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# CALCIUM ALKOXYALANATES

## III [*]. REDUCTION OF ORGANIC FUNCTIONAL GROUPS BY CALCIUM TETRAKIS(ALKOXY)ALANATES

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## Summary

Calcium tetrakis(alkoxy)alanates obtained from different alcohols reduce aldehydes, ketones, acids, esters, acid chlorides and anhydrides to alcohols in high yields. Good results are achieved in the reduction of amides to amines. The reductions of nitrile and oxime groups and dehalogenation reactions are more difficult. Selectivity is possible in the reduction of organic epoxides.

## Introduction

In previous papers [1,2] we described the synthesis of calcium alkoxyalanates (CAA), derived from the partial replacement of hydride hydrogens of calcium alanate by alkoxy groups, according to the general formula I.

$$\mathrm{Ca[AlH_{4-n}(OR)_n]_2 \cdot x\ THF}$$

(I)

$n = 0.5$—$3.5$; $x = 0, 1, 2$

These compounds can be prepared by partial alcoholysis of calcium alanate [1] or by methods [2] utilizing readily available reagents. Among the various alcohols examined, branched aliphatic alcohols give CAA, usually as complexes with THF, for which, with a few exceptions, X-ray and IR investigations support definite chemical structures [1].

Metal hydrides have found extensive application in the stoichiometric reduction of organic compounds [3] and their use is increasing [4]. Since the stability,

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TABLE 1

SOLUBILITY OF CALCIUM TETRAKIS(ALKOXY)ALANATES IN ORGANIC SOLVENTS

| Solvent | Solubility (%) [a] (g of compound for 100 ml of solution) | |
|---|---|---|
| | $Ca[AlH_2(O\text{-}i\text{-}C_3H_7)_2]_2 \cdot THF$ | $Ca[AlH_2(O\text{-}i\text{-}C_4H_9)_2]_2 \cdot THF$ |
| Diethyl ether | 35 | 60 |
| Methyl t-butyl ether | 25 | 55 |
| Tetrahydrofuran | 45 | 65 |
| Dioxan | 35 | 55 |
| Cyclohexane | 25 | 55 |
| Benzene | >60 [b] | >70 [b] |
| Toluene | >60 [b] | >70 [b] |

[a] Determined as weight of solid for 100 ml of solution at 25°C. [b] The limit is given by the increasing viscosity of solution. Fluid solutions at higher concentration are obtainable directly by concentration of the preparation solution.

solubility and safety of CAA from branched alcohols are generally excellent, we decided to assess their reducing power towards organic reagents. Of the possible CAA, our attention was focused on calcium tetrakis(alkoxy)alanates (TTCAA), $Ca[AlH_2(OR)_2]_2 \cdot THF$, which show a good balance of stability, solubility and hydride hydrogen content. Depending on the nature of the alkoxy group, pure TTCAA can be isolated as crystalline or amorphous solids [1], stable under nitrogen. They show decomposition temperatures as high as 150°C. In the presence of air, their decomposition is slow, with a gradual loss of hydride hydrogens. In contact with water, they quickly decompose, but no ignition was noted for small laboratory samples. TTCAA are soluble in ethereal solvents, aromatic hydrocarbons, cyclohexane, and, depending on the size of R, in aliphatic hydrocarbons. For illustration, the solubilities of $Ca[AlH_2(O\text{-}i\text{-}C_3H_7)_2]_2 \cdot THF$ (CAPAL) and $Ca[AlH_2(O\text{-}i\text{-}C_4H_9)_2]_2 \cdot THF$ (CABAL) are shown in Table 1.

This paper deals with the first testing of the behaviour of TTCAA as reducing agents for several organic functional groups.

## Results and discussion

Table 2 summarizes the results obtained by reducing organic substrates bearing various functional groups with CAPAL, CABAL, and TTCAA from cyclohexanol (CAHAL) and 2-ethylhexanol (CAEAL). Aromatic hydrocarbons were found to be suitable as the reaction medium. For reactions with CAEAL n-hexane, in which the reagent shows good solubility, was used. The CAA solution was added to the substrate with stirring. Interaction of alanate with organic molecules (except for hydrocarbyl halides) led to soluble intermediates that were hydrolyzed to yield the reduced products. Hydrolysis was carried out with aqueous acid solutions, or in the special case of amines with aqueous alkali. Except for 1,4-butanediol, the products were separated from aluminum and calcium salts or hydroxides by extraction with the organic solvent; 1,4-butanediol was isolated by taking up the residue obtained by evaporation of the aqueous layer in ethanol. Tetrahydrofuran and alcohols derived from the starting alanate could be removed by distillation.

The results in Table 2 indicate that aldehydes, ketones, esters, and acid chlorides are easily reduced to alcohols at room temperature. Acids and anhydrides are also reduced to alcohols in high yields, but higher temperatures are needed. Good results were also achieved in the reduction of amides to amines. Preparation of amines from nitrile and oxime groups was more difficult, as was the dehalogenation. The reduction of propene oxide was selective, yielding isopropanol; styrene oxide gave both 1- and 2-phenylethanol, with the former predominating. Generally the olefinic double bond is not reduced, unless it is activated, e.g. by a C=O group. In this case reduction of the C=O group dominates, but with excess CAA the C=C bond is also reduced.

These results can be used to reach some conclusions about the reducing power of TTCAA compared with the more usual metal hydrides. The reducing activities of the latter compounds towards typical organic groups have been compared in the literature [4,5]. Derivatives of aluminum hydride such as $LiAlH_4$ (II), $Al(i\text{-}C_4H_9)_2H$ (III), $NaAl(C_2H_5)_2H_2$ (IV) and $NaAlH_2(OCH_2CH_2OCH_3)_2$ (V) are active reducing agents for a large number of functional groups, with II the most powerful. The spectrum of organic functional groups reduced by borane derivatives is narrower. $NaBH_4$ reduces only aldehydes, ketones and acid chlorides. The reducing power of boranates of other alkali or alkali-earth metals is only slightly higher. Other boranes are used for highly selective reductions [6]. We have attempted to place TTCAA in the context of these observations (Table 3). It appears that TTCAA have a reducing power close to the other more active derivatives of aluminum hydride, and can be regarded as multi-purpose reducing agents.

## Experimental

### *Reagents and solvents*

Calcium tetrakis(alkoxy)alanates were obtained as described previously [1,2]. Organic substrates were pure commercial products. Liquids were further purified by distillation and dried over molecular sieves. Solids were dried by heating under vacuum or by storing their hydrocarbon solutions over molecular sieves. All reagents and solvents were handled and all reduction reactions were carried out under nitrogen up to the hydrolytic quenching.

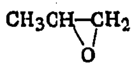
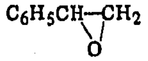
### *Analyses*

The results of the reduction reactions were evaluated by gas chromatography using either a C. Erba Fractovap C model or a Perkin-Elmer Sigma 3 B apparatus. Various chromatographic columns appropriate to the separation of the various reduction products were used: Carbowax 20 M 8% and 10% on Chromosorb P (benzyl, 2-phenylethyl, cinnamic alcohol); Carbowax 20 M 5% (2-heptyl, cyclohexyl alcohol) or 10% on Chromosorb W (hexamethyleneimine); Carbowax 1500 10% on teflon (n-propyl, isopropyl, n-butyl, neopentyl, n-hexyl, 2-cyclohexylethyl, benzyl, 1-phenylethyl alcohol, diphenylcarbinol); Carbowax 6000 10% on teflon (n-butyl, n-hexyl alcohol, 1,4-butandiol), all C. Erba products; Tenax (amines) Supelco. The yield of 3-pyridylmethanol was calculated by separating the product by distillation. Purity was evaluated by chemical analysis, and NMR and IR spectroscopy. The method of chemical analyses of alanates was previously described [1].

*(continued on p. 27)*

TABLE 2

REDUCTION OF ORGANIC COMPOUNDS BY CALCIUM TETRAKIS(ALKOXY)ALANATES

| Run | Organic compound | $Ca[AlH_2(OR)_2]_2 \cdot THF$ R | Ratio [a] | Solvent ($Q$) [b] | Temp. (°C) | Time (h) | Product (yield, %) |
|---|---|---|---|---|---|---|---|
| 1 | $n\text{-}C_3H_7CHO$ | $CH_2CH(C_2H_5)C_4H_9$ | 0.375 | hexane (3) | 20 | 0.5 | $n\text{-}C_4H_9OH$ (≥99) |
| 2 | $C_6H_5CHO$ | $i\text{-}C_3H_7$ | 0.275 | toluene (3) | 25 | 3 | $C_6H_5CH_2OH$ (98) |
| 3 | $C_6H_5CH{=}CHCHO$ | $i\text{-}C_4H_9$ | 0.25 | toluene (3) | 20 | 20 | $C_6H_5CH{=}CHCH_2OH$ (84) |
| 4 | $C_6H_5CH{=}CHCHO$ | $i\text{-}C_4H_9$ | 0.875 | toluene (4) | 100 | 6 | $C_6H_5(CH_2)_3OH$ (≥99) |
| 5 | $CH_3CO(CH_2)_4CH_3$ | $i\text{-}C_3H_7$ | 0.275 | toluene (3) | 25 | 0.5 | $CH_3CHOH(CH_2)_4CH_3$ (97) |
| 6 | $(CH_2)_5CO$ | $i\text{-}C_4H_9$ | 0.375 | toluene (2.5) | 20 | 0.5 | $(CH_2)_5CHOH$ (≥99) |
| 7 | $CH_3COC_6H_5$ | $CH_2CH(C_2H_5)C_4H_9$ | 0.375 | hexane (3) | 20 | 0.5 | $CH_3CHOCH_6H_5$ (≥99) |
| 8 | $(C_6H_5)_2CO$ | $i\text{-}C_4H_9$ | 0.30 | toluene (3) | 25 | 5 | $(C_6H_5)_2CHOH$ (70) |
| 9 |  $CH_3\underset{\diagdown O \diagup}{CH-CH_2}$ | $i\text{-}C_4H_9$ | 0.375 | toluene (4) | 70 | 3 | $CH_3CHOHCH_3$ (84) |
| 10 |  $C_6H_5\underset{\diagdown O \diagup}{CH-CH_2}$ | $i\text{-}C_4H_9$ | 0.375 | toluene (3) | 25 | 1 | $C_6H_5CH_2CH_2OH$; (69)<br>$C_6H_5CHOHCH_3$ (27) |
| 11 | $n\text{-}C_3H_7COOH$ | $CH_2CH(C_2H_5)C_4H_9$ | 1.125 | hexane (6.5) | reflux | 2.5 | $n\text{-}C_4H_9OH$ (92) |
| 12 | $n\text{-}C_5H_{11}COOH$ | $i\text{-}C_3H_7$ | 0.825 | toluene (4) | 85 | 2 | $n\text{-}C_6H_{13}OH$ (≥99) |
| 13 | $C_6H_5COOH$ | $i\text{-}C_4H_9$ | 1 | toluene (4) | 80 | 2 | $C_6H_5CH_2OH$ (68) |
| 14 | $n\text{-}C_3H_7COOC_2H_5$ | $C_6H_{11}$ | 0.75 | benzene (6.5) | 20 | 1 | $n\text{-}C_4H_9OH$ (≥99) |
| 15 | $n\text{-}C_5H_{11}COOC_2H_5$ | $i\text{-}C_3H_7$ | 0.55 | toluene (3) | 25 | 1 | $n\text{-}C_6H_{13}OH$ (92) |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| 16 | $(CH_2)_5CHCOOC_2H_5$ | $CH_2CH(C_2H_5)C_4H_9$ | 0.75 | toluene<br>(5) | 20 | 1 | $(CH_2)_5CHCH_2OH$<br>(⩾99) |
| 17 | $C_6H_5COOC_2H_5$ | $i\text{-}C_4H_9$ | 1.1 | toluene<br>(3) | 60 | 0.25 | $C_6H_5CH_2OH$<br>(⩾99) |
| 18 | $C_5H_4NCOOC_2H_5$ | $i\text{-}C_4H_9$ | 0.55 | toluene<br>(1) | 80 | 0.5 | $C_5H_4NCH_2OH$<br>(73) |
| 19 | $\overline{O(CH_2)_3C}O$ | $i\text{-}C_4H_9$ | 0.75 | toluene<br>(3) | 20 | 1 | $HO(CH_2)_4OH$<br>(⩾99) |
| 20 | $n\text{-}C_5H_{11}COCl$ | $i\text{-}C_4H_9$ | 0.625 | toluene<br>(4) | 80 | 0.5 | $n\text{-}C_6H_{13}OH$<br>(⩾99) |
| 21 | $C_6H_5COCl$ | $i\text{-}C_4H_9$ | 0.625 | toluene<br>(3) | 25 | 1 | $C_6H_5CH_2OH$<br>(⩾99) |
| 22 | $C_6H_5CH{=}CHCOCl$ | $i\text{-}C_3H_7$ | 0.55 | toluene<br>(3) | 25 | 1 | $C_6H_5CH{=}CHCH_2OH$<br>(⩾99) |
| 23 | $C_6H_5CH{=}CHCOCl$ | $i\text{-}C_4H_9$ | 1.25 | toluene<br>(6) | 100 | 5 | $C_6H_5(CH_2)_3OH$<br>(62) |
| 24 | $(CH_3CH_2CO)_2O$ | $C_6H_{11}$ | 1.87 | benzene<br>(12.5) | reflux | 2.5 | $n\text{-}C_3H_7OH$<br>(⩾99) |
| 25 | $[(CH_3)_3CCO]_2O$ | $i\text{-}C_3H_7$ | 1.1 | toluene<br>(4) | 80 | 2 | $(CH_3)_3CCH_2OH$<br>(91) |
| 26 | $(C_6H_5CO)_2O$ | $i\text{-}C_3H_7$ | 1.1 | toluene<br>(4) | 100 | 3 | $C_6H_5CH_2OH$<br>(92) |
| 27 | $C_6H_5CONH_2$ | $i\text{-}C_4H_9$ | 1.5 | benzene<br>(4) | reflux | 3 | $C_6H_5CH_2NH_2$<br>(62) |
| 28 | $CH_3CONHC_6H_5$ | $i\text{-}C_4H_9$ | 1.1 | benzene<br>(4) | reflux | 4 | $CH_3CH_2NHC_6H_5$<br>(93) |
| 29 | $\overline{NH(CH_2)_5C}O$ | $i\text{-}C_4H_9$ | 0.9 | toluene<br>(4) | 80 | 2 | $(CH_2)_6NH$<br>(70) |
| 30 | $C_6H_5CH{=}NOH$ | $i\text{-}C_4H_9$ | 1 | toluene<br>(4) | 90 | 3 | $C_6H_5CH_2NH_2$<br>(43) |
| 31 | $C_6H_5CH_2CN$ | $i\text{-}C_4H_9$ | 1 | toluene<br>(5) | reflux | 3 | $C_6H_5(CH_2)_2NH_2$<br>(35) |
| 32 | $n\text{-}C_5H_{11}Br$ | $C_6H_{11}$ | 0.375 | toluene<br>(3) | 90 | 18 | $n\text{-}C_5H_{12}$<br>(65) |
| 33 | $C_6H_5CH_2Cl$ | $C_6H_{11}$ | 0.375 | benzene<br>(3.5) | reflux | 4 | $C_6H_5CH_3$<br>(55) |

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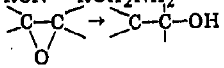
[a] Molar ratio of calcium tetrakis(alkoxy)alanate to organic compound. [b] *Q* indicates ml of solvent used for mmol of organic compound.

TABLE 3

REDUCING ACTIVITY OF METAL HYDRIDES TOWARDS TYPICAL ORGANIC GROUPS [a]

| Reduction reaction | $LiAlH_4$ | $NaAlEt_2H_2$ | $NaAlH_2(OR)_2$ [b] | $CaAlH_2(OR)_2$ [c] | $Al(i\text{-}Bu)_2H$ | $LiBH_4$ | $LiBEt_3H$ | $NaBH_4$ | $LiAl(O\text{-}t\text{-}Bu)_3H$ |
|---|---|---|---|---|---|---|---|---|---|
| $RCHO \rightarrow RCH_2OH$ | + | + | + | + | + | + | + | + | + |
| $R_2CO \rightarrow R_2CHOH$ | + | + | + | + | + | + | + | + | + |
| $RCOOH \rightarrow RCH_2OH$ | + | + | + | + | —[d] | — | — | — | — |
| $RCOOR' \rightarrow RCH_2OH$ | + | + | + | + | —[d] | + | + | —[f] | — |
| $(RCO_2)_2O \rightarrow RCH_2OH$ | + | + | + | + | + | + | +[e] | — | — |
| $RCOCl \rightarrow RCH_2OH$ | + | + | + | + | + | + | + | + | —[d] |
| $RCON< \rightarrow RCH_2N<$ | + | + | + | + | + | — | —[e] | —[g] | — |
| $RCN \rightarrow RCH_2NH_2$ | + | + | + | + | —[d] | — | —[e] | — | — |
|  | + | + | + | + | + | + | + | — | — |
| $Rhal \rightarrow RH$ | + | + | + | + | — | — | + | — | |
| $>C{=}C< \rightarrow HC{-}CH$ [h] | — | — | — | — | + | — | —[e] | — | — |

[a] + indicates that the reduction reaction occurs as described; — indicates that this reduction does not take place. [b] OR is $OCH_2CH_2OCH_3$. [c] OR is the alkoxy group from branched alcohols (see Table 2). [d] The reduction gives RCHO. [e] There is a lack of information; the activity is estimated on the basis of a reduction potential similar to that of $LiBH_4$ [3]. [f] Very slow reduction to $RCH_2OH$ can be achieved in some cases. [g] RCN is formed from $RCONH_2$. [h] Non-activated olefin.

### *Reduction reactions*

Typical procedures are as follows.

*A. Reduction of pivalic anhydride.* A toluene solution (3.8 ml) of $Ca[AlH_2(O\text{-}i\text{-}C_3H_7)_2]_2 \cdot THF$ (5.5 mmol) was added dropwise to a stirred and cooled solution of $[(CH_3)_3CCO]_2O$ (5 mmol) in toluene (18 ml). The solution was stirred for 2 h at 80°C, and the cooled mixture was then decomposed by addition of 25% aqueous $H_2SO_4$. The water layer was washed 3 times with toluene and the organic layers were combined and dried over molecular sieves. Analysis by gas-chromatography showed the yield of neopentanol to be 91%.

*B. Reduction of acetanilide.* A benzene solution (4.0 ml) of $Ca[AlH_2(O\text{-}i\text{-}C_4H_9)_2]_2 \cdot THF$ (5.5 mmol) was added dropwise to a stirred and cooled solution of $CH_3CONHC_6H_5$ (5 mmol) in benzene (18 ml). The solution was refluxed for 2 h. Part of the reaction mixture was decomposed by addition of 20% aqueous NaOH solution. The water layer was washed 3 times with benzene and the organic layers were combined and dried over molecular sieves. Analysis by gas chromatography showed the yield of *N*-ethylaniline to be 87.5%. The remaining reaction solution was further refluxed and the formation of *N*-ethylaniline was again tested, as reported above, after 2 h. The yield was 93%.

*C. Reduction of ethylnicotinate.* A toluene solution (40 ml) of $Ca[AlH_2(O\text{-}i\text{-}C_4H_9)_2]_2 \cdot THF$ (55 mmol) was added dropwise during 10 minutes to a stirred solution of ethylnicotinate (100 mmol) in toluene (80 ml) heated at 80°C. The solution was stirred for 30 minutes at 80°C, and then cooled and decomposed by addition of 30 ml of water. The mixture was filtered, and the solid residue was extracted with $CO_2$ saturated methanol (200 ml). The methanol solution was combined with the previously filtered liquids, and the mixture was evaporated. The residue was taken up in diethyl ether and the solution was dried over anhydrous $K_2CO_3$, then evaporated, and the oily residue was distilled at reduced pressure (ca. 20 Torr, 144°C) to yield 73% of pure 3-pyridylmethanol.

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## References

1 S. Cucinella, G. Dozzi and G. Del Piero, J. Organometal. Chem., 224 (1982) 1.
2 G. Dozzi, S. Cucinella and M. Bruzzone, J. Organometal. Chem., 224 (1982) 13.
3 N.G. Gaylord, Reduction with Complex Metal Hydrides, Interscience Publ. Inc., New York, 1956; H. Hajós, Komplexe Hydride, und ihre Anwendung in der Organischen Chemie, Veb Deutscher Verlag der Wissenschaften, Berlin, 1966; A. Hajós, Complex Hydrides and Related Reducing Agents in Organic Synthesis, Elsevier, Amsterdam, 1979.
4 S.C. Stinson, Chem. Eng. News, Nov. 3, 1980, p. 18.
5 E.R.H. Walker, Chem. Soc. Reviews, 5 (1976) 23.
6 H.C. Brown, Boranes in Organic Chemistry, Cornell Univ. Press, London, 1972; H.C. Brown, Organic Synthesis via Boranes, J. Wiley, New York, 1975; G.M.L. Cragg, Organoboranes in Organic Chemistry, M. Dekker Inc., New York, 1973.