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A NOVEL SYNTHESIS OF AROMATIC α-DIKETONES FROM ELECTRON TRANSFER REACTIONS OF AROMATIC ACIDS WITH EITHER LITHIUM 4,4′-DI-*T*-BUTYLBIPHENYL RADICAL ANION OR LITHIUM METAL

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Summary: Some aromatic α-diketones were directly synthesized in high yields from ultrasound-promoted reactions of the corresponding acids with excess lithium in dry THF. Use of a catalytic amount of 4,4′-di-*t*-butylbiphenyl (DBB) enhanced the coupling reaction rate.

We recently reported the unique reducing properties of lithium DBB radical anion in carbonyl systems such as xanthone[1] and aliphatic and aromatic carboxylic esters.[2] During an effort to broaden our study and to exploit this approach in other systems, we have discovered the remarkable unexpected behavior of aromatic acids. We report here our preliminary results of this study which describe a simple direct conversion of aromatic acids to α-diketones promoted by ultrasonic waves.

In a typical reaction, a mixture of 1 equiv of aromatic acid, 4 equiv of lithium and 0.1 equiv of DBB in dry THF was placed in a laboratory ultrasonic bath and sonicated at room temperature under nitrogen atmosphere for an extended period of time. The progress of the reaction was accompanied by color changes (white ⇒ yellow ⇒ brown ⇒ green-blue) and was monitored by TLC and GC/MS methods. Quenching with dilute hydrochloric acid and extraction with dichloromethane afforded as products the corresponding α-diketones in high yields (Table). The formation of corresponding bibenzyl derivatives should be noted (14% and 21% yields, respectively, in entries 4 and 5).[3] Repetition of the same experiment in the absence of DBB resulted in a slower reaction rate, but improved the reaction yield. It was also found that the rate of the reaction was greatly dependent on whether the reaction mixture was sonicated or mechanically stirred. When sonication was used the reaction was completed after several hours, whereas if mechanical stirring was employed, little or no reaction had occurred after the same time period. This is consistent with much evidence that the use of ultrasonic irradiation to promote organic syntheses is in a maturing and growing state and that the list of uses includes a variety of reactions.[4-7]

Our earlier studies with xanthone and aromatic and aliphatic esters had indicated a difference in the behavior of lithium and sodium metals.[1,2] Because of this, we sought also to study the reactions of carboxylic acids with sodium metal alone as well as in the presence of DBB. Treatment of benzoic acid or *p-t*-butylbenzoic acid with either sodium metal alone or with DBB indicated that the corresponding sodium carboxylate was formed, that it was stable for more than 5 days, and that it did not undergo a coupling reaction. This discrepancy may be attributed to two major factors. The first is the relationship between the identity of the alkali metal and the tendency to form ion pairs. In situations where all the cations form contact ion pairs, lithium binds most strongly with the anions.[8,9] The second factor is the reducing ability of lithium and DBB compared to sodium and DBB in THF. As a result of the reaction of sodium benzoate with lithium and DBB to give benzil in 83% yield and the lack of reaction of lithium benzoate in the presence of sodium and DBB (as determined from recovery of benzoic acid upon workup), we conclude that the first factor is not playing the predominant role in this reaction. We are currently investigating the importance of the second factor by experimental and theoretical methods.

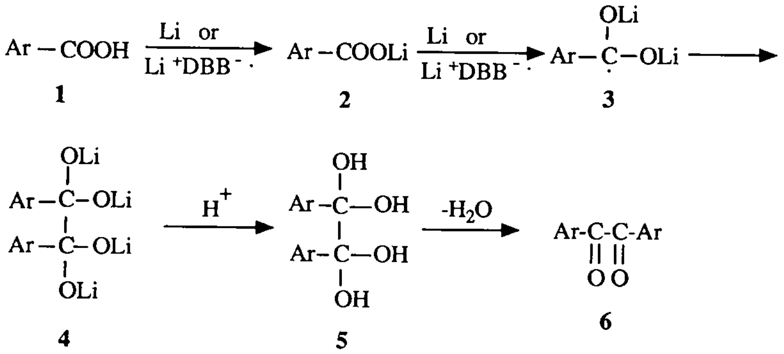
Table. Reductions of Aromatic Acids with Lithium or Lithium/DBB in THF

Entry	Substrate (**1**)	Yield of α-Diketone (**6**)[a,b,c] Li Time, h	Li %	Li/DBB[d] Time, h	Li/DBB[d] %
1	Benzoic Acid	170	27[c,f]	72	79
2	" "	>120	0[g]	>120	0[g]
3	*p*-Toluic Acid	54	91	48	85
4	*m*-Toluic Acid	28	74	17	61[h]
5	*p-t*-Butylbenzoic Acid	29	77	17	64[i]
6	" "	>120	0[g]	>120	0[g]
7	Sodium Benzoate	--	--	42	83[f]
8	Lithium Benzoate	--	--	48	0[g]

[a] The substrate (10 mmol) was sonicated with 40 mmol of Li in 50 mL of dry THF under N_2 for the indicated time. [b] Isolated yields except as indicated. [c] The products were identified by ^1H and ^{13}C NMR and GC/MS spectral methods. [d] One mmol of DBB was used. [e] 73% recovery of acid. [f] The yield was estimated from the ^1H NMR spectrum. [g] Sodium was used in place of lithium in this experiment. The substrate was recovered as the benzoic acid upon workup. [h] The corresponding bibenzyl product was also obtained in 14% yield. [i] The corresponding bibenzyl product was also obtained in 21% yield.

The results shown in the Table can be understood in terms of the mechanism depicted in the Scheme. The first step of the reaction is neutralization of the acid by lithium. In the second step, lithium transfers one electron to the carbonyl of salt **2** to form the dilithium radical **3**, which can then undergo dimerization to give **4**. The last step is hydrolysis of **4** to form the unstable intermediate **5** which then undergoes dehydration to the final product, α-diketone **6**.

In order to gain further insight into the modes of the reaction, 1 mmol of *p*-toluic acid was sonicated with 4 mmol of lithium in 1 mL of THF-d_8 and the reaction mixture was monitored by ^{1}H and ^{13}C NMR spectroscopy. The monitoring results indicated a gradual disappearance of the acid and the formation of a new product which was stable for more than one week. Its ^{13}C NMR spectrum did not show any signal in the region expected of a carbonyl carbon. Quenching with dilute hydrochloric acid led to the formation of the corresponding α-diketone. These results strongly suggest the intermediacy of a species such as **4**.[10]



Scheme

There are reports in the literature which describe the synthesis of α-diketones from oxidation of acyloins with copper(II) acetate[11] or bismuth(III) oxide[12] or by reductive coupling of acid chlorides promoted by reducing agents such as samarium(II) iodide,[13] lithium,[14] or pyrophoric lead.[15] The method reported here is novel since it shows for the first time that carboxylic acids themselves can be reduced to α-diketones by using lithium metal in THF. This is in contrast to what is observed in the reactions of carboxylic acids with lithium in amine solvents. Those conditions give mixtures of alcohols and aldehydes.[16,17]

The results presented so far may be summarized by saying that aromatic acids can be used in the direct preparation of aromatic α-diketones by an electron-transfer reaction using either lithium alone or lithium and DBB in THF as a solvent.

Further work is underway to extend the scope of this method, especially in the preparation of dissymmetric aromatic α-diketones.

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