

**ELECTRON TRANSFER REACTIONS OF ALIPHATIC ESTERS TO THE
CORRESPONDING ALIPHATIC KETONES BY LITHIUM 4,4'-DI-*t*-BUTYLBIPHENYL
RADICAL ANION**

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Summary: Sonication of some representative aliphatic esters with lithium in the presence of catalytic amounts of 4,4'-di-*t*-butylbiphenyl (DBB) in dry THF under N₂ afforded the corresponding aliphatic ketones in good yields. Monitoring studies by GC/MS and ¹H-NMR spectroscopy after quenching indicate the intermediacy of the corresponding β-ketoesters.

The reduction of aliphatic and aromatic esters by sodium and potassium metals is well known. The reactions may proceed through radical anion intermediates which, in the absence of hydroxylic solvents, give the corresponding acyloins.¹⁻⁶ Recently we have found that aromatic esters undergo facile dimerization and reductive elimination to bibenzyl derivatives when they are sonicated with lithium DBB radical anion in THF solvent.⁷ In an effort to define the scope and limitations of this method we have extended our studies to include aliphatic esters. We now report our preliminary findings that, in sharp contrast to the behavior of the aromatic esters, aliphatic esters with α hydrogens react with lithium in the presence of catalytic amounts of DBB to give good yields of the corresponding aliphatic ketones, whereas those without α hydrogens give only acyloins.

In a typical reaction, a mixture of 1 equiv of ester (1), 0.15 equiv of DBB and 3.5 equiv of lithium in 25 mL of dry THF was placed in an ultrasonic bath and held for an extended period of time. The progress of the reaction was monitored by GC/MS and ¹H-NMR spectral methods following quenching with saturated aqueous ammonium chloride solution and extraction with dichloromethane. The results show the slow intermediate formation of the corresponding β-ketoester (4)⁸ which then undergoes gradual decomposition to the corresponding ketone (11). Repetition of the experiment beginning with known samples of the corresponding β-ketoesters (synthesized by reacting aliphatic esters with potassium hydride)⁹ gave the expected ketones in good yields.¹⁰ The results of several experiments are summarized in the Table.

The mechanism shown in the Scheme is a reasonable explanation of these results. It is suggested that the first step of the reaction involves electron transfer from lithium DBB radical anion onto a molecule of ester 1 to give radical anion 2, as in the first step of acyloin condensations mediated by

sodium metal.⁶ This can then be followed by loss of hydrogen (either by abstraction as an atom or, following additional electron transfer, as hydride) to give lithium enolate **3**. In a following step the enolate may react with another molecule of ester **1** to form β -ketoester (**4**, Claisen-type condensation). In further steps, **4** then may react with lithium DBB radical anion as shown to finally give ketone **11** upon hydrolysis. Use of less than one equiv of lithium metal led to formation of β -ketoester with little evidence of further conversion to ketone. Preliminary results of MNDO calculations and labeling experiments support the mechanism (pathway **4-10**) shown in this Scheme.¹⁰

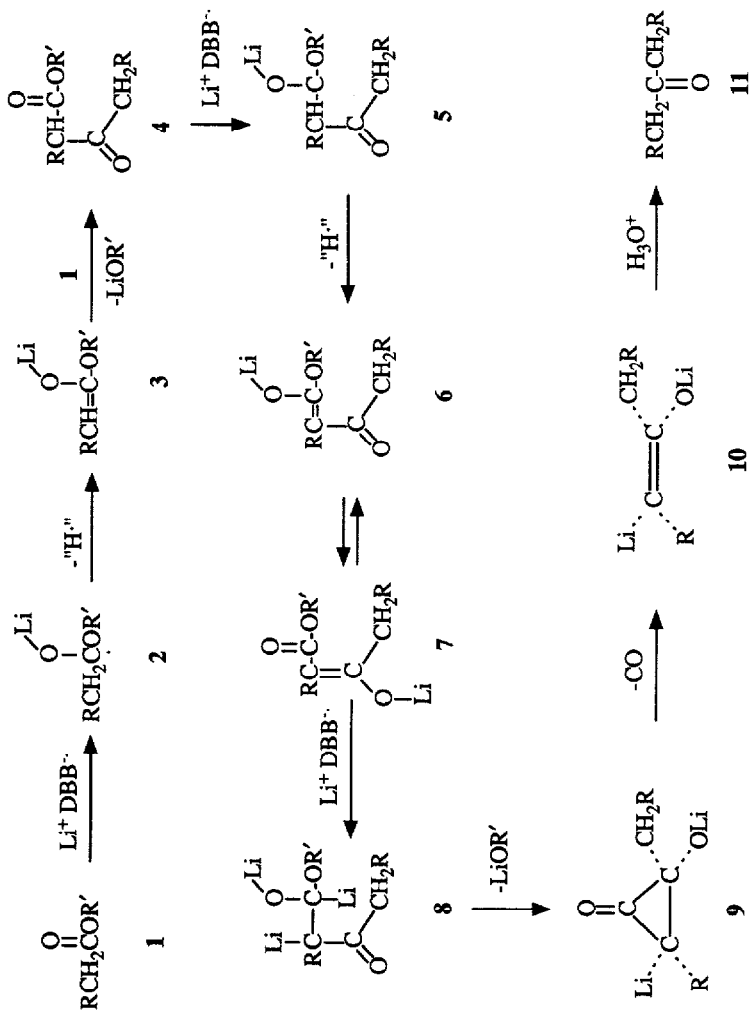
Table. Reductions of Aliphatic Esters with Metal(Li or Na)/DBB in THF

Substrate (1)	Metal	Time, h	% Yield of Products ^{a,b}	
			Acyloin	Ketone
Methyl caprylate	Li	60	0	55
	Li ^c	36	0	4 ^d
	Na	8	82	0
Ethyl phenylacetate	Li	60	0	73
	Li ^c	36	0	2 ^e
	Na	12	42	5
Methyl laurate	Li	60	0	48
	Na	12	95	0
Methyl 1-adamantyl-carboxylate	Li	60	68	0
Methyl α,γ -diheptyl-acetoacetic ester	Li	3.5	0	77
Ethyl α,γ -diphenyl-acetoacetic ester	Li	8	0	82
Methyl α,γ -diundecyl-acetoacetic ester	Li	3.5	0	68

^aThe substrate (10 mmol) was sonicated with 35 mmol of either Li or Na and 1.5 mmol of DBB in 25 mL of dry THF under N₂ for the indicated time. ^bIsolated yields except as indicated. ^c2:1 equiv ratio of ester to lithium metal. Analysis by ¹H NMR. ^dAlso formed 43% β -ketoester with 53% recovery of ester. ^eAlso formed 57% β -ketoester with 41% recovery of ester.

It is noteworthy that when aliphatic esters were treated with sodium and DBB under the same conditions which led to ketones when lithium was the metal, only the corresponding acyloins were obtained in high yields. Moreover, no reaction was observed when β -ketoester **4** was treated with sodium in the presence of DBB.¹¹ This indicates a unique behavior of lithium attributable to the formation of a more covalent bond (or tighter ion pair) between lithium and oxygen or carbon than in the case of sodium. Also consistent with the suggested mechanism is the observation that the aliphatic ester without α -hydrogen atoms, methyl 1-adamantylcarboxylate, reacts with lithium DBB radical anion to give only the corresponding acyloin.

In the presence of lithium metal, but in the absence of DBB, no reaction was observed. Thus



Scheme

DBB serves a key role as an electron-transfer reagent from the lithium metal onto the carbonyl compound.¹²⁻¹⁴

Although the conversion of β -ketoesters to ketones is well known and may be achieved by such means as either the classical sequence of alkaline hydrolysis, acidification, and thermal decarboxylation¹⁵ or by decarboxylation effected by heating in wet DMSO,¹⁶ the method reported here is interesting from a mechanistic point because it is based on unusual electron-transfer reactions. Further work is underway to explore the mechanism of this unique reaction¹⁰ and to determine its applicability for the synthesis of a number of interesting compounds.

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References and Notes

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