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[4+2] Cycloadditions between 2-Pyrones and Benzyne. Application to the Synthesis of Binaphthyls.

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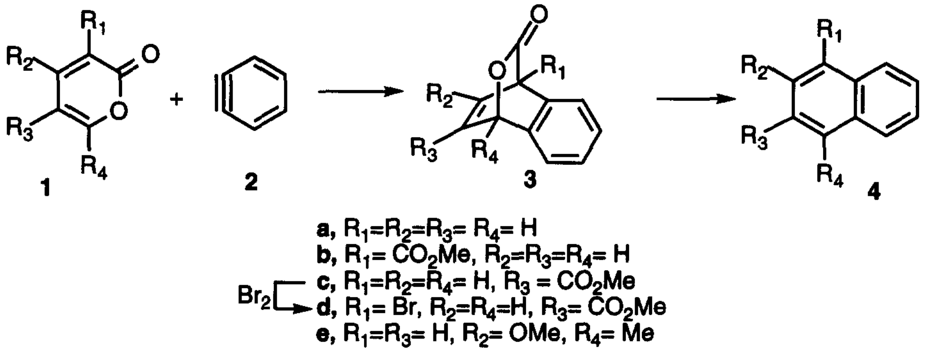
Abstract. Cycloaddition of benzyne to 2-pyrones affords the corresponding naphthalene derivatives, the intermediate bicyclic adduct not being detected. Benzopyrones do not react with benzyne under similar conditions probably because this would require the fused aromatic ring to lose aromaticity in the Diels-Alder transition state, which is therefore destabilized. 4-Bromo-2-naphthoic acid methyl ester (obtained by cycloaddition of benzyne to 3-bromo-5-carboxymethylpyran-2-one) can be transformed into 3,3'-dicarboxymethyl-1,1'-binaphthyl by Ni-mediated dimerization. © 1997 Elsevier Science Ltd.

2-Pyrones are valuable as synthetic building blocks owing to their capability to react with dienophiles in Diels-Alder reactions,[1] affording adducts with a bicyclic [2.2.2] structure which, though sometimes isolable, may undergo a retro Diels-Alder with loss of CO_2 reaction under the reaction conditions. This retro Diels-Alder reaction is usual when the dienophile is an alkyne, since it affords an aromatic ring. Thus 2-pyrone (**1a**) reacts with benzyne (**2**) to yield naphthalene (**4a**) in 36% yield - a reaction reported many years ago,[2] since when there have been only sporadic reports of similar reactions between 2-pyrones and arynes.[3]

In view of these precedents and the potential of this reaction for the synthesis of aromatic compounds, we decided to investigate the cycloaddition of benzyne to easily accessible 2-pyrones **1b-e**.[4] In each case, the procedure was as follows. The pyrone was dissolved in 1,2-dimethoxyethane and the solution was heated to reflux. Benzyne was generated *in situ* by thermal decomposition of benzenediazonium 2-carboxylate, which was added in portions to the pyrone solution.[5] When all the starting pyrone has been consumed (tlc monitoring), heating was stopped and the reaction mixture was worked up. Chromatographic purification of the crude products afforded the corresponding naphthalene **4** in good yields (see Table 1).[6]

In all cases the initial cycloadduct **3** underwent retro Diels-Alder reaction to afford the naphthalene **4**, this reaction being favoured by both enthalpic (aromatization of the substrate) and entropic (loss of CO_2) factors.



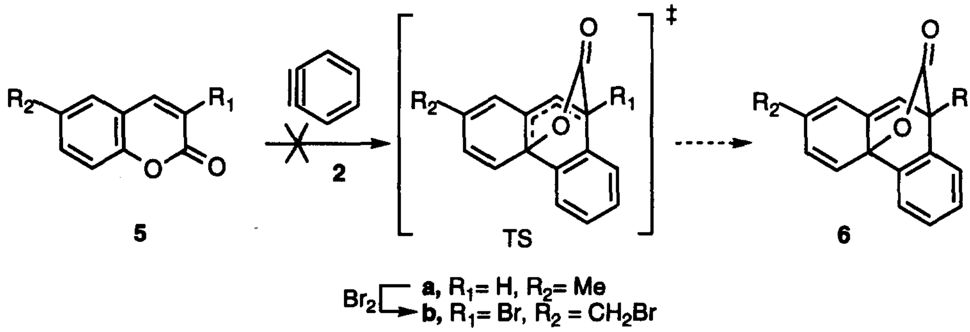
a, $R_1=R_2=R_3=R_4=H$
b, $R_1=CO_2Me$, $R_2=R_3=R_4=H$
c, $R_1=R_2=R_4=H$, $R_3=CO_2Me$
d, $R_1=Br$, $R_2=R_4=H$, $R_3=CO_2Me$
e, $R_1=R_3=H$, $R_2=OMe$, $R_4=Me$

Scheme 1

Table 1

Pyrone	Naphthalene	Yield (%)
1b	**4b**	71
1c	**4c**	80
1d	**4d**	93
1e	**4e**	59

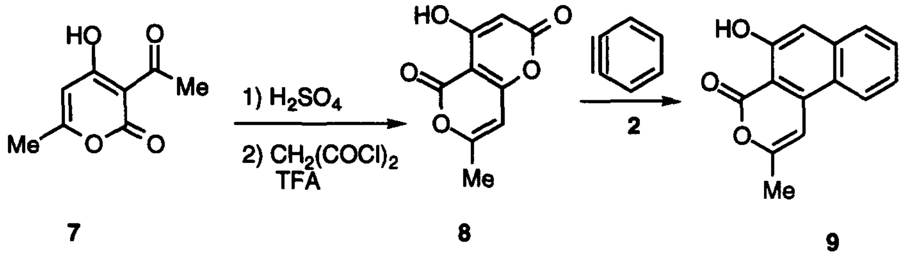
Encouraged by these results for the cycloaddition of simple pyrones, we next examined this reaction of two benzopyrones, the coumarins **5a** and **5b**,[7] under the same conditions. In both cases the starting compounds were recovered unchanged. We attribute the reluctance of these coumarins (as compared to 2-pyrones **1**) to react with benzyne to an increse in the energy of activation of the Diels-Alder reaction due to loss of the aromaticity of the benzene ring in the transition state (see TS, Scheme 2).



a, $R_1=H$, $R_2=Me$
b, $R_1=Br$, $R_2=CH_2Br$

Scheme 2

Next, we examined the possibility of converting a compound containing two pyrone units into a pyrene by a double Diels-Alder/retro Diels-Alder reaction sequence. To this end, benzyne was generated in the presence of compound **8**, which was prepared from dehydroacetic acid (**7**) by a published procedure.[8]



Scheme 3

The adduct obtained (75% yield) showed a molecular ion at m/z 226 (100%) in its mass spectrum, indicating that only one pyrone moiety had reacted with benzyne. This result and most of the NMR data were consistent with structures **9** and **10**, which result from reaction through the upper or lower pyrone, respectively (see orientation in Scheme 3).

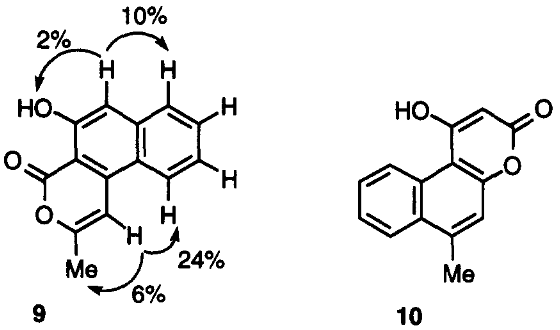


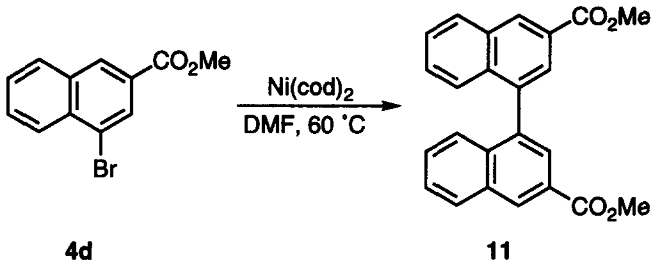
Figure 1

The results of nOe experiments carried out to determine the correct structure of the reaction product (Figure 1) led us to propose structure **9** for this compound.

As occurred for 2-pyrones **1**, no intermediate bicyclic adduct was detected. The fact that compound **9** did not react further with benzyne, neither as a diene through the second pyrone moiety nor as a nucleophile through the phenolic oxygen, may in the former case be attributed to the presence of a fused aromatic ring; and, in the latter case to a hydrogen-bonding interaction between the OH and the carbonyl group.

Finally, we recognized that naphthalenes prepared by the above reaction may be useful as precursors of binaphthyl derivatives, which are used as ligands in many important reactions. To examine the potential of this approach, we carried out the Ni-mediated dimerization of naphthalene **4d**, using Ni(cod)$_2$. Chromatographic purification of the mixtured obtained afforded unchanged **4d** (26%) and the binaphthyl derivative **11** (50%, 70% based on unrecovered **4d**; yields not optimized).

As far as we are aware, this combination of cycloaddition of benzyne to a pyrone and Ni-mediated dimerization of the resulting naphthalene is a new route to binaphthyls. Work is in progress to investigate the scope of this procedure and. in particular, to examine the possibility of effecting chiral induction at the coupling stage.



4d **11**

Scheme 4

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