

Mass spectrometric studies of self-condensation products of cyclohexanone under alkaline conditions and synthesis of dodecahydrotriphenylene and triphenylene from easily available reactants

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LC-MS was used to study products of cyclohexanone self-condensation under alkaline conditions. Improved methods (as compared to those described in the literature) for the preparation of dodecahydrotriphenylene and highly pure sublimed triphenylene were suggested based on the easily available and cheap reactants. Possible reasons of the low yield of the target dodecahydrotriphenylene in the step of oligomerization of cyclohexanone were identified.

Key words: triphenylene, cyclohexanone, trimerization, aromatization.

At the present time, triphenylene (**1**) and its derivatives are of considerable interest because of a possibility of their application as a base for the preparation of electroluminescent materials,¹ discotic liquid crystals,^{2,3} and as chemosensors and sensor materials.^{4,5} Unsubstituted triphenylene can be easily functionalized: in the literature, there are described methods for the preparation of its monobromo,^{6,7} hexabromo,^{8,9} monoiodo derivatives,¹⁰ various acyl derivatives,^{11,12} as well as triphenylene-2-carbaldehyde.¹³ Thus, triphenylene **1** is a key compound in the preparation of a wide variety of its derivatives necessary for different purposes. The present work is devoted to the development of an approach to the synthesis of triphenylene **1** from easily available reagents.

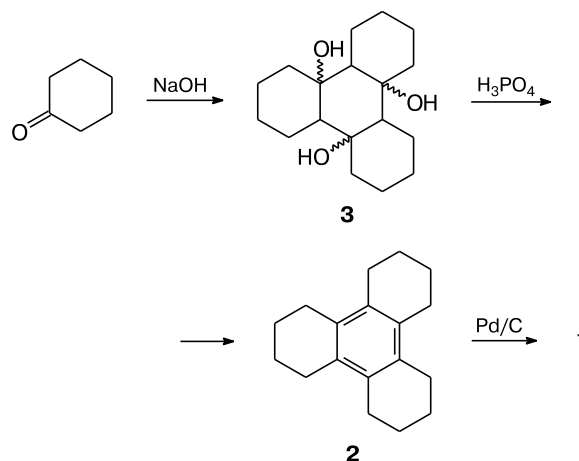
A number of methods for the preparation of triphenylene **1** are described in the literature. In particular, a preparative synthesis of triphenylene can be accomplished using aryne intermediates,^{14–17} cross-coupling reactions,¹⁸ metal-catalyzed arylation,^{19,20} cyclization based on 9,10-phenanthrenequinone.²¹ These methods have a disadvantage of very expensive starting reagents and catalysts, as well as a necessity to purify triphenylene in order to obtain highly pure product.

At the same time, one of the most promising methods for the preparation of triphenylene is dehydrogenation^{22,23} of dodecahydro derivative in the presence of palladium-on-charcoal, which in turn can be obtained according to

well known methods which use readily available reagents, in particular, cyclohexanone.^{24,25}

An approach to the preparation of dodecahydrotriphenylene **2** by the reaction of cyclohexanone with an alkali described by German authors²⁶ seems the most promising, since it compares favorably with other methods by the absence of expensive reactants and catalysts (Scheme 1). The triol **3** results from the reaction of cyclohexanone with the alkali at room temperature and its subsequent dehydration with orthophosphoric acid gives dodecahydrotriphenylene **2**. We have chosen this procedure as a basic one in the present work.

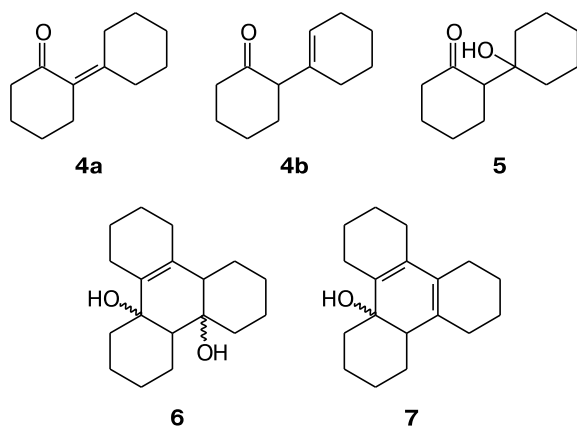
Scheme 1



The authors of the work²⁶ found that the cyclic trimer **3** was the only product of the reaction of cyclohexanone with an alkali, whose existence was confirmed by IR spectroscopy and elemental analysis.

However, attempted reproduction of this method showed that oligomerization of cyclohexanone is accompanied by the formation of considerably more complicated mixture of products. It should be also noted that the yields of dodecahydrotriphenylene **2** obtained by this procedure varied from low to moderate. To find possible reasons for this, we studied the composition of the reaction mixtures formed upon oligomerization of cyclohexanone by LC-MS.

According to the LC-MS data, the reaction mixture obtained by treatment of cyclohexanone with NaOH for three days contains the following intermediate compounds: dehydrated dimers of cyclohexanone **4** (two isomers), dimer of cyclohexanone **5**, and isomers of cyclohexanone trimers with different degree of dehydration **3**, **6**, and **7** (Table 1, Fig. 1, 2).



The peaks $[M + H]^+$ of compounds with m/z 179.1436 (compounds **4a,b**) and m/z 259.2042 (compound **7**) have the highest integral intensities.

The starting cyclohexanone was absent in the reaction mixture: the distillation of the reaction mixtures gave no fraction with b.p. 155 °C, and no $[M + H]^+$ peak of cyclohexanone with m/z 99.08 was observed according to the LC-MS data.

Analysis of trimeric products of condensation of cyclohexanone **3** (three isomers), **6** and **7** (four isomers) showed that, despite the presence of such products (see Table 1) in the reaction mixture, the integral intensities of the peaks of these compounds are low, therefore, a suggestion that the low yield of the reaction is explained by the parallel processes of trimerization, leading to the products incapable of further cyclization to dodecahydrotriphenylene **2**, was not confirmed. It can be supposed that the oligomerization reaction of cyclohexanone is kinetically controlled, since the best results were obtained after a prolonged standing of the reaction

Table 1. The LC-MS data for the reaction mixture obtained upon oligomerization of cyclohexanone under alkaline conditions^a

Com- pound	Chromatographic separation		MS, m/z , [M + H] ⁺		Molecular formula
	τ_{ret} /min	I_{int}^c (rel. units)	Found	Calculated	
Dimers					
4a	19.7	114239	179.1436	179.1436	C ₁₂ H ₁₈ O
4b	17.2	326589	179.1436	179.1436	C ₁₂ H ₁₈ O
5	17.2	6445	197.1532	197.1536	C ₁₂ H ₂₀ O ₂
Trimers					
3	15.8	17703	295.2236	295.2268	C ₁₈ H ₃₀ O ₃
	16.0	17609	295.2237	295.2268	C ₁₈ H ₃₀ O ₃
	17.3	25190	295.2233	295.2268	C ₁₈ H ₃₀ O ₃
6	22.5	8700	277.2113	277.2162	C ₁₈ H ₂₈ O ₂
7	20.5	11660	259.2042	259.2056	C ₁₈ H ₂₆ O
	22.5	47939	259.2042	259.2056	C ₁₈ H ₂₆ O
	24.5	15084	259.2039	259.2056	C ₁₈ H ₂₆ O
	28.9	13772	259.2031	259.2056	C ₁₈ H ₂₆ O

^aReaction conditions: cyclohexanone : NaOH = 3.8 : 1, 20 °C, 3 days.

^bCalculated based on the mass spectrometric data.

^cIntegral intensity.

mixtures at room temperature; heating gave lower yields of the target triphenylene **1**. We also found that cyclohexanone dimers **4a,b** and **5** are present in the reaction mixture in large amounts, whereas the starting cyclohexanone is completely absent. To sum up, there are no precondition for the formation of the trimer and, therefore, of dodecahydrotriphenylene **2**, whereas tetramer is present

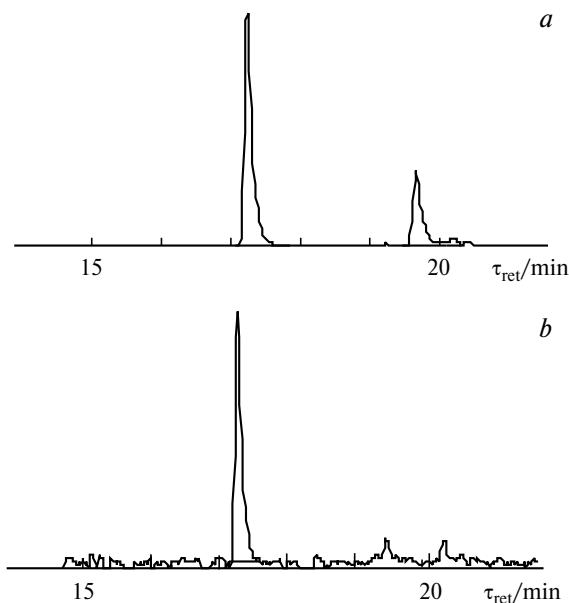


Fig. 1. Chromatography pattern of cyclohexanone dimers **4a,b** (a) and **5** (b).

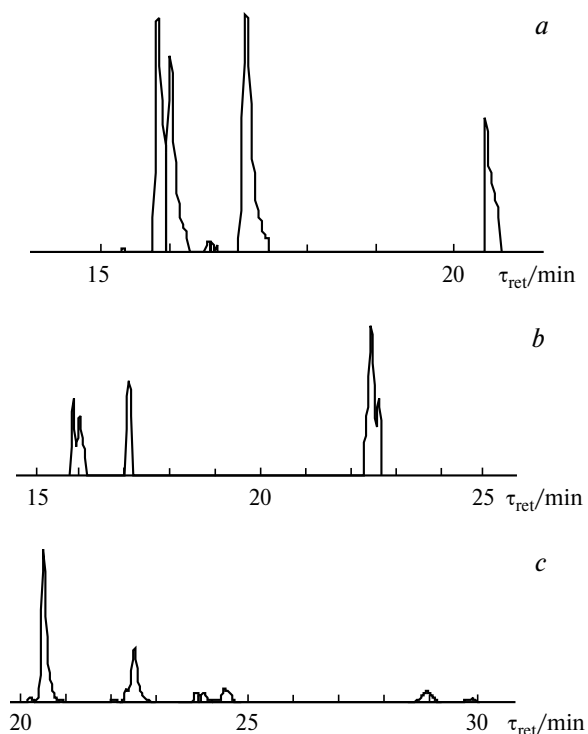


Fig. 2. Chromatography pattern of cyclohexane trimers **3** (a), **6** (b), and **7** (c).

in insignificant amount (one isomer with the low integral intensity of the peak).

One of the major reasons of low efficiency of the process can be a low rate of cyclization reaction of the open-chain trimer to the cyclic structure **3**, as well as to its dehydrated forms **6** and **7**, which were also identified in the reaction mixture.

We assume that in order to increase the yield of the target dodecahydrotriphenylene **2**, it is necessary to periodically add the starting cyclohexanone to the reaction mixture and to increase reaction time.

It should be also noted that, despite considerable amount of side products formed in the first step of the process, the modified procedure used by us allows obtaining dodecahydrotriphenylene **2** with sufficient purity without additional purification.

We further made a number of changes in the procedure used for the preparation of dodecahydrotriphenylene **2** (the dehydration step). In particular, we used polyphosphoric acid instead of orthophosphoric acid because this reactant is more convenient in handling. Besides, we also changed the procedure used for the isolation of product **2**: we applied continuous extraction with light petroleum using a Soxhlet extractor.

Dehydrogenation of **2** leading to triphenylene **1** was also effected according to a modified procedure:²² the reaction was carried out under argon with the preparation of sublimed triphenylene in 99% yield, which

is considerably higher than that in the methods described earlier.

In conclusion, in the present work we developed an approach to the synthesis of highly pure sublimed triphenylene starting from inexpensive commercially available reactants. LC-MS was used to study composition of the mixture of products obtained upon oligomerization of cyclohexanone in the presence of an alkali, possible reasons decreasing the yield of the target dodecahydrotriphenylene in this step were identified. Taking into account commercial value of triphenylene, this method seems promising, despite a moderate yield of the target product.

Experimental

¹H and ¹³C NMR spectra were recorded on a Bruker Avance-400 spectrometer (400 and 100 MHz, respectively) in CDCl₃, using Me₄Si as an internal standard. Melting points were measured on a Boetius heating stage. Electron impact mass spectra (EI) were measured on a SHIMADZU GCMS-QP2010 Ultra instrument.

The mass analyzer was a Bruker Daltonics (Bremen, Germany) MicrOTOF-Q II mass spectrometer with an electrospray ionization source, a 6-port divert valve and syringe pump kd Scientific appliance with the flow rate 180 μL h⁻¹, and an Agilent 1200 chromatograph with a diode array detector (DAD). The instrument controls were performed with micrOTOFcontrol 2.3 patch 1 (Bruker Daltonics) software. The nominal resolution of the instrument was 17500. The instrument was operated in the positive ion mode with *m/z* range 50–900 Da. A 6 point external instrument mass scale was performed before each sequence with lithium formate clustered by infusing 10 mmol L⁻¹ of lithium hydroxide in a mixture of isopropanol–0.2% aqueous formic acid (1 : 1, v/v). The chromatograph was equipped by an Agilent Eclipse XDB C18 column (150×4.6 mm) and worked in the gradient mode (eluent acetonitrile–water, from 5 to 95% of acetonitrile in the channel B from 0 to 30 min at the flow rate 1.0 mL min⁻¹).

Dodecahydrotriphenylene (2). Calcined anhydrous sodium hydroxide (6 g, 0.15 mol) was added to anhydrous freshly distilled cyclohexanone (60 mL, 0.58 mol) and the mixture obtained was stirred at room temperature for three days. Then, water (150 mL) was added to the reaction mixture with stirring, a precipitate was filtered off, washed with 10% aqueous HCl and water, and dried. The mixture of intermediate products without additional purification was added to polyphosphoric acid (40 g) and stirred for 2 h at 150 °C. Then, the reaction mixture was mixed with anhydrous sodium sulfate (100 g), placed into a Soxhlet extractor, and the product was continuously extracted with light petroleum (b.p. 40–70 °C). A precipitate was filtered off, washed with hexane, and dried. The yield was 24 g (52%), m.p. 229–231 °C. Found (%): C, 89.88; H, 10.01. C₁₈H₂₄. Calculated (%): C, 89.94; H, 10.06. ¹H NMR, δ: 1.78 (m, 12 H, ArCH₂CH₂); 2.58 (m, 12 H, ArCH₂CH₂). ¹³C NMR, δ: 23.23, 26.98, 132.77. MS (EI), *m/z* (%): 240 [M]⁺ (100).

Triphenylene (1). *A.* Dodecahydrotriphenylene **2** (24 g, 0.1 mol) and 10% palladium/Sibunit (4 g) were heated for 10 h at 300 °C under argon over the surface cooled with running water. The

sublimed product was mechanically removed from the surface. The yield was 22.57 g (99%), m.p. 196–198 °C. Found (%): C, 94.56; H, 5.21. C₁₈H₁₂. Calculated (%): C, 94.70; H, 5.30. ¹H NMR, δ: 7.66 (m, 6 H); 8.66 (m, 6 H). ¹³C NMR, δ: 123.33, 127.23, 129.85. MS (EI), *m/z* (%): 228 [M]⁺ (100).

B. The synthesis was carried out similarly, using 10% Pd/C and using no argon. The yield of triphenylene was 80%.

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