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# ALKYLATION OF β-DIKETONES THROUGH THEIR Co(II), Co(III) AND Zn(II) COMPLEXES. 1-BROMOADAMANTANE AS ALKYLATING AGENT.

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Summary: α-(1-Adamantyl)-β-diketones are now accessible by the alkylation of Co(II) complexes of β-diketones with 1-bromoadamantane. The intermediacy of adamantyl cation is proposed. Co(II), Co(III) and Zn(II) complexes of pentane-2,4-dione react with alkyl halides precursors of stabilized carbenium ions, to give 3-alkylpentane-2,4-diones.

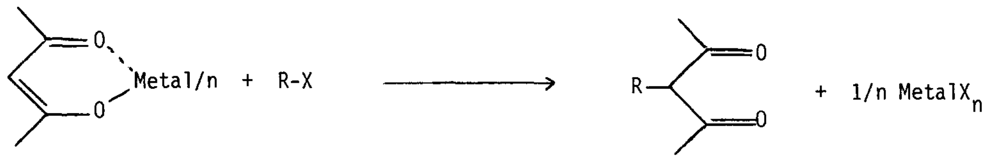
The α-alkylation of β-dicarbonyl compounds is an important C-C bond forming reaction[1]. With the aid of a base, the β-dicarbonyl compound is converted into the enolate anion which in turn undergoes $S_N2$ reactions with proper alkyl halides or tosilates.

Unfortunately only $S_N2$ active compounds such as methyl, allyl, benzyl and some other primary alkyl halides afford reasonable yields. Some of the problems usually found are: lack of regiospecificity (C vs. O alkylation), polyalkylation, and cleavage of the β-dicarbonyl compound.

Previously we have reported that alkylations of pentane-2,4-dione (acetylacetone, acacH) by activation through its cobalt(II) complex offer clear advantages over the classical methods for $S_N1$ active halides[2].

We wish to report here the broadening of the scope of this procedure to Co(III) and Zn(II) acetylacetonates, Co(II) β-dicarbonyl complexes, and to some alkyl halides of particular interest like 1-bromoadamantane. It is well known that 1-halogenosubstituted bridgehead compounds are very unreactive toward nucleophilic substitution reactions. Different adamantyl intermediates such as ion pairs[3], radical anions[4], or simply radicals[5] have been suggested in these reactions. Although 1-bromoadamantane and 1-iodoadamantane react with nucleophiles in good yields by the $S_{RN}1$ mechanism[6] they fail to alkylate carbanionic nucleophiles such as ketone enolate anions[7]. 1-Bromoadamantane α-alkylate carbonyl compounds via the corresponding silyl enol ethers in the presence of Lewis acids[8], in a reaction that has a slight resemblance with the one reported here. However, this procedure has not been applied to β-dicarbonyl compounds.

Table 1. Reactions of alkyl halides with several acetylacetonates[a].




| Alkyl halide | Reaction Product | Reaction yields (%)[b] starting from: Co(acac)$_2$ | Co(acac)$_3$ | Zn(acac)$_2$ |
|---|---|---|---|---|
| $\underline{p}$-$NO_2$-$C_6H_4CH_2Br$ | 3-$\underline{p}$-nitrobenzylpentane-2,4-dione | 6 | 0 | 0 |
| $C_6H_5CH_2Br$ | 3-benzylpentane-2,4-dione | 53[d] | 59 | 65 |
| | 3,3-dibenzylpentane-2,4-dione | 6[d] | 6 | 21 |
| $\underline{p}$-$CH_3O$-$C_6H_4CH_2Br$ | 3-$\underline{p}$-methoxybenzylpentane-2,4-dione | 88 | 77 | c |
| $C_6H_5CH(CH_3)Br$ | 3-(1-phenylethyl)pentane-2,4-dione | 75 | 58 | 61 |
| $(C_6H_5)_2CHBr$ | 3-benzhydrylpentane-2,4-dione | 97 | 96 | 87 |
| $(C_6H_5)_3CCl$ | 3-tritylpentane-2,4-dione[e] | 29[d] | c | 18 |
| 1-bromoadamantane | 3-(1-adamantyl)pentane-2,4-dione | 81 | c | 75 |

a) Standard conditions used : $CHCl_3$ refl., 17h. For trityl chloride the reaction time was reduced to 3h. $C_6H_5Cl$ refl. 24h were the conditions used in the reaction between $(acac)_2Co$ and 1-bromoadamantane. b) All previously known products were characterized by comparison with authentical samples. The new products 3-$\underline{p}$-methoxybenzylpentane-2,4-dione, m.p. 69-70°C, and 3-(1-adamantyl)pentane-2,4-dione, m.p. 54-5°C, showed the expected spectral characteristics and correct elemental analyses. c) Reaction not attempted. d) Results taken from ref. 2. e) Product not stable in the reaction conditions.

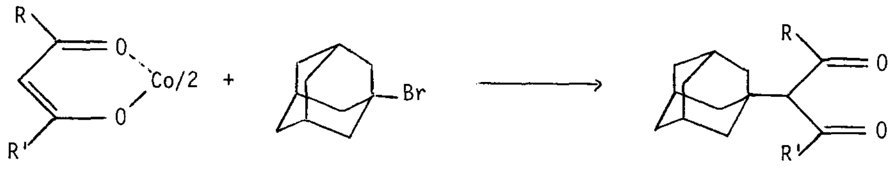
In Table 1, the yields of acetylacetone C-alkylation products obtained from the reactions of its Co(II), Co(III) and Zn(II) complexes with several alkyl halides are reported and compared. No O-alkylation products were detected. From this Table 1 we can conclude that our method is suitable for alkyl halides susceptible of positive charge stabilization (typical

$S_N1$ substrates) going the yields in those cases from reasonable to good.

It turned out that isopropyl, <u>sec</u>-butyl and cyclohexyl bromides failed to alkylate the Co(II), Co(III) and Zn(II) acetylacetone complexes in various conditions, probably due to the fact they are not $S_N1$ active enough[8]. The starting halide was recovered unaltered in those cases. In sharp contrast, aryl activated alkyl bromides (other than p-nitrobenzyl) underwent smooth reactions in refluxing chloroform. In spite of the known unreactivity of 1-bromoadamantane, 3-(1-adamantyl)acetylacetone was obtained in very good yield. Other tert-alkyl halides (like tert-butyl bromide) failed to alkylate the acetylacetone complexes in preparative yields. The starting halide was not recovered in these cases pointing out that elimination probably becomes competitive when steric hindrance slows down the substitution reaction.

Although bridgehead compounds are unreactive toward nucleophilic substitution reactions we have been able to alkylate several β-dicarbonyl compounds with 1-bromoadamantane through their Co(II) complexes. Preparative useful yields were obtained. Table 2 shows these results, proving our method general for a broad spectrum of β-dicarbonyl compounds.

Table 2. Reactions of Co(II) β-dicarbonyl complexes[a] with 1-bromoadamantane.[b]




| R | R' | Yield (%) | Product[c] m.p. (°C) |
|---|---|---|---|
| $CH_3$ | $CH_3$ | 81 | 54-5 |
| Ph | $CH_3$ | 89 | 70-1 |
| Ph | Ph | 80 | 210-1 |
| OEt | $CH_3$ | 38 | oil |

a) All the starting complexes were prepared following standard literature methods[9-11].
b) Standard conditions were: $C_6H_5Cl$ refl.,24h. c) All the products gave correct elemental analyses and exhibited spectroscopic behavior as expected.

In Table 1 we can also observe the very similar results obtained with the three complexes studied. This fact is not so evident from electronic considerations since $Co(acac)_3$ and $Zn(acac)_2$ are isoelectronic and coordinatively saturated and therefore electronically different from $Co(acac)_2$. $Co(acac)_3$ and $Zn(acac)_2$ can not act as Lewis acids (activating the halide) without loosing at least one ligand.

Some other important features of these reactions were studied using α-phenylethyl bromide as a more representative halide. To prove them general, $Co(acac)_2$ and $Co(acac)_3$ were used as substrates. Reactions in the presence of galvinoxyl (powerful radical scavenger) showed no effect on the yields suggesting that electron-transfer and radical processes were not operative in our reactions. This test was also carried out for the reaction between 1-bromoadamantane and $Co(acac)_2$ with the same result. Reactions in the presence of $K_2CO_3$ showed a dramatic drop of yields, the starting materials being recovered. This suggest the necessity of a trace of acid (normaly associate to our halides) to activate the metallic complex and trigger the reaction. Reactions in the presence of anhydrous $CoCl_2$ worked at room temperature indicating that $CoCl_2$ was in some way a catalyst and that our reactions could be autocatalyzed. Both substrates, $Co(acac)_2$ and $Co(acac)_3$ gave similar results thus confirming the conclusion extracted from Table1, suggesting a similar pathway (carbenium ion process) in our reactions. The necessity of a trace of acid can be related with partial chelate cleavage that would leave free some coordination positions needed to activate the alkyl halide.

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