Efficient Synthesis of Acetals Catalysed by Rare Earth Chlorides

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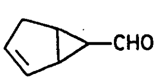
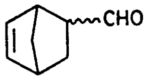
Summary Rare earth chlorides are efficient catalysts for the acetalization of aldehydes.

ELEMENTS of the rare earths series and their derivatives have received scarce attention from organic chemists, although their use for synthetic purposes seems to be promising.[1] We now report that the rare earths chlorides are highly efficient catalysts for the acetalization of aldehydes.

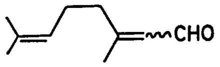
Acetalization and dioxolan formation are the most efficient and usual methods for the protection of aldehyde and ketone groups.[2] In the presence of an alcohol, these compounds form acetals in an acid-catalysed, equilibrated reaction. Usually the transformation is brought to completion by the presence of 2,2-dimethoxypropane or trimethyl orthoformate.[2,3] Several methods using various catalysts, such as protic acids[4] or Lewis acids ($FeCl_3$, NH_4NO_3, BF_3, $ZnCl_2$),[5] have been described.



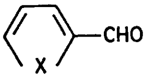
(1)



(2)



(3)



(4) X = O
(5) X = S

When an aldehyde is dissolved in a methanolic solution of a rare earth chloride, the aldehyde–acetal equilibrium is reached almost instantaneously. It can be shifted to the optimum acetal concentration by addition of trimethyl orthoformate [reaction (1)]. Various lanthanoids have been tested, and the results are in the Table.

The reaction mixtures contain only starting material and the corresponding acetal, with no by-products. The

$$\text{R-CHO} + \text{MeOH} \xrightarrow[\text{HC(OMe)}_3]{\text{LnCl}_3} \text{R-CH(OMe)}_2 \qquad (1)$$

maximum acetal formation depends on the lanthanoid ion. Lanthanum, cerium, and neodymium are effective for acetalization of aliphatic aldehydes, although for aromatic, bicyclic, and heterocyclic aldehydes, the best results are obtained with erbium and ytterbium chlorides. The reaction is very easy to perform and the maximum yield is obtained within a few minutes at room temperature. These conditions are especially valuable for acid sensitive reactants, in contrast to methods which employ higher temperatures or stronger acids.[4] For example, bicyclo[3.1.0]-hex-2-ene-6-carbaldehyde is quantitatively transformed to its dimethyl acetal in the presence of ytterbium chloride, whereas rearrangement products are obtained when sulphuric or toluene-*p*-sulphonic acid is used. Zinc chloride was ineffective as a catalyst for acetalization under our experimental conditions. The presence of trimethyl orthoformate as a water scavenger allows the use of commercially available hydrated forms of the lanthanoid salts.[6]

The precise role of the catalyst has not yet been studied. Examples show that the yield of the acetals increases with the atomic number of lanthanoid used. As the ionic radius decreases from lanthanum to ytterbium, the greater catalytic effect of the latter may be explained in terms of a reduced steric hindrance of the approach to the reactants, or a more acidic character. As a further example *p*-nitrobenzaldehyde was not acetalized after 20 h in the presence of $ErCl_3$, whereas it was totally transformed after the same time in the presence of $YbCl_3$.

TABLE. Acetalization of aldehydes with lanthanoid chlorides as catalysts (reaction 1).

	% Yield of acetal[a,b]				
Aldehyde	$LaCl_3$	$CeCl_3$	$NdCl_3$	$ErCl_3$	$YbCl_3$
$C_5H_{11}CHO$	90	100		100 (96)[b]	
$C_7H_{15}CHO$		100		100 (95)	
Cyclohexanecarbaldehyde		95		95 (85)	
(1)	95	95	95	95	100 (96)
(2)	70	70		80	100 (92)
(3)		95		95 (87)	
PhCH=CH–CHO		75	80	100 (95)	
PhCHO	85	90	90	100 (95)	
p-$MeOC_6H_4CHO$	60	70	80	95 (71)[c]	
p-BrC_6H_4CHO		80		85	100 (92)
(4)		90	90	95	100 (98)
(5)	50	60		80	100 (98)

[a] Typically, the aldehyde (1 mmol) was dissolved in methanolic $LnCl_3.nH_2O$ (2·5 ml; 0·4 M) and trimethyl orthoformate (n+1 mmol) was added. The solution was kept at room temperature for 10 min then poured into aqueous sodium hydrogen carbonate. The mixture was extracted (ether), and the extract washed (sat. aqueous NaCl), dried (Na_2SO_4), and evaporated. The crude mixture was analysed by n.m.r. spectroscopy, then purified (neutral Al_2O_3 chromatography). The isolated acetals were identified by the usual spectroscopic techniques (i.r., n.m.r.) and by regeneration of starting material [hydrolysis with wet silica gel (F. Huet, A. Lechevallier, M. Pellet, and J. M. Conia, *Synthesis*, 1978, 63) or H_2SO_4]. [b] The yields of acetals were obtained by n.m.r. analysis of the crude mixture (JEOL PMX 60, CCl_4 solution with Me_4Si as internal standard). Figures in parentheses are isolated yields of pure compounds. [c] Partial decomposition during the isolation process.

The acetalization of ketones, which leads to unexpected results, will be discussed elsewhere.

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