

ALKYLATIONS OF α -METHYL SUBSTITUTED β -DIKETONES THROUGH THEIR Cu(II) COMPLEXES.
PREPARATION OF STERICALLY CONGESTED β -DIKETONES.

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Summary: The copper(II) complexes of 3-methylpentane-2,4-dione and 2-methyl-1-phenylbutane-1,3-dione are good substrates for C-alkylation with several alkyl bromides including 1-bromoadamantane and 9-bromofluorene. Sterically congested β -diketones have been prepared.

Alkylation of β -diketones in the form of their nickel(II)¹ and cobalt(II) complexes offers some advantages over the most conventional methods based on the use of strongly basic media. Thus, cobalt(II) complexes of β -dicarbonyl compounds have been used in alkylations with easily dehydrohalogenable alkyl halides^{2a}, non active halides such as 1-bromoadamantane^{2b} and other special halides such as 9-bromofluorene.^{2c} These procedures have been particularly useful in the regioselective alkylation of methyl 3,5-dioxohexanoate, a β,δ -diketoester considered as a polyketide model³ and in the preparation of highly hindered β -diketones amenable to conformational analysis through a combined technique of Molecular Mechanics calculations and dipole moments determinations.⁴ Mechanistic studies on the cobalt mediated alkylations showed that two different mechanisms operate; one of them involves a non radical chain containing oxidative addition to Co(I) and reductive elimination from Co(III) steps and being initiated by inner sphere electron transfer induced by Co(II). This mechanism operates at high concentrations (>0.73M in cobalt)⁵.

Copper complexes are quite inert as alkylation substrates⁶ and have even been used for protection of intercarbonyl positions.^{3,7} However, two examples of alkylations through copper complexes can be found in the literature, one of them by reaction with benzhydryl bromide³ and the other with thiuronium salts which means a sulphur based leaving group.⁸

We report in this letter that the stable and easily prepared copper bis(3-methylpentane-2,4-dionato), 1,⁹ and copper bis(2-methyl-1-phenylbutane-1,3-dionato), 2,⁹ are efficiently alkylated upon treatment with several alkyl bromides in concentrated chloroform solutions at 100-115°C in closed reactors (See Table). The isolated diketones are disubstituted at the intercarbonyl position and the introduction of an 1-adamantyl group as for 3e and 4e gives products with two vicinal quaternary centers. Diketone 4c exhibited slow rotation around sigma bonds as evidenced by two sets of singlets in 1H-NMR spectroscopy at 2.44 and 2.17 and at 2.07 and 1.67. Upon standing the oily 4c solidifies and the 1H-NMR spectrum of the solid sample presents only signals at 2.07 and 1.67.

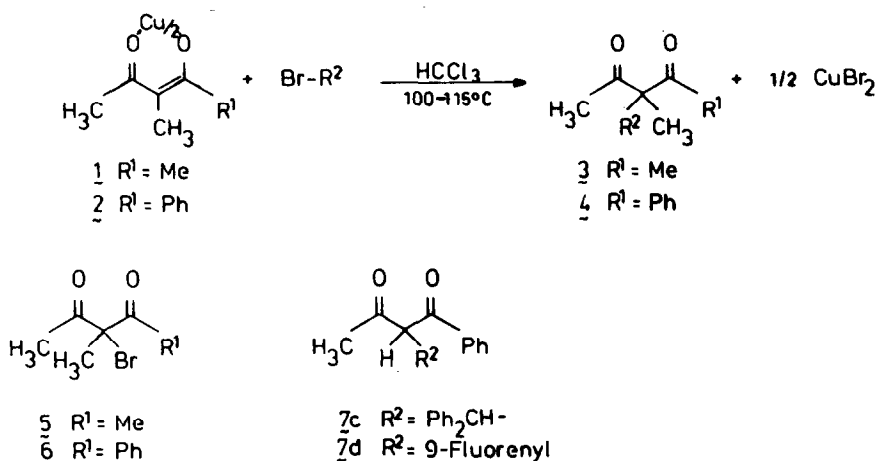


TABLE.- Preparation of products 3^a and 4^a from complexes 1 and 2 and alkyl bromides.

R ¹	R ²	[1] or [2] ^b	3 or 4 (%)	M.p. (or b.p.)	Other products (%)
Me	Ph-CH ₂ -	2.15M	3a (80)	(94-6°C/0.05mmHg)	
Me	CH ₂ =CH-CH ₂ -	0.86M	3b (88) ^c		
Me	Ph ₂ CH-	0.86M	3c (44)	81-2°C	5 (18), (Ph ₂ CH) ₂ O (17)
Me		0.86M	3d (65)	64-6°C	
Me		0.86M	3e (25)	88-90°C	Di-1-adamantyl ether (20) ^f
Ph	Ph-CH ₂ -	0.60M	4a (43)	103-4°C ^d	6 (12)
Ph	CH ₂ =CH-CH ₂ -	0.60M	4b (30)	(220-5°C/15mmHg) ^e	6 (10)
Ph	Ph ₂ CH-	0.60M	4c (76)	low melting solid	7c (11)
Ph		0.60M	4d (30)	136-8°C	6 (12), 7d (3)
Ph		0.60M	4e (1)	82-4°C	2-methyl-1-phenyl-1,3-butane-dione (59)

^aNew diketones 3 and 4 gave correct elemental analyses but 4e that was characterized spectroscopically. ^bIn terms of solvent volume. No correction has been made for the volume of added reagents. ^cAnalyzed as bis-2,4-dinitrophenylhydrazone, m.p. 228-30°C. ^dLit.¹⁰ m.p. 96.5-97°C. ^eLit.¹⁰ b.p. 95-105°C. ^fM.p. 177-81°C; lit.¹¹ m.p. 179-82°C.

Bromodiketones 5 and 6 were also formed probably by the action of copper(II) bromide, which has Br⁺ donor properties. The demethylated products 7c (m.p. 148-51°C; lit.¹² m.p. 149-50°C) and 7d (m.p. 104°C; lit.^{2c} m.p. 97-9°C) were not formed during the reaction but in the separation procedure which included chromatography through silica gel. This was shown by careful examination (NMR monitoring) of the reaction crudes and by an independent experiment in which a mixture of compound 4c (1.49g), silica gel (Chromagel 60 A CC from "SDS" company) (10g) and hexane/dichloromethane (1:1) (20 mL), left one week at room temperature afforded, after filtration and evaporation, a mixture of 4c (67%) and 7c (33%). The chemistry of these congested β -diketones will be published in the future.

Copper(II) complexes are more stable than those of cobalt(II) and this represents an experimental improvement when severe reaction conditions are required. Good alkylation reactions have been achieved under high concentration conditions in spite of the known low reactivity of copper(II) complexes.⁶ These experimental conditions, the type of alkylating agents and the general features of the reactions resemble the analogous reactions with Co(II) complexes when the chain mechanism is elicited. Co(II) and Cu(II) are radicaloid species (d⁷ and d⁹) and a similar chain mechanism through a Cu(I)-Cu(III) cycle can operate for the here reported reactions. Cu(III) species have been proposed as intermediates¹³ and have also isolated in stable form.¹⁴

A typical experimental procedure was as follows:

3-(1-Adamantyl)-3-methylpentane-2,4-dione, 3e.— A mixture of complex 1 (2.50g, 8.6 mmole), 1-bromoadamantane (3.71g, 17.2 mmole) and ethanol-free chloroform (10 mL) was heated at 100°C for 48 hours in a glass closed reactor. During that time a white precipitate was observed. The cooled mixture was partitioned between dichloromethane (200 mL) and 1N HCl (3 x 100mL). The organic layer was dried and evaporated and the residue chromatographed through a column of silica gel. The eluted products were di-(1-adamantyl) ether (m.p. 177-81 °C; lit¹¹ m.p. 179-82°C) and diketone 3a (1.10 g, 25%), m.p. 88-90°C (from dichloromethane/hexane): ir(KBr) 1715, 1689 cm⁻¹; 1H-NMR (CDCl₃) 2.14 (s, 6H), 1.59-2.07 (m, 15H), 1.43 (s, 3H); 13C-NMR (CDCl₃) 16.4, 28.8, 30.6, 36.8, 36.9, 39.7, 70.3, 208.4. Anal. Calcd. for C₁₆H₂₄O₂: C, 77.38; H, 9.74. Found: C, 77.17; H, 10.05.

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