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CROSSED ALDOL REACTION MEDIATED BY DIETHYLALUMINUM 2,2,6,6-TETRAMETHYLPIPERIDIDE (DATMP)

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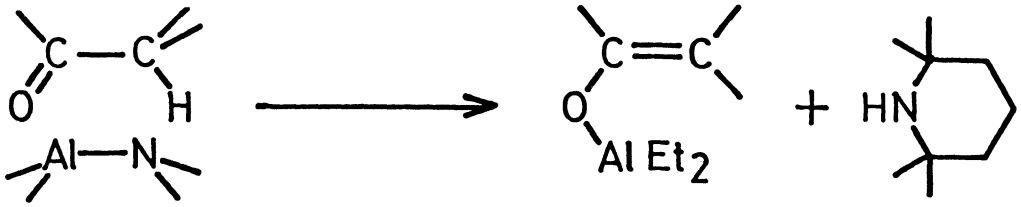
An efficient way of producing organoaluminum enolates of *t*-butyl acetate and of ketones is based on the title aluminum amide. Subsequent addition to a carbonyl moiety of various substrates affords the desired aldol adducts in fair to excellent yields.

Recently disclosed observation of the aldolic cyclization of 2,15-hexadecanedione by means of dialkylaluminum alkoxide-amine system[1] has prompted the authors to publish independent findings on the title reactions.

An organoaluminum enolate has been postulated to intervene the reaction of α-halocarbonyl compounds with various carbonyl substrates in the presence of zinc and diethylaluminum chloride.[2] However, the possibility of a zinc enolate, instead of the aluminum one, actually mediating the C-C bond formation has not been excluded. The title organoaluminum amide, DATMP, was previously introduced as a reagent isomerizing a 2-alkyloxirane into an allylic alcohol.[3] The logical extension should provide a means of transforming a carbonyl compound into the respective diethylaluminum enolate:



Experiments have shown that tetrahydrofuran is the best solvent for the reaction. A typical procedure (A) for the addition of an ester enolate to an aldehyde[4] would therefore be as follows: Diethylaluminum chloride (1.5 M solution in hexane, 2.0 ml. 3.0 mmol) was added to a solution of lithium TMP derived from *n*-BuLi (3.0 mmol) and TMP (0.42 g, 3.0 mmol) in THF (15 ml) at 0 °C. After 30 min at 0 °C, a solution of *t*-butyl acetate (0.35 g, 3.0 mmol) in THF (2.0 ml) was added at -23 °C and stirring was continued at this temperature for 1 h. The resulting pale yellow solution was treated with benzaldehyde (0.16 g, 1.5 mmol) and the mixture was stirred at -23 °C for 1 h and 25 °C for 30 min. Work up (ether, 2N HCl), followed by preparative TLC (hexane/ether (1 : 1)), gave the desired β-hydroxy ester (0.31 g, 92%) as a colorless oil which was spectrometrically identical with an authentic sample.[4] Another procedure (B) for the cross aldol addition of a ketone enolate to a carbonyl compound follows: To a solution

of DATMP (3.0 mmol) prepared as above, was added a solution of cyclohexanone (0.20 g, 2.0 mmol) in THF (2.0 ml) at -78 °C and stirring was continued for 1 h. Benzaldehyde (0.21 g, 2.0 mmol) was added and the mixture was stirred at -78 °C for 2 h and 25 °C for 30 min. Extractive work-up followed by TLC purification afforded β-hydroxy ketone as a colorless oil (0.32 g, 78%). Other examples are given below (*e/t=erythro/threo*).[5]

Table: ALDOLIC ADDITION MEDIATED BY DATMP

$R^1CH=C(OAlEt_2)R^2$		R^3COR^4		Procedure	$R^3 \diagdown R^4 C(OH)-CHR^1-COR^2$	
R^1	R^2	R^3	R^4		Y% (*e/t*)	IR(neat) cm^{-1}
H	$OC(CH_3)_3$	Ph	H	A	92	3450, 1720
H	$OC(CH_3)_3$	$-(CH_2)_5-$		A	87	3500, 1710
$CH_2=CH$	$OC(CH_3)_3$	Ph	H	A	68[a] (1/1)	3475, 1725
$-(CH_2)_4-$		Ph	H	B	78 (4/5)	3490, 1700
H	Ph	CH_3	CH_3	B[b]	65	3460, 1670
H	Ph	$-(CH_2)_5-$		B	63	3530, 1675
$-CH_2CH_2CH_2CH(CH_3)-$		Ph	H	B	72[c]	3500, 1700
$-CH_2CH_2CH_2CH(CH_3)-$		$(CH_3)_2CH-$	H	B	55[c]	3470, 1710

a) None of the γ-addition isomer was detected in this reaction of *t*-butyl crotonate. The same regioselectivity was observed in the reaction between methyl 4-bromocrotonate and benzaldehyde by means of Zn/Et_2AlCl system. See ref. 2. b) An excess of acetone (6 equiv) was used. c) Only the kinetically controlled products, 6-substituted 2-methylcyclohexanones, were obtained as a mixture of stereoisomers.

Literature and Footnotes

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4) For aldolic reactions of acetates, see (a) K. Sisido, H. Nozaki, and O. Kurihara, J. Am. Chem. Soc., 74, 6254 (1952), (b) M. W. Rathke and D. F. Sullivan, ibid., 95, 3050 (1973) and literature cited therein.

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