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ASYMETRIC ALKYLATION OF CARBONYL COMPOUNDS WITH CHIRAL LITHIUM ALKOXY-TRIBUTYL ALUMINATE.

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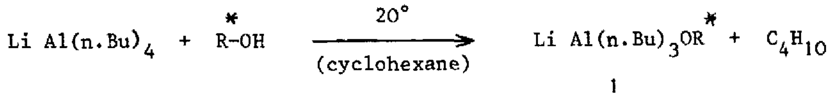
We have shown previously that aluminium "ate" complexes, Li $Al(n.Bu)_4$ and Na Al Et_4, are able to alkylate carbonyl compounds and epoxides (1, 2). Moreover reduction of prochiral ketones by chiral lithium alkoxyaluminohydrides to secondary alcohols, sometimes with fairly good optical yields, has been reported (3, 4).

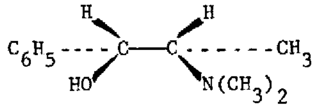
These results have enabled us to prepare a new organometallic reagent 1, useful for asymetric alkylation, by combining equimolar amounts of lithium tetrabutyl aluminate and (-)-N-methylephedrin according to reaction scheme I :



$$\text{Li Al(n.Bu)}_4 + \overset{*}{R}\text{-OH} \xrightarrow[\text{(cyclohexane)}]{20°} \text{Li Al(n.Bu)}_3\text{O}\overset{*}{R} + C_4H_{10} \qquad \text{(I)}$$

1

$\overset{*}{R}$-OH =



Indeed, we observed that compound 1, prepared *in situ*, could alkylate aldehydes and ketones, leading respectively to the secondary and tertiary alcohols 2, in good yields, with very few reduction by-products 3. Futhermore, the alcohols 2 were obtained with rather high optical activities. These results appear on scheme II and table :

$$\text{Li Al(n.Bu)}_3\text{O}\overset{*}{R} + R_1 - \overset{\overset{O}{\|}}{C} - R_2 \longrightarrow R_1 - \underset{OH}{\overset{R_2}{C}} - \text{n.Bu} + R_1 - \underset{OH}{\overset{R_2}{C}} - H \qquad \text{(II)}$$

2 3

$R_1 = C_2H_5$, $R_2 = H$
$R_1 = C_6H_5$, $R_2 = H$
$R_1 = C_6H_5$, $R_2 = CH_3$

experimental

A solution of (-)-N-methylephedrin (0,01 mole) in cyclohexane (100 ml) was added within one hour, with stirring, to Li $Al(n.Bu)_4$ (0,01 mole) covered with cyclohexane (10 ml), at 20°, under nitrogen. Subsequently a solution of the ketone or aldehyde (0,01 mole) in cyclohexane (10 ml) was added, within 10 min. After hydrolysis of the mixture by water (10 ml), the organic layer was washed three times with 10 ml of 2N HCl, to separate the amine, which was thus quantitatively recovered. Analysis of the organic layer, dried over K_2CO_3, was made by G.C., and alcohol 2 was purified by preparative G.C. for the determination of $[\alpha]_D$.

table

carbonyl compound	yield (%) of 2 [c]	$[\alpha]^t_D$ of 2	optical yield (%) for 2
C_2H_5-CHO [a]	70	$[\alpha]^{25}_D = -1{,}92°$ (ethanol, c = 10)	24 (5)
C_6H_5-CHO [b]	79	$[\alpha]^{20}_D = -1{,}60°$ (liquide, l = 1)	8 (6)
C_6H_5-$COCH_3$ [a]	56	$[\alpha]^{22}_D = -3{,}40°$ (ethanol, c = 11,8)	31 [d]

- reaction times at 20° : [a] 24 h. ; [b] 4 h.
- [c] evaluated by GC, using the internal standard method. Reactions give always about 5% of 3. With acetophenone 39% of the ketone was recovered.
- [d] evaluated by NMR with the aid of chiral shift reagent Eu $(t.fac.cam)_3$ (7).

In conclusion the lithium alkoxy-tributyl aluminate 1, prepared *in situ*, can alkylate carbonyl compounds, as well as lithium tetrabutyl aluminate, although it is by far less reactive. This new alkylating agent leads to optically active alcohols 2, with optical yields much higher than those previously reported in similar reactions (3, 8). Futhermore it can be prepared and used very easily.

Owing to the great interest of the chiral alkali metal alkoxy-trialkyl aluminates, $M^+ (AlR_3,OR')^-$, whose compound 1 is the first example, for the synthesis by alkylation reactions of pure optically active compounds, we will now extend our studies in this field.

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