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THE USE OF 8-ACYLOXYQUINOLINE METAL COMPLEX IN THE ACYLATION REACTION AND THE KETONE SYNTHESIS. THE METAL ION PROMOTED REACTIONS OF 8-ACYLOXYQUINOLINE I.

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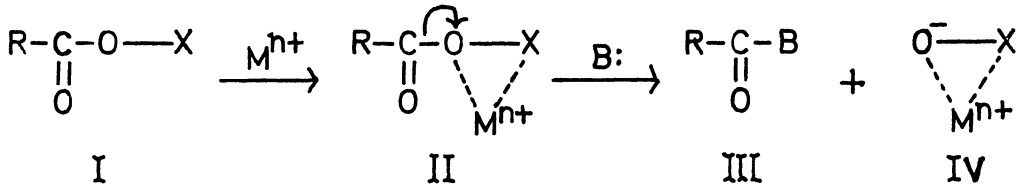
8-Acyloxyquinoline metal complexes were discussed of their possible use as an active acylating agent. In this connection, the reaction of 8-acyloxyquinolines with the Grignard reagent was found to be useful as a novel synthetic method for ketones.

Metal ions have been shown to promote a large number of organic reactions, including the hydrolysis of α-amino acid esters,[1] glycine amide,[2] N-carbo-(8-quinoloyl)-derivatives of amines,[3] and acylguanidine,[4] or the hydration of carbonitriles,[5] the decarboxylation[6] and the aldol condensation.[7]

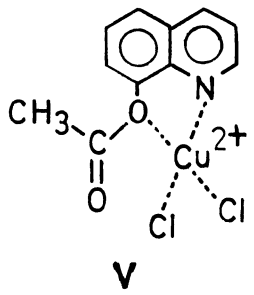
When a carboxylic acid derivative I is capable of such coordination with a metal ion both at the etheral oxygen atom and certain suitably positioned donor atom in a group X, forming a complex compound II, it appears to be relatively more susceptible to nucleophilic attack (nucleophile, B:) on the carbonyl carbon as the result of a considerable shift of electron density toward the metal ion resulting in cleavage of carbon-oxygen bond to form an acylated species III and an another chelated complex IV. This nucleophilic reaction will be remarkably accelerated, if the final chelated complex IV is a very stable one, because it can act as an excellent leaving group.



I II III IV

Now we wish to report one of such metal ion promoted reactions. We have chosen 8-acyloxyquinoline for these purposes,because its easy hydrolysis promoted by metal ions has been reported.[3] 8-Acetoxyquinoline affords a Cu(II)-complex V, $C_{11}H_9O_2N.CuCl_2$, m.p. above 280°, IR(KBr): 1790, 1180, 1160 cm^{-1}, as a green precipitate with cupric chloride in absolute tetrahydrofuran. The structure V is elucidated from its elementary analysis and the IR spectrum which shows that the cupric ion is chelated with phenolic and not with carbonyl oxygen atom. The infrared spectra of solid metal-α-amino acid ester complexes show the decreases in the carbonyl stretching frequency compared to the free esters, indicating the formation

of metal-carbonyl oxygen bonding.[8] However the spectrum of V shows increase in the carbonyl streching frequency and decrease in the ester bands compared to 8-acetoxyquinoline; IR(KBr): 1750, 1200(broad) cm^{-1}. Therefore, the five-membered chelate structure V is reasonable. In this complex the carbonyl carbon atom appears to be more reactive to a nucleophilic reagent owing to both the polarization of the carbon-oxygen bond induced by the chelation and the well known large stability of the Cu-complex of 8-hydroxyquinolinate anion. This reagent has the ability not only to act as an acylating agent as shown in table 1, but also to cleave some ether under a mild acidic condition (tetrahydrofuran ⟶ 4-chlorobutyl acetate). Further works in these areas will be reported in detail at a later date.

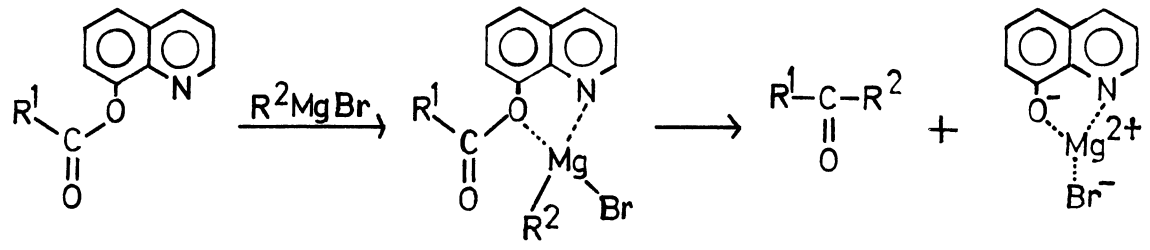


V

Table 1. The use of the Cu-complex V as an acylating agent

Substrate	Solvent	Temperature, Time	Product	Yield(%)
$C_6H_5NH_2$	THF	room temp. 2 days	$CH_3CONHC_6H_5$	83
$C_6H_5CH_2OH$	THF	43° 4 hr. and reflux one hour		
			$CH_3CO_2CH_2C_6H_5$	50
C_6H_5OH	benzene	reflux 2 hr.	$CH_3CO_2C_6H_5$	52

We furthermore considered the reaction of a 8-acyloxyquinoline metal complex which bears an active nucleophilic group as one of its ligands. The metal ion in such a complex will play a role of a match-maker for a reaction of the activated acyl group with the nucleophile R^2. This presumably assists the reaction by making the entropy of activation more positive. These considerations led us to study the reaction of 8-acyloxyquinolines with the Grignard reagents. The Grignard reagents are not so ionic as metal ions, but it seems to be possible to coordinate with 8-acyloxyquinolines, affording a similar type complex VI with two activated ligands so suitably located that the reaction proceeds smoothly.



VI

Each Grignard reagent, prepared carefully from 4.0 mM of alkyl or aryl bromide and 4.0 mg atom of magnesium in 10 ml absolute ether under oxygen free nitrogen, was added slowly with vigorous stirring to a solution of 3.6 mM of 8-acyloxyquinoline in 10 ml of absolute ether or 15 ml of absolute benzene at 0° during 30 minutes. A white precipitate immediately formed. The stirring was continued at the same temperature for one hour and then at room temperature for more one hour. The precipitate of the Mg-complex of 8-hydroxyquinolinate anion was removed by filtration. The filtrate was washed with 2N HCl and water, and dried

over sodium sulfate. After removal of the solvent, the products were purified by distillation, crystallisation or GLC. In the cases that ether was used as the solvent, decomposition of the precipitate with 6N HCl gave an additional amount of ketone. We obtained ketones in fairly good yields as ahown in table 2.

Table 2. The reaction of 8-acyloxyquinoline with the Grignard reagents

R^1	R^2	Solvent	Ketone	Yield (%)	
CH_3	C_6H_5	a	$CH_3COC_6H_5$	64	
CH_3	$n\text{-}C_6H_{13}$	a	$CH_3COC_6H_{13}$	90	
CH_3	$C_6H_5CH_2CH_2$	a	$CH_3COCH_2CH_2C_6H_5$	98	
CH_3	$C_6H_5CH_2$	a	$CH_3COCH_2C_6H_5$	0	u)
C_6H_5	C_2H_5	b	$C_6H_5COC_2H_5$	56	v)
		c		61	w)
C_6H_5	C_6H_5	b	$C_6H_5COC_6H_5$	54	x)
		c		82	y)
C_6H_5	$n\text{-}C_6H_{13}$	b	$C_6H_5COC_6H_{13}$	50	z)
		c		75	
C_6H_5	$C_6H_5CH_2CH_2$	b	$C_6H_5COCH_2CH_2C_6H_5$	71	
		c		82	

a: Ether, b: ether and tetrahydrofuran, c: ether and benzene.
The yields of by-products; u) $CH_3C(OCOCH_3)(CH_2C_6H_5)_2$ quantitatively, derived from the further attack of the Grignard reagent to the ketone produced, followed by acetylation by 8-acetoxyquinoline,.
v) $C_6H_5C(OH)(C_2H_5)_2$ 24%, w) $C_6H_5C(OH)(C_2H_5)_2$ 7%, x) $(C_6H_5)_3COH$ 11%, y) $(C_6H_5)_3COH$ 9%, z) $C_6H_5CH(OCOC_6H_5)C_6H_{13}$ 20%

Generally, ketones are prepared from the Grignard reagents and acyl halides, by the use of low temperatures, inverse addition, excess acyl halides, etc. But the yields are usually low, because of the tendency of the Grignard reagent to undergo addition to the carbonyl group of the ketone produced to form tertiary alcohols.[9] In the present case, the yields of tertiary alcohols are generally poor, except in benzylmagnesium bromide which gave quantitatively the acetate of dibenzyl methyl carbinol. Since almost all of the Grignard reagents are probably consumed by the immediate formation of the chelate-complex intermediate VI, the chance of further reaction of the ketone produced to a tertiary alcohol is largely reduced.

The similar type of reactions with other organometallic compounds, or with other chelated compounds seems to be very promising for organic synthesis. Further studies along these lines are in progress.

Footnotes and References

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