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Thermal Reactions Of Benzocyclobutenone With Alcohols

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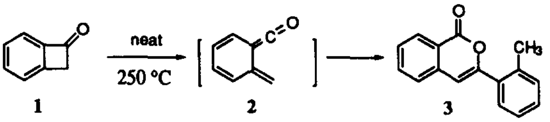
Abstract: Thermolysis of benzocyclobutenone alone at 250 °C yielded the isocoumarin **3** in 60% yield. In the presence of alcohols at 170-200 °C, the corresponding 2-methylbenzoates **4a-e** and **5a-c** were formed in quantitative yields.

Thermolysis or photolysis of benzocyclobutenone (**1**) generates a reactive intermediate of considerable interest in organic synthesis, α-oxo-*o*-quinodimethane (**2**), which undergoes facile [4+2] cycloaddition reaction with aldehydes, ketones and dienophiles such as maleic anhydride, dimethyl fumarate, benzoquinones and [60]fullerene.[1,2,3] Besides the diene moiety, another intriguing group in **2** is the ketene. Ketenes are highly reactive towards a variety of compounds such as alcohols, amines and carboxylic acids.[4] Irradiation of **1** in alcoholic solution at room temperature resulted in the formation of 2-methylbenzoates in high yield,[5] demonstrating a coupling reaction between the ketene group in **2** and alcohols. Surprisingly, the same ester-forming reaction of **1** and alcohols was not investigated under thermal conditions, although the thermal coupling reaction should be quite useful for certain applications.

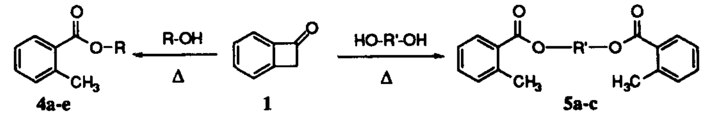
We then examined thermal reactions of **1** with and without alcohols. Thermolysis of **1** at 220-250 °C produced the isocoumarin **3** in 60% yield, along with some unidentified oligomers (Scheme 1). The same isocoumarin was also isolated in 40% yield from the reaction of *o*-(trimethylsilylmethyl)benzoyl chloride with cesium fluoride in refluxing acetonitrile, in which the intermediate **2** underwent self [4+2] cycloaddition followed by a 1,5-hydrogen shift in the dimer.[2]

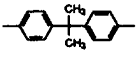
Scheme 1:



In the presence of alcohols, heating **1** at relatively lower temperatures (170-200 °C) yielded the corresponding 2-methylbenzoates (e.g., **4a-e**) in quantitative yields (Scheme 2). Both aliphatic and aromatic diols of low or high molecular weights also react with **1**, giving the corresponding bis-2-methylbenzoates **5a-c** in 100% yield. The reaction is very simple to run and does not produce any other by-products.

Scheme 2:



4a, R = $-CH_2(CH_2)_6CH_3$	**5a**, R' = $-CH_2CH_2-$
4b, R = $-CH_2Ph$	
4c, R = -Ph-p-Bu-t	**5b**, R' = 
4d, R = $-CH(CH_3)(CH_2)_5CH_3$	
4e, R = $-C(CH_2CH_2)_3$	**5c**, R' = $-(CH_2CH_2O)_n-$

A typical procedure follows: Benzocyclobutenone (0.56 g) was placed in a sealed tube and heated at 250 °C for 4 h. The resulting dark viscous liquid was cooled to room temperature and added into methanol. The methanol solution was filtered and the filtrate was concentrated. The residue was purified by chromatography using ethyl acetate/hexane (20/80) to give the isocoumarin **3**: 0.33 g (60%); mp 84-85 °C (lit.[2] mp 63-65 °C). For ester formation, **1** and an alcohol were placed in a flask or a sealed tube and heated in an oil bath at 170-210 °C for 2-30 h. The products were obtained without further purification in most cases when using stoichiometric amounts of reactants. The ratio of reactants, reaction temperature and time, and yield are summarized in Table 1.

Table 1. Reactions of benzocyclobutenone (**1**) with alcohols.

Run	Alcohol	Amount (meq)[a]	Temp. (°C)	Time (h)	Product[b]	Yield (%)[c]
1	1-octanol	4.0	200	21	**4a**	94.0
2	1-octanol	1.00	200	30	**4a**	79.3
3	benzyl alcohol	1.00	210	5	**4b**	100
4	4-t-butylphenol	1.00	200	2	**4c**	100
5	2-octanol	1.00	200	26	**4d**	80.5
6	2-octanol	12	170	56	**4d**	83.3
7	3-ethyl-3-pentanol	1.00	170	24	(**4e**)[d]	100
8	ethylene glycol	0.50	200	18	**5a**	100
9	bisphenol A	0.50	200	2	**5b**	100
10	poly(ethylene glycol)[e]	0.50	190	18	**5c**	100

a, molar equivalent to **1**. b, all products were fully characterized by spectroscopic means.
c, isolated yield based on **1**. d, 2-toluic acid and 3-ethyl-2-penpenee were obtained. e, Mw = 600.

By comparing the reaction time and yield, aromatic and benzylic alcohols react with **1** more readily than aliphatic alcohols. In run 7 with a tertiary alcohol, 2-toluic acid and 3-ethyl-2-penpene were obtained quantitatively. Under the same conditions (170 °C, 24 h), thermolysis of a mixture of **1** and water afforded 2-toluic acid as well, but 3-ethyl-3-pentanol did not yield water and 3-ethyl-2-penpene. Therefore, the corresponding ester **4e** was formed in run 7 but thermally decomposed to give 2-toluic acid and 3-ethyl-2-penpenee. The esterification went to completion, in most cases, using a stoichiometric amount of an alcohol (e.g., runs 4, 8, 9, 10). Thus, **1** can be considered as a latent 2-toluic acid, which forms an ester without any by-products (e.g., water). Since benzocyclobutenone and its substituted analogues are readily available,[6,7] this thermal reaction can be an alternative method for the esterifcation of alcohols. Given the fact that the diols react with equimolar **1** quantitatively (runs 8-10), it is highly conceivable that this coupling reaction based on **1** can be utilized as a polymer forming and/or curing reactions.

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References

1. Schiess, P.; Eberle, M.; Huys-Francotte, M.; Wirz, J.*Tetrahedron Lett.* **1972**, *25*, 2201.
2. Kessar, S. V.; Singh, P.; Venugopal, D.*J. Chem. Soc. Chem. Commun.* **1958**, 1258.
3. Tomioka, H.; Yamamoto, K.*J. Chem. Soc. Chem. Commun.* **1995**, 1961.
4. Blake, P. in *The Chemistry of Allenes, Ketenes and Related Compounds*, Part 1; Patai, S., ed., Wiley: Chicherster, **1980**, p 309-328.
5. Cava, M. P.; Spangler, R. J. *J. Am. Chem. Soc.* **1967**, *89*, 4550.
6. (a) Spangler, J.; Kim, J. H.*Tetrahedron Lett.* **1972**, *25*, 1249. (b) Hedaya, E.; Kent, M. E. *J. Am. Chem. Soc.* **1970**, *92*, 2149. (c) Liebeskind, L. S.; South, M. S.*J. Org. Chem.* **1982**, *47*, 3815.
7. (a) Schiess, P.; Heitzmann, M. *Angew. Chem. Int. Ed. Engl.* **1977**, *16*, 469. (b) Hart, H.; Hartlage, J. A. *J. Am. Chem. Soc.* **1967**, *89*, 6672. (c) Krohn, K.; Rieger, H.; Broser, E.; Shiess, P.; Chen, S.; Strubin, T. *Liebig Ann.Chem.* **1988**, 943. (d) Stevens, R. V.; Bisacchi, G. S. *J. Org. Chem.* **1982**, *47*, 2393.

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