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Reactions of 4-Acyl-2-phenyl-1,3,4-oxadiazoline-5-thiones with Alcohols in the Presence of Metal Ions

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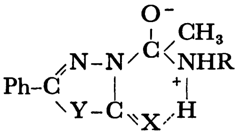
Synopsis. 4-Acetyl- and 4-benzoyl-2-phenyl-1,3,4-oxadiazoline-5-thiones reacted with alcohols in the presence of metal ions to give the corresponding esters in good yields.

It is known that metal ions promote some reactions, such as the hydrolysis of α-amino acid esters[1,2] and 8-acyloxy-quinolines,[3,4] the aminolysis of thiol esters,[5] and the alcoholysis of 8-acyloxyquinolines[6] and *S*-(2-pyridyl) thio carboxylates.[7]

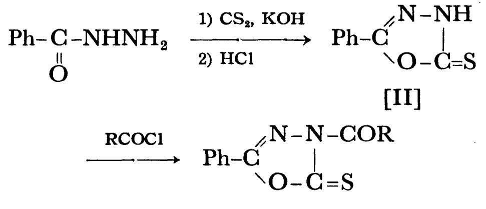


[I]

X=O, Y=O or S
X=S, Y=O or S

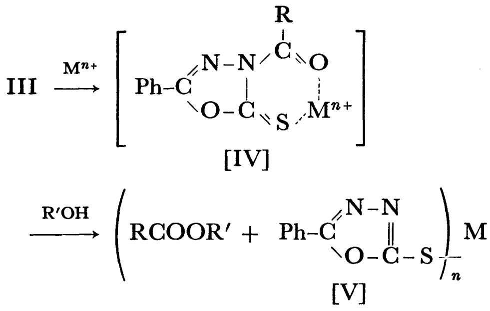
We have reported that 4-acetyl-2-phenyl-1,3,4-oxa-(thia)diazoline-5-ones(thiones) are 10^2—10^7 times more reactive than *p*-nitrophenyl acetate in the aminolysis by cyclohexylamine, unusually rapid aminolysis being due to the intramolecular base catalyzed reactions as illustrated in I.[8] However, the acetyl derivatives scarcely react with alcohols even under refluxing for several hours. This paper describes the reactions of 4-acyl-2-phenyl-1,3,4-oxadiazoline-5-thiones(IIIa, b) with alcohols in the presence of various metal ions, and with phenylmagnesium bromide.

2-Phenyl-1,3,4-oxadiazoline-5-thione(II), its 4-acetyl compound(IIIa) (yield 78%, mp 115—116 °C), and 4-benzoyl-2-phenyl-1,3,4-oxadiazoline-5-thione(IIIb) (yield 92%, mp 134.5—136 °C) were prepared by the method reported.[8]



[IIIa]: R=CH$_3$ [IIIb]: R=Ph

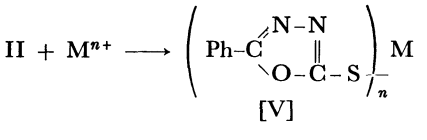
When 4-acyl-2-phenyl-1,3,4-oxadiazoline-5-thiones(III) is coordinated with metal ions as shown in IV, it might be subjected to nucleophilic attack on carbonyl carbon atom, as the consequence of activation of carbonyl group by such coordination. This reaction would also be remarkably accelerated if the final product (V) is mercaptide which is an excellent leaving group because of its high stability.



At first, the reactions of 2-phenyl-1,3,4-oxadiazoline-5-thione(II) with various metal ions were examined. Ag$^+$, Cu^{2+}, Hg^{2+}, and Pb^{2+} formed mercaptides (V) with II, but metal ions, such as Sn^{4+}, Mg^{2+}, Zn^{2+}, and Co^{2+} gave no mercaptides in methanol or acetonitrile at room temperature. The results are given in Table 1. The mercaptides obtained were confirmed by IR spectra and elemental analyses.

Table 1. Mercaptide formation of II with metal ions

Metal ions	Ag$^+$	Cu^{2+}	Hg^{2+}	Pb^{2+}
n	1	2	2	2
Yield (%)	99	98	91	95



The reactions of III with alcohols in the presence of metal ions, which form mercaptides with II, were carried out at room temperature for 15 h. A white (mercury(II) salt) precipitate and a dark grey (silver salt) one were formed in a few minutes. In the case of copper(II) chloride, the reaction mixture was heterogeneous during the course of reaction because of the

Table 2. Reactions of III with alcohols in the presence of metal ions[a)]

Compound	R′	Solvent	Metal salt	Yields of ester (%)[b)]
IIIa	PhCH$_2$	CH$_3$CN	none	0
〃	〃	〃	CuCl$_2$	100
〃	〃	Acetone	〃	92
〃	〃	CH$_3$CN	AgNO$_3$	65
〃	〃	〃	HgCl$_2$	54
〃	〃	〃	AgClO$_4$	41
〃	〃	〃	HgCl$_2$[c)]	36
〃	〃	〃	Pb(NO$_3$)$_2$	0
〃	C$_6$H$_{13}$	〃	AgNO$_3$	70
IIIb	PhCH$_2$	〃	CuCl$_2$	40
〃	C$_6$H$_{13}$	〃	〃	55

a) Equimolar reaction; reagents 4 mmol; solvent 30 ml; room temp, 15 h. b) Determined by NMR spectrum. c) Half molar of HgCl$_2$ used.

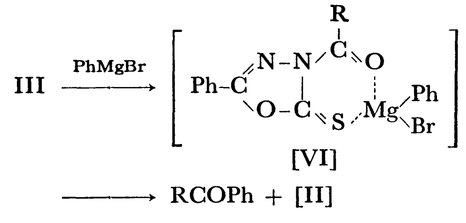
TABLE 3. REACTIONS OF IIIa WITH BENZYL ALCOHOL IN THE PRESENCE OF METAL IONS[a)]

Solvent	Metal salt	Yields of ester (%)[b)]
THF	Bu_2SnCl_2	75
CH_2Cl_2	$SnCl_4$	70
CH_3CN	$Mg(ClO_4)_2$	57
Acetone	$ZnCl_2$	14
CH_3CN	$CoCl_2$	6

a) Equimolar reaction; reagents 4 mmol; solvent 30 ml; room temp, 15 h. b) Determined by NMR spectrum.

low solubility of copper(II) chloride. As shown in Table 2, all the metal ions, except Pb^{2+}, capable of mercaptide formation, are effective for the acceleration of these reactions, copper(II) chloride being the most remarkable. Lead nitrate did not promote the reaction since it is insoluble in acetonitrile. The precipitates were confirmed to be mercaptides consisting of 1 : 1 molar ratio of II and metal ions by elemental analyses and IR spectra. It was observed that the reactions of IIIa with benzyl alcohol in the presence of metal ions, such as Sn^{4+}, Mg^{2+}, Zn^{2+}, and Co^{2+} which can not form mercaptides with II proceed homogeneously. The results given in Table 3 indicate that tin(IV) salt is very effective for activation of IIIa. Thus, in the deacylation of III with alcohols, the coordination effect of some metal ions on acyl function might be much more important than the increasing stability of the leaving group. If the coordination (IV) assumed above is strong, the shift of C=O and C=S absorption bands of IIIa would be observed in IR spectra. However, no shift of the absorption bands was noted even in the solution of IIIa and Bu_2SnCl_2 or $Mg(ClO_4)_2$. The results indicate that even the weak interaction which can not be observed in IR spectra is also effective for promotion of these reactions.

We have investigated the reactions of III with phenylmagnesium bromide. III was allowed to react with equimolar amount of phenylmagnesium bromide in THF at *ca.* −20 °C for 4 h followed by hydrolysis to give the desired ketones. Thus, acetophenone and benzophenone were obtained from IIIa and IIIb in 76 and 78% yields, respectively. This is compatible with the above results.



Experimental

Mercaptides Formation of II with Metal Ions. A mixture of II (0.72 g, 4 mmol) and 4 mmol of metal ions in acetonitrile (30 ml) was stirred for 4 h at room temperature. The mercaptides obtained were filtrated and washed with dry acetonitrile three times, and dried at reduced pressure. The composition of mercaptides (Table 1) was determined by elemental analysis.

Reactions of III with Alcohols in the Presence of Metal Ions. Typical Procedure: A mixture of 0.88 g (4 mmol) of IIIa, 0.43 g (4 mmol) of benzyl alcohol, and 0.59 g (4 mmol) of copper(II) chloride in acetonitrile was stirred for 15 h at room temperature. The reaction mixture was poured into water, and the solution was extracted with ether. The extract was dried over anhydrous magnesium sulfate. After the solvent had been removed in a vacuum, the residue was distilled to afford 0.69 g of benzyl acetate quantitatively.

Reactions of III with Phenylmagnesium Bromide. Typical Procedure: To a solution of IIIa (1.76 g, 8 mmol) in dry THF (20 ml) was added a solution of phenylmagnesium bromide (1.45 g, 8 mmol) in dry THF (20 ml) over 30 min at −20 °C. After the mixture had been stirred at −20 °C for 4 h then at 25 °C for the same period, the reaction mixture was poured into water. The solution was extracted with ether, and the extract was dried over anhydrous magnesium sulfate. After removal of the solvent, the residue was distilled in a vacuum to afford 0.73 g (76%) of acetophenone.

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