discussion

The pyrolysis conditions described above were deduced from a series of optimization runs, in which the

nature and flow rate of the carrier gas and the working temperature were varied. At nitrogen flow rates of 50 or 100 ml/min, pyrolysis temperatures of 700 °C or lower led to incomplete conversion of the starting material **2** or its complete conversion to insoluble black deposits, regardless of whether the pyrolysis tube was open or filled with quartz saddles. At 775 °C **2** was no longer present in the effluent from the open tube. At 50 ml/min flow rate, or if the tube was packed, only black insoluble material resulted, but after an increase of the flow rate to 100 ml/min in an open tube, about half of the starting **2** was converted into **1** and **3** while the rest was still lost as black deposit on the reactor walls. We also tried to use argon as carrier gas but all our attempts resulted in the recovery of starting **2**. This is surprising because there are reports [27] of using argon under similar conditions and at least **3** was obtained.

It is quite possible that further optimization will lead to an increased yield of the desired product **1**. The observation that a re-pyrolysis of the fractions that contained mostly the side product **3** did not increase the content of **1** however suggests that both **1** and **3** are

formed directly from **2** in parallel competing reactions and that the conversion of **3** to **1** is difficult if not impossible, and this does not bode well for attempts to increase the yield of **1**.

The main advance reported presently is the in-situ chemical cleaning of the reaction tube, which saves much time otherwise needed for disassembly and mechanical cleaning or flaming of the U-tube. It is based on the realization that the insoluble black residue most likely is partially hydrogenated elemental boron, which could be expected to react with chlorine gas at elevated temperatures to give volatile products.

#### 4. Conclusion

We developed a convenient procedure for the small scale batch synthesis of **1** from **2** under laboratory conditions. The procedure is safe, rapid, and reproducible, and it provides a 27% yield of pure **1**, superior to those described earlier. A key novelty is the introduction of an in-situ apparatus cleaning procedure that avoids the most onerous part of the original process and reduces considerably the down time.

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