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Cannizzaro's $(C_7H_6)_n$ conundrum resolved: [1.1.1]orthocyclophane was first made 150 years ago

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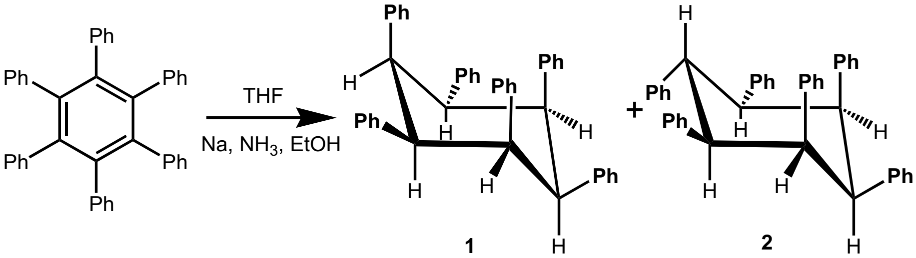
Abstract

The product of the reaction of benzyl alcohol with a number of Lewis acids was shown by Cannizzaro in 1854 to have the empirical formula $(C_7H_6)_n$, and this material has been the subject of much controversy for many decades. Its attribution as an isomer of 1,2,3,4,5,6-hexaphenylcyclohexane is shown to be incorrect, and instead it has been identified as 10,15-dihydro-5*H*-tribenzo[*a*,*d*,*g*]cyclononene, **3**, the parent [1.1.1]orthocyclophane, the X-ray crystal structure of which is reported.

Keywords: Cannizzaro; Benzyl cations; Trimerisation; X-ray crystallography

In a very recent report from this laboratory, it was shown that the Birch reduction of hexaphenylbenzene led, surprisingly, to *cis*- and *epi*-1,2,3,4,5,6-hexaphenylcyclohexane, **1** and **2**, respectively (Scheme 1).[1] These sterically very crowded products were unequivocally characterised by X-ray crystallography, and by ^1H and ^{13}C NMR spectroscopy. In light of these observations, a routine literature search was carried out in an attempt to find any prior reports of the existence of $C_6H_6Ph_6$; this search opened up a fascinating historical story that we now describe.

In 1854, Cannizzaro reported that the action of a variety of compounds, including boron trifluoride, sulfuric acid, phosphorus pentoxide or zinc chloride, either on benzyl alcohol or on dibenzyl ether gave a hydrocarbon with the formula $(C_7H_6)_n$.[2] Subsequently, other researchers described the preparation of related $(C_7H_6)_n$ compounds, some of them resinous and apparently polymeric where



Scheme 1. Products of the Birch reduction of hexaphenylbenzene.

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the value of '*n*' ranged up to 18;[3] there were also numerous claims to have prepared 1,2,3,4,5,6-hexaphenylcyclohexane by this procedure.[4] In 1939, Calcott et al. reported that the treatment of benzyl alcohol with anhydrous hydrogen fluoride furnished 1,2,3,4,5,6-hexaphenylcyclohexane, but no experimental data were provided.[5] Furthermore, the reaction of benzyl chloride with a wide range of metals was also reported to yield 'the $(C_7H_6)_n$ hydrocarbon'.[6] Indeed, over the ninety years following Cannizzaro's initial report, the question of the identity of this material was the subject of more than thirty publications, and a comprehensive historical survey has been provided.[7] We are aware of only two substantive reports of the possible resolution of this problem: in 1941, Shriner and Berger observed that, when a large quantity of benzyl alcohol was heated for 12 h at 180 °C with boric acid, a very small amount of a pure product, **3**, (mp 278–280 °C) could be obtained after recrystallisation from benzene.[7] A molecular weight determination by Rast's method (depression of the freezing point of camphor)[8] gave a value of 556—$(C_7H_6)_6$ requires 540—and, based also on the microanalytical results, these data led the authors to suggest that compound **3** was 'one of the isomeric 1,2,3,4,5,6-hexaphenylcyclohexanes'. There was even some mechanistic speculation concerning the possible trimerisation of stilbene to yield **3**, but this was eventually discounted. Subsequently, in 1956, Gerrard and Kilburn noted that, when $[PhCH_2CH(Ph)O]_4Si$ was treated with HCl, a liquid was formed with bp 229 °C at 0.03 mm Hg; this was assigned as 'sym-hexaphenylcyclohexane'.[9] However, in the absence of clear spectroscopic or crystallographic evidence, these previous claims for the existence of 1,2,3,4,5,6-hexaphenylcyclohexane must remain unproven.

Because of the lack of any structural or spectroscopic data from the earlier work, the only viable historical links are the melting points of the products. In all of those studies over the past 150 years, the only reported melting point (278–280 °C) is that of the crystalline $(C_7H_6)_n$ product, **3**, reported by Shriner and Berger;[7] however, this does not correlate with those found recently (190–191 °C for *cis*-**1**, 216–217 °C for *epi*-**2**),[1] showing that they are different from the material reported in 1941. Nevertheless, such a discrepancy in melting points did not rule out the possibility that Cannizzaro's original product was indeed one of the other geometric isomers of 1,2,3,4,5,6-hexaphenylcyclohexane, such as the energetically favoured *all-equatorial* (*scyllo*) structure that apparently is not produced under the low temperature Birch conditions, where kinetic factors presumably dominate.[1] We thus decided to repeat the Shriner and Berger synthesis so as to establish the identity of their crystalline material using modern analytical methods.

After considerable time and effort, a small quantity of a crystalline product was eventually obtained; it exhibited a sharp melting point of 279 °C, in excellent accord with that previously reported for **3**. The NMR spectra of **3** were surprisingly simple, immediately eliminating any isomer of 1,2,3,4,5,6-hexaphenylcyclohexane as a possibility. The ^1H NMR spectrum exhibited an AB pair of doublets ($J = 13.3$ Hz) at 3.76 and 4.91 ppm, clearly a methylene group, and two pseudo-triplets (9 Hz) of doublets (3.5 Hz) (each 2 H) at 7.09 and 7.38 ppm entirely characteristic of a symmetrically *ortho*-disubstituted benzene. This interpretation was consistent with the observed ^{13}C NMR spectrum which revealed a CH_2 absorption at 37.3 ppm, two aromatic CHs at 127.1 and 130.2 ppm and one other aromatic resonance at 139.6 ppm.

One was drawn to the conclusion that the molecule is a cyclic $[ortho\text{-}C_6H_4\text{–}CH_2\text{–}]_n$ system, in accord with Cannizzaro's empirical formula. A literature search immediately revealed that the trimer, 10,15-dihydro-5*H*-tribenzo[*a*,*d*,*g*]cyclononene, prepared either by acid-catalysed cycloaddition of benzene with 2,2′-bis(hydroxymethyl)diphenylmethane under high dilution conditions,[10] or with bis(bromomethyl)diphenylmethane and a Lewis acid such as $TiCl_4$ or Nafion,[11] was known to have a melting point of 278–279 °C, strongly suggesting it to be the true identity of **3**. Moreover, the NMR data listed above for **3** correspond to those previously reported for 10,15-dihydro-5*H*-tribenzo[*a*,*d*,*g*]cyclononene.[12] As expected for the trimeric

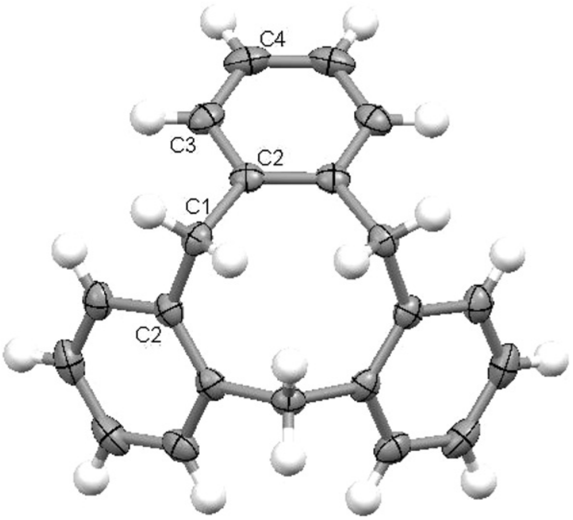


Fig. 1. *Mercury*[14] representation of the X-ray crystal structure of **3**; a bird's eye view emphasising the threefold symmetry.

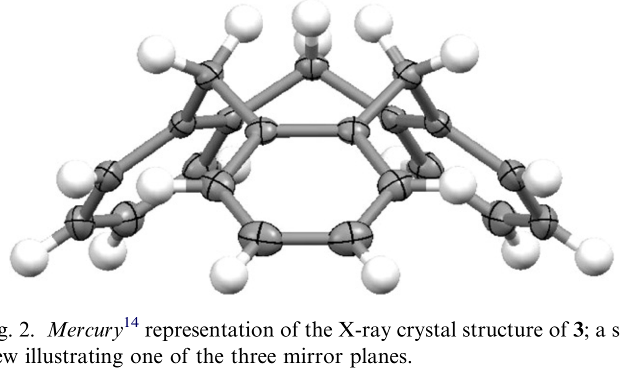
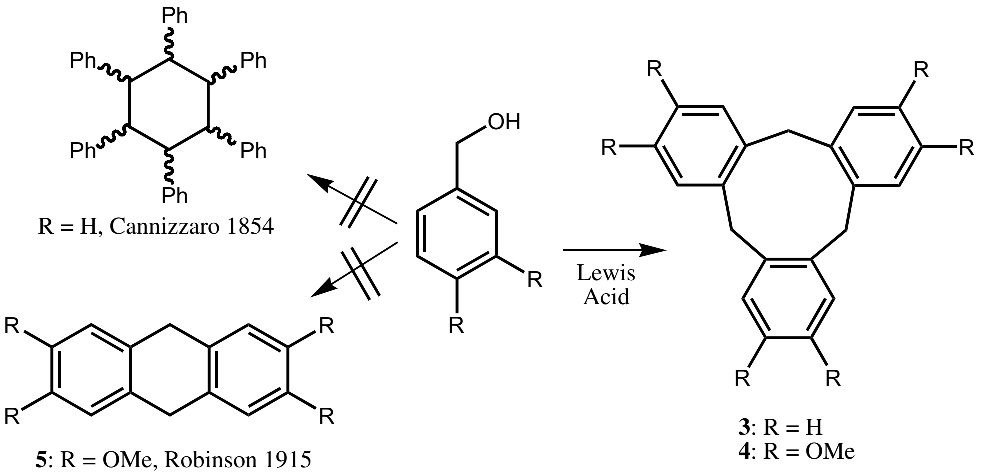


Fig. 2. *Mercury*[14] representation of the X-ray crystal structure of **3**; a side view illustrating one of the three mirror planes.



Scheme 2. Reactions of benzyl alcohols with Lewis acids.

material, the mass spectrum of **3** exhibited a parent peak at *m*/*z* 270.

Finally, as depicted in Figures 1 and 2, the structure of **3** was conclusively established by X-ray crystallography which confirmed the C_{3v} symmetry of the *all-cis*, crown-shaped isomer. The interplanar angles between the arene rings were found to be 68°, the ring-centroid–ring-centroid distances to be 4.84 Å, and the benzo-ring–carbon–CH_2 distances, C(1)–C(2), were 1.522 Å, and in all cases very similar to those found in cyclotriveratrylene, **4**.[13]

Interestingly, as shown in Scheme 2, there are historical parallels between the current identification of **3** as a cyclic trimer and the belated recognition of the correct structure for cyclotriveratrylene, **4**, which has since become a very widely-used host in supramolecular chemistry. In 1915, Robinson suggested that the reaction of *o*-dimethoxybenzene and formaldehyde gave 2,3,6,7-tetramethoxy-9,10-dihydroanthracene, **5**,[15] and it was only 50 years later that Lindsey was able to show conclusively that the product was in fact a trimer. Even more relevant to the present case is the subsequent observation that cyclotriveratrylene, **4**, is preparable in good yield by the acid-catalysed trimerisation of 3,4-dimethoxybenzyl alcohol;[16] of course, in the latter case, the benzyl cation benefits very greatly from the presence of a methoxy substituent.

We suggest that the early claims for the synthesis of 1,2,3,4,5,6-hexaphenylcyclohexane appear to have been unjustified, and that the identity of 'the $(C_7H_6)_n$ hydrocarbon', which has been the source of some controversy for more than 150 years, has now been resolved. It would appear that, in the earlier work, too much reliance was placed on the molecular weight determination by Rast's method that gave much too high a value of 556. Nevertheless, one must admire the determination and experimental expertise of those early pioneers of organic chemistry who tackled such problems without the benefit of the powerful spectroscopic and structural techniques that are readily available today. Furthermore, one can now see that Cannizzaro and his successors had in fact prepared the parent compound of the [1.1.1]orthocyclophane series, albeit in very low yield, more than a century before designed syntheses of **3** were reported.

Acknowledgements

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Supplementary data

Experimental procedures for **3**, as well as X-ray crystallographic collection and refinement details and structural data. Crystal data for **3** have been deposited with the Cambridge Crystallographic Data Centre (CCDC # 668372). Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.12.094.

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