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REACTION OF ENOL ACETATE WITH ACETAL AND CARBONYL COMPOUND IN THE PRESENCE OF LEWIS ACID

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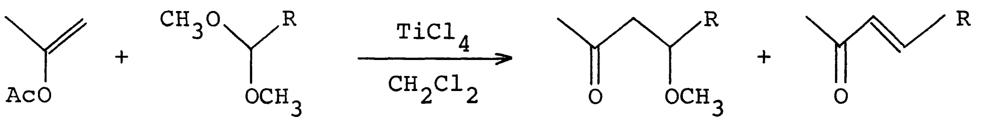
It was found that, in the presence of Lewis acid such as $TiCl_4$, $AlCl_3$, $SnCl_4$, $ZnCl_2$, and $BF_3 \cdot O(C_2H_5)_2$, enol acetate reacts with various acetals and benzaldehyde to afford the corresponding aldol-type addition products in good yields.

In the course of our continuing studies[1] on the exploration of useful synthetic reactions by using $TiCl_4$, it was found that enol acetate reacts easily with acetals and benzaldehyde to give the corresponding aldol-type addition products in good yields.[2]

In a typical procedure, to a mixture of isopropenyl acetate (2.8 mmol) and β-phenylpropionaldehyde dimethyl acetal (2.5 mmol) in 10 ml of dichloromethane was added a solution of $TiCl_4$ (2.5 mmol) in 5 ml of dichloromethane within 10 min at -10°C under an argon atmosphere, and this homogeneous reaction mixture was stirred for additional 2 hr at -10°C. After washing off the titanium compound by aqueous alkaline solution, 4-methoxy-6-phenylhexan-2-one and 6-phenyl-3-hexen-2-one were isolated in 89% and 1% yields, respectively, by silica gel column chromatography.

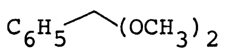
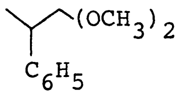
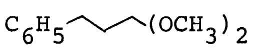
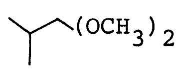
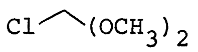
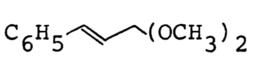
In a similar manner, the aldol-type addition reactions of isopropenyl acetate with various acetals, derived from benzaldehyde, α-phenylpropionaldehyde, isobutyraldehyde, chloroacetaldehyde and cinnamaldehyde, were carried out and the results are listed in the table.

This reaction can be explained by assuming an initial formation of $TiCl_4$-acetal complex (3), which in turn immediately reacts with isopropenyl acetate to



(1) (2)

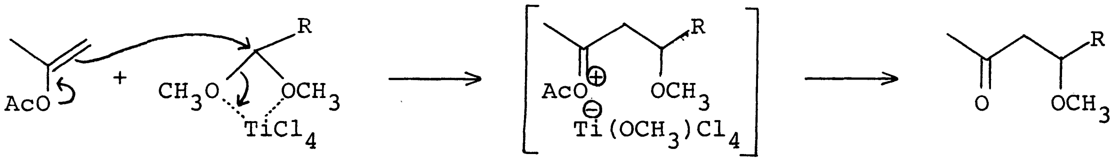
Table 1. The Reaction of Various Acetals with Isopropenyl Acetate

Acetal	Temp. (°C)	Time (hr)	Product, Yield (%) (1)	(2)
	-78	1	81	5*
	-10	2	79	6
	-10	2	89	1
	-10	2	92	0
	0	5	41	0
	-40	1	0	65**

* 4-Chloro-4-phenylbutan-2-one was also isolated in 14% yield as the minor product.

** According to the tlc of the reaction mixture, 4-methoxy-6-phenyl-5-hexen-2-one was a major product, but only 6-phenyl-3,5-hexadien-2-one was isolated by the usual work-up.

give the addition product, i.e., β-alkoxyketone (1).



(3) (1)

Next, it was found that isopropenyl acetate similarly reacts with benzaldehyde in the presence of various Lewis acids such as $TiCl_4$, $AlCl_3$, $SnCl_4$, $BF_3 \cdot O(C_2H_5)_2$, and $ZnCl_2$ to afford the corresponding aldol-type addition products in good yields.

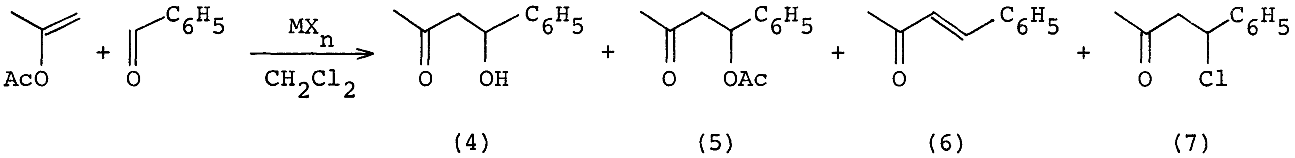
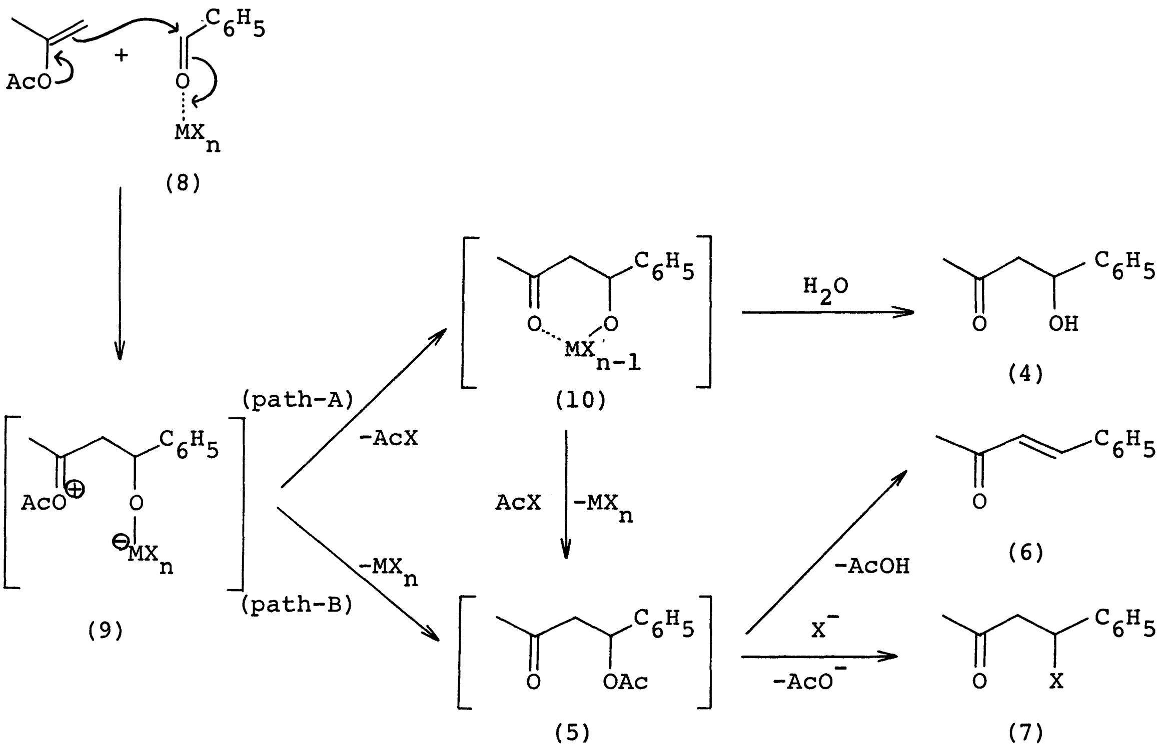


Table 2. The Reaction of Benzaldehyde with Isopropenyl Acetate in the Presence of Various Metal Halides

MX_n	Temp. (°C)	Time (hr)	Product, Yield (%)				
			(4)	(5)	(6)	(7)	(4+5+6+7)
$TiCl_4$	r.t.	0.5	0	3	14	74	91
	-10	5	65	16	6	5	92
$AlCl_3$	r.t.	3	0	0	27	55	82
	-10	5	0	57	11	16	84
$SnCl_4$	r.t.	5	0	23	23	39	85
	-10	5	0	38	5	50	93
$BF_3 \cdot O(C_2H_5)_2$	r.t.	5	0	51	30	—	81
	-10	5	0	71	9	—	80
$ZnCl_2$	r.t.	72	0	58	15	0	73

Based on these results, the reaction of benzaldehyde with isopropenyl acetate can be similarly explained by assuming an initial formation of the metal halide (Lewis acid)-aldehyde complex (8), which immediately affords an addition compound (9) by the further reaction with isopropenyl acetate. There are two alternative pathways of decomposition of (9) according to the nature of the Lewis acids used; namely, (path-A) the formation of metal alkoxide (10) accompanying the elimination of acetyl halide; and/or (path-B) the formation of β-acetoxyketone (5) with the elimination of metal halide. When the reaction is carried out in the presence of $TiCl_4$ at -10°C, the alkoxide (10) is kept stable in the reaction mixture to afford the corresponding β-hydroxyketone (4) on hydrolysis (path-A), and at an elevated temperature, (10) is converted to (5), which is further led to the formation of α,β-unsaturated ketone (6) and β-chloroketone (7: X=Cl) as sketched on next page. On the other hand, in the cases of the other Lewis acids, the reactions proceed only through the path B to yield (5), probably because of the facile cleavage of the metal-oxygen bond as compared with the titanium-oxygen bond.



It is noted that isopropenyl acetate is a unique alkylating reagent for various acetals and benzaldehyde in the presence of various Lewis acids. Further reactions of other enol esters with acetals, carbonyl compounds and other electrophiles are now in progress.

REFERENCES

1) T. Mukaiyama, K. Narasaka, and K. Banno, Chem. Lett., 1011 (1973); T. Mukaiyama and M. Hayashi, ibid., 15 (1974).

2) Up to this time, there has been no report about the aldol-type addition reaction of enol ester with acetal or carbonyl compound under an acidic condition except in case of the reaction of vinyl acetate and chloromethyl alkyl ether in the presence of $ZnCl_2$. S. A. Vartanyan, Sh. A. Gevorkyan, and E. V. Dangyan, Izv. Akad. Nauk Arm. SSR, Khim. Nauki, 18, 415 (1965) [Chem. Abstr., 63, 17886 (1965).].

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