



Improved Synthesis of Benzocyclobutenone by Flash Vacuum Pyrolysis

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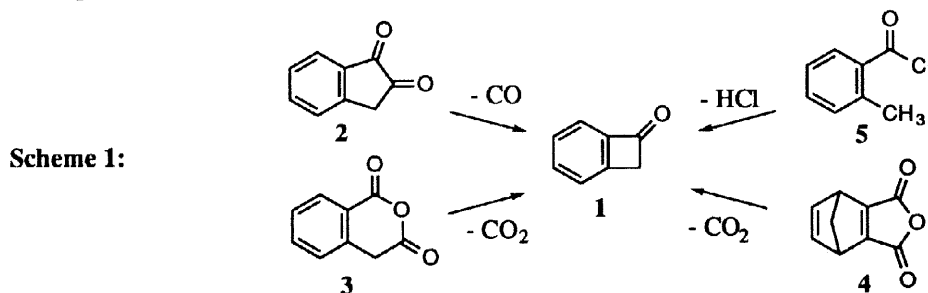
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Abstract: Flash vacuum pyrolysis of *o*-toluoyl chloride at 780 °C under 0.5 mmHg afforded benzocyclobutenone in higher yield (80%) than previously reported one (28 %).

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Benzocyclobutenone (bicyclo[4.2.0]octa-1,3,5-triene-7-one, **1**) is known to react with dienophiles, carbonyl compounds and nucleophiles.¹ Reaction of **1** with C₆₀ gave the Diels-Alder adduct where a carbonyl group is introduced directly onto the fullerene core.² Compound **1** is also a precursor to benzocyclobutenedione which has been used to produce a variety of cyclopentenones^{3a} and quinones.³ Benzocyclobutenedione monoketal has been used for the synthesis of quinone-type antibiotics,⁴ as well as complex organic molecules with potential antiviral activity.⁵ Benzocyclobutenone was first synthesized in 42% yield by oxidation of benzocyclobutenol.⁶ The only large-scale (80 g) synthesis of **1**, reported by Liebeskind et al. was done via cycloaddition of benzyne and vinylidene chloride.⁷ However, this synthetic route, like the others involving benzyne as an intermediate,⁸ requires the use of large quantities of solvent, and generates a large amount of solid wastes. On the other hand, flash vacuum pyrolysis (FVP) is a gas-phase reaction and is a more environment-friendly process as no solvent is needed and no or little solid wastes are produced. Several compounds were reported to yield benzocyclobutenone by FVP. 1,2-Indandione (**2**),⁹ homophthalic anhydride (**3**),¹⁰ bicyclo[2.2.1]hepta-2,5-diene-2,3-carboxylic anhydride (**4**)¹¹ and *o*-toluoyl chloride (**5**)¹² generate benzocyclobutenone, by loss of CO, CO₂, CO₂ and HCl, in 54%, 45%, 11%, and 28% yields, respectively (Scheme 1).

In connection with the studies on benzocyclobutenone and its applications in polymers, we needed to have compound **1** in large quantities. Our efforts were directed towards gas-phase pyrolysis, rather than the solution process. We chose to use *o*-toluoyl chloride as it is easily derived from inexpensive *o*-toluic acid (**5**). Whereas compounds **2**, **3** and **4** have to be made by multistep synthesis, rendering them less readily available.

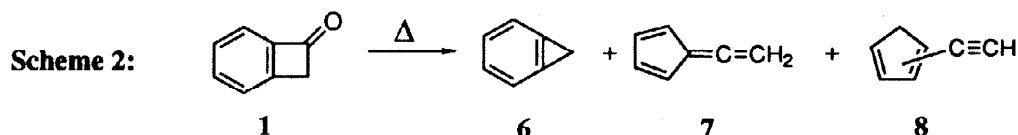


The reported pyrolysis was carried out at 630 °C and 14 mmHg, producing **1** in 28 % yield (run 1, Table 1).¹² The formation of **1** was accompanied by the evolution of hydrochloric acid. We studied the pyrolysis of *o*-toluoyl chloride under different conditions by varying the pyrolysis temperature and the system pressure (Table 1). We found that the pyrolysis of *o*-toluoyl chloride was very sensitive to slight changes in pressure and temperature in the system. These parameters can greatly affect the yield.

Table 1. Parameters for the pyrolysis of *o*-toluoyl chloride.

Run	1	2	3	4	5	6	7	8
Column Temperature (°C)	630	630	780	780	780	800	800	780
Pressure (mmHg)	14	5	5	5	1.75	1.75	1.5	0.5
yield (%)	28	53	59	60	35	32	75	80

The yield of **1** was significantly increased when decreasing the system pressure (run 2). The reactant **5** must stay in the hot reaction zone long enough for the reaction to occur, but not too long so as to prevent any further side reactions. Furthermore, the product **1** should be removed from the hot zone as quickly as possible in order to avoid thermal decomposition. Some of the thermal decomposition products from **1** were identified, e.g., benzocyclopropene (**6**),⁹ fluvenallene (**7**)^{9,10} and ethynylcyclopentadiene (**8**) (Scheme 2).⁹ An increase in the column temperature from 630 to 780 °C had little effect on the yield (runs 3 and 4). A decrease of the system pressure lowered the yield (run 5). Comparing runs 5 and 6, the yield dropped slightly (32%) at higher temperature (800 °C, run 6). However, a significant increase in yield (75%) was observed when the pressure was further decreased to 1.5 mmHg (run 7). After further fine tuning, an optimized condition (e.g., 780 °C, 0.5 mmHg) was established, which allowed a large-scale (>200 g) synthesis of **1** in high yield (e.g., 80%, run 8).



A typical pyrolysis is as follows: A horizontal type of FVP apparatus was used. A quartz tube (30 cm x Φ 2 cm) filled with quartz beads (1 cm x Φ 0.4 cm) was placed horizontally in a tube furnace. The reactant **5** was placed in a round-bottomed flask which was connected to the hot tube. The reactant was distilled under vacuum at 90-100 °C (oil bath temperature). The pyrolyzate was collected in a cold trap (-78 °C) attached at the end of the tube. Hydrochloric acid gas was trapped into a column packed with solid potassium hydroxide pellets. The collected pyrolyzate was then diluted with diethyl ether and was washed with aqueous potassium carbonate solution (5%) and water. The organic phase was dried over anhydrous MgSO_4 , concentrated and vacuum distilled to give benzocyclobutenone: $\text{Bp}_{0.05}$ 35-37 °C (lit¹³: $\text{Bp}_{0.1}$ 50 °C).

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