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THE REACTION OF ENOL ETHERS WITH ALDEHYDES PROMOTED BY TITANIUM TETRAISOPROPOXIDE AND TITANIUM TETRACHLORIDE

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The equimolar reactions of enol ethers with various aldehydes in the coexistence of $Ti(OPr\text{-}i)_4$ and $TiCl_4$ afford 3-isopropoxy acetals or α,β-unsaturated carbonyl compounds in good yields under mild conditions.

As a part of our continuing studies[1)] on the $TiCl_4$-promoted aldol reaction of enols, such as silyl enol ether, enol acetate and diketene, with carbonyl compounds, the reactions of enol ethers with aldehydes were tried. Several investigators[2-4)] reported that, in the presence of $BF_3 \cdot OEt_2$, enol ether reacts with more than two molar amounts of aldehyde to afford 1,3-dioxane derivative, which is in turn refluxed in dil.HCl for a several hours to give α,β-unsaturated aldehyde in moderate yield. In this paper, we wish to report the preparation of cross aldol by an equimolar reaction of enol ether and aldehyde in the presence of titanium compounds under mild conditions.

After a number of investigations, it was found that the reaction of enol ether with aldehyde did not afford aldol when $TiCl_4$ or $Ti(OPr\text{-}i)_4$ was used as an activator. On the other hand, only when $Ti(OPr\text{-}i)_4$ and $TiCl_4$ were used together, enol ether reacted with aldehyde to give cross aldol, i.e., 3-isopropoxy acetal[5)] or α,β-unsaturated carbonyl compound in good yield as shown in the following examples [A] and [B].

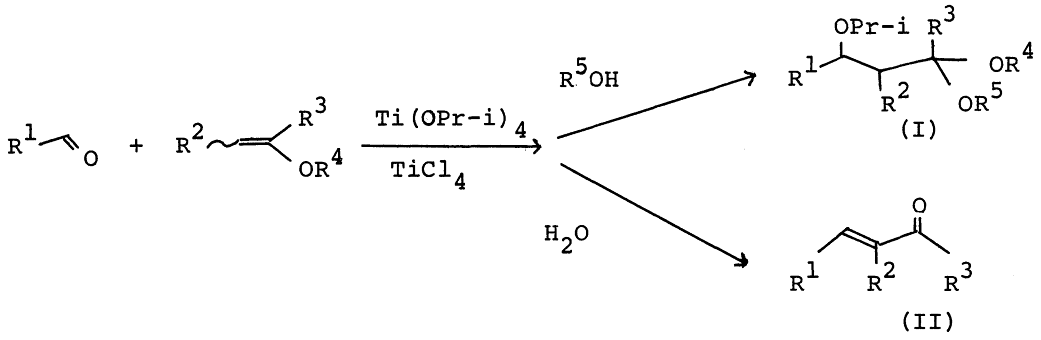
[A]: To a stirred solution of aldehyde (2.0 mmol) in dichloromethane (10 ml) was added $Ti(OPr\text{-}i)_4$ (2.0 mmol) at the temperature indicated in the Table under an argon atmosphere, and the solution was stirred for a few minutes. After adding $TiCl_4$ (2.0 mmol), a solution of enol ether (2.2 mmol) in dichloromethane (10 ml) was added dropwise within 30 min at the same temperature, and the mixture was stirred for additional half an hour to 2 hr, followed by the addition of alcohol (2 ml). After stirring for 3 hr at room temperature, the reaction mixture was quenched with sat. $NaHCO_3$ solution (100 ml), and titanium compound was filtered off. The filtrate was extracted with dichloromethane (80 ml), and the extract was concentrated under reduced pressure. The purification of the residue with silica gel column or thin layer chromatography gave 3-isopropoxy acetal.5)

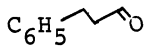
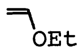
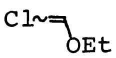
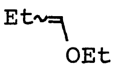
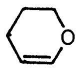
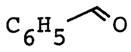
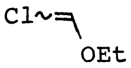
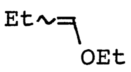
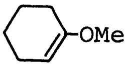
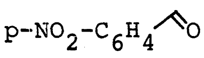
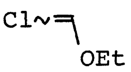
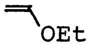
According to this procedure, various cross aldols were obtained from aldehydes and enol ethers, such as ethyl vinyl ether, 2-chlorovinyl ethyl ether, 1-butenyl ethyl ether, dihydropyran and 1-hexenyl methyl ether, as shown in the Table.

[B]: Enol ether was allowed to react with aldehyde as described in [A], and the reaction mixture was quenched with sat. $NaHCO_3$ solution (20 ml). The corresponding α,β-unsaturated carbonyl compounds were obtained after the similar work-up as described in [A].

According to the present procedure, 2-ethyl-5-phenyl-2-pentenal and 2-benzylidenecyclohexanone7) were isolated in 58% and 71% yields, respectively (see the Table).

Further works on the utility and the mechanism of the reactions are now in progress.



Aldehyde	Enol Ether	Conditions		Procedure	Yield(%)	
		°C	hr		(I)	(II)
		-78	0.5	A[a]	quant.	—
		-30	2	A[a]	96	—
		-30	2	A[a]	56	—
		-30	2	B	—	58
		-30	2	A[b]	quant.	—
		0	1	A[a]	quant.[6]	—
		0	1	A[a]	73	—
		0	1	B	—	71
		0	1	A[c]	81	—
		-30	2	A[a]	61	—

quenched with [a] EtOH, [b] MeOH, [c] i-PrOH

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3) R. I. Hoaglin and D. H. Hirsh, U. S. 2628257 (1953) [Chem. Abstr., 48, 1423, (1954).].

4) S. Satsumabayashi, K. Nakajo, R. Soneda, and S. Motoki, Bull. Chem. Soc. Japan, 43, 1586 (1970).

5) The isopropoxy group of the acetal may be originated in Ti(OPr-i)$_4$.

6) nmr (δ_{TMS}ppm, CCl_4): 0.95 ~ 1.35 (m, 12H), 3.30 ~ 3.90 (m, 5H), 4.05 (d × d, J=6 Hz, 1H), 4.43 (d, J=6 Hz, 1H), 4.67 (d, J=6 Hz, 1H), 7.28 (s, 5H). ir (neat): ν_{C-O} 1070 cm^{-1}. The other 3-isopropoxy acetals indicated similar nmr and ir spectra.

7) nmr (δ_{TMS}ppm, CCl_4): 1.40 ~ 1.95 (bs, 4H), 2.20 ~ 2.55 (bs, 2H), 2.55 ~ 2.85 (bs, 2H), 7.30 (s, 5H), 7.40 (s, 1H). ir (neat): $\nu_{C=O}$ 1675 cm^{-1}.

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