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A FACILE SYNTHESIS OF BICYCLO[4.2.0]OCTA-1,3,5-TRIEN-3-OL

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ABSTRACT: Bicyclo[4.2.0]octa-1,3,5-trien-3-ol (**2**) has been synthesized in good yield via a Baeyer-Villiger reaction of the corresponding aldehyde **5** with permonophosphoric acid.

Benzocyclobutene (bicyclo[4.2.0]octa-1,3,5-triene) based polymers are gaining importance because of their special properties.[1] In order to incorporate the benzocyclobutene moiety into a wide variety of polymer systems, functionalized benzocyclobutene derivatives are required. One such derivative is bicyclo[4.2.0]octa-1,3,5-trien-3-ol (**2**). Although **2** is a known compound, efficient synthetic methods have not been reported. The literature procedures[2,3] are based on diazotization of the corresponding amino compound **3** which itself is not easily accessible.[2-5] We report herein a new and efficient method for the synthesis of bicyclo[4.2.0]octa-1,3,5-trien-3-ol via Baeyer-Villiger reaction of the aldehyde **5**, which is obtained in high yield from either

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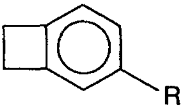
bromobenzocyclobutene **4**[5] or benzocyclobutene (**1**) by conventional methods.[6,7]



1 : R = H
2 : R = OH
3 : R = NH_2
4 : R = Br
5 : R = CHO
6 : R = COOH

Although aromatic aldehydes containing electron releasing groups in the ortho or para positions have been converted to the corresponding phenols in good yields under Baeyer-Villiger reaction conditions,[8,9] unactivated aromatic aldehydes are known to give predominantly the corresponding acids. When aldehyde **5** was subjected to Baeyer-Villiger reaction conditions employing either peracetic acid, trifluoroperaetic acid or sodium perborate, carboxylic acid **6** was the major product. However, aldehyde **5** smoothly underwent Baeyer-Villiger rearrangement on treatment with permonophosphoric acid[10] in acetonitrile to afford almost exclusively phenol **2** in 70% yield. The corresponding acid **6** was not formed in any significant amount. Permonophosphoric acid has been used before for the conversion of aromatic ketones to the corresponding phenols, but it has not been used for the conversion of aromatic aldehydes to phenols, to our knowledge. Extension of this methodology to benzaldehyde resulted in the formation of benzoic acid and phenol in 1.4 : 1 ratio.

The aldehyde **5** was obtained in 90% yield by treating the Grignard reagent derived from bromobenzocyclobutene **4** with dimethyl formamide followed by quenching with ammonium chloride. Alternatively, reaction of benzocyclobutene (**1**) with dichloromethyl methyl ether in the presence of titanium tetrachloride and subsequent aqueous workup furnished the aldehyde **5** in 70% yield.

In conclusion, we have demonstrated a new and efficient synthetic route to the phenol **2** starting from easily accessible benzocyclobutene derivative **5**.

EXPERIMENTAL

Bicyclo[4.2.0]octa-1,3,5-triene-3-carboxaldehyde (5)

a) From Bromobenzocyclobutene (**4**)

To a stirred solution of Grignard reagent prepared from 4.8 g of magnesium and 18.3 g of **4** in 40 mL of tetrahydrofuran at 0°C under nitrogen atmosphere, 15 mL of dimethyl formamide was added dropwise. The mixture was slowly warmed to room temperature and poured into 100 mL of saturated ammonium chloride solution. The mixture was extracted with ethyl acetate, the organic layer washed with water and brine and dried over anhydrous magnesium sulfate. Removal of the solvent followed by distillation under reduced pressure gave 11.9 g (90%) of the aldehyde **5**: bp 90°C (3.5 mm); IR (neat) 2930, 2820, 2730, 1685, 1595 cm^{-1}; ^1H-NMR ($CDCl_3$) δ 9.94 (s, 1H), 7.73 (d, J = 7.53 Hz, 1H), 7.57 (s, 1H), 7.21 (d, J = 7.53 Hz, 1H) and 3.24 s, 4H); ^{13}C-NMR ($CDCl_3$) δ 193.00, 154.10, 146.89, 135.95, 130.61, 123.10, 123.04, 29.84 and 29.11; HRMS: m/e 132.0579 (calcd for C_9H_8O, 132.0575).

b) From Benzocyclobutene (**1**)

To a stirred solution of 2.08 g of benzocyclobutene in 25 mL of methylene chloride at 0°C, 7.26 g of titanium tetrachloride was added over a period of 10 minutes. After 10 minutes, 2.3 g of dichloromethyl methyl ether in 5 mL of methylene chloride was added dropwise. The mixture was stirred for one more hour at 0°C and poured into 100 g of crushed ice. Extraction with ethyl acetate followed by workup as described above afforded 1.85 g (70%) of the aldehyde **5**. The physical properties and spectral data were identical with the sample prepared from bromobenzocyclobutene (**4**).

Preparation of Permonophosphoric Acid

To a stirred suspension of 14.2 g of phosphorus pentoxide in 60 mL of acetonitrile at 0°C, 10 g of 70% hydrogen peroxide in 20 mL of acetonitrile was added over a period of 45 minutes. The mixture was slowly warmed to room temperature and stirred for 16 hours (initially a milky white solution was formed and slowly turned into a colorless liquid). This solution was used immediately for the reaction.

Bicyclo[4.2.0]octa-1,3,5-trien-3-ol (**2**)

To a stirred solution of permonophosphoric acid, prepared as described above, 5 g of **5** in 10 mL of acetonitrile was added dropwise over a period of 30 minutes. The reaction mixture was stirred for an additional 2 hours and cooled to 0°C. Water (20 mL) was added, and the excess per acid was destroyed by addition of sodium bisulfite solution (tested with starch iodide paper). The organic solvent was removed by rotary evaporation, sodium hydroxide solution added until alkaline, and the mixture cooled to 0°C, acidified and extracted with ethyl acetate. The organic layer was washed with water, bicarbonate solution and brine. Drying and removal of the solvent followed by flash chromatography using 10% ethyl acetate in hexanes afforded 3.19 g of pure **2** (70%) as solid. A small portion was recrystallized from pentane: mp 47°C (lit.[3] 44-47°C); IR (neat) 3280 (br), 2920, 1595, 1450, 1160 cm^{-1}; ^{1}H-NMR (CDCl$_3$) δ 6.86 (d, J = 7.89 Hz, 1H), 6.64 (dd, J = 7.89 and 2.2 Hz, 1H), 6.58 (d, J = 2.2 Hz, 1H), 5.50 (s, 1H) and 3.06 (s, 4H); ^{13}C-NMR (CDCl$_3$) δ 154.70, 146.68, 137.41, 123.45, 113.99, 110.28, 28.83 and 28.56.

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