

CALCIUM ALKOXYALANATES

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

S. CUCINELLA **, G. DOZZI and M. BRUZZONE

ASSORENI, 20097 San Donato Milanese, Milano (Italy)

(Received July 31st, 1981)

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.



(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,

* For part II see ref. 2.

** To whom correspondence should be addressed.

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-i-C ₃ H ₇) ₂] ₂ · THF	Ca[AlH ₂ (O-i-C ₄ H ₉) ₂] ₂ · 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[AlH₂(OR)₂]₂ · 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[AlH₂(O-i-C₃H₇)₂]₂ · THF (CAPAL) and Ca[AlH₂(O-i-C₄H₉)₂]₂ · 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), $\text{Al}(\text{i-C}_4\text{H}_9)_2\text{H}$ (III), $\text{NaAl}(\text{C}_2\text{H}_5)_2\text{H}_2$ (IV) and $\text{NaAlH}_2(\text{OCH}_2\text{CH}_2\text{OCH}_3)_2$ (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].

TABLE 2


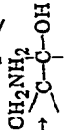


REDUCTION OF ORGANIC COMPOUNDS BY CALCIUM TETRAKIS(ALKOXY)ALANATES

Run	Organic compound	$\text{Ca}[\text{AlH}_2(\text{OR})_2]_2 \cdot \text{THF}$ R	Ratio ^a	Solvent ^b (Q)	Temp. (°C)	Time (h)	Product (yield, %)
1	$n\text{-C}_3\text{H}_7\text{CHO}$	$\text{CH}_2\text{CH}(\text{C}_2\text{H}_5)\text{C}_4\text{H}_9$	0.375	hexane (3)	20	0.5	$n\text{-C}_4\text{H}_9\text{OH}$ (≥99)
2	$\text{C}_6\text{H}_5\text{CHO}$	$i\text{-C}_3\text{H}_7$	0.275	toluene (3)	25	3	$\text{C}_6\text{H}_5\text{CH}_2\text{OH}$ (98)
3	$\text{C}_6\text{H}_5\text{CH}=\text{CHCHO}$	$i\text{-C}_4\text{H}_9$	0.25	toluene (3)	20	20	$\text{C}_6\text{H}_5\text{CH}=\text{CHCH}_2\text{OH}$ (84)
4	$\text{C}_6\text{H}_5\text{CH}=\text{CHCHO}$	$i\text{-C}_4\text{H}_9$	0.875	toluene (4)	100	6	$\text{C}_6\text{H}_5(\text{CH}_2)_3\text{OH}$ (≥99)
5	$\text{CH}_3\text{CO}(\text{CH}_2)_4\text{CH}_3$	$i\text{-C}_3\text{H}_7$	0.275	toluene (3)	25	0.5	$\text{CH}_3\text{CHOH}(\text{CH}_2)_4\text{CH}_3$ (97)
6	$(\text{CH}_2)_5\text{CO}$	$i\text{-C}_4\text{H}_9$	0.375	toluene (2.5)	20	0.5	$(\text{CH}_2)_5\text{CHOH}$ (≥99)
7	$\text{CH}_3\text{COOC}_6\text{H}_5$	$\text{CH}_2\text{CH}(\text{C}_2\text{H}_5)\text{C}_4\text{H}_9$	0.375	hexane (3)	20	0.5	$\text{CH}_3\text{CHOCH}_2\text{C}_6\text{H}_5$ (≥99)
8	$(\text{C}_6\text{H}_5)_2\text{CO}$	$i\text{-C}_4\text{H}_9$	0.30	toluene (3)	25	5	$(\text{C}_6\text{H}_5)_2\text{CHOH}$ (70)
9	$\text{CH}_3\text{CH}-\text{CH}_2$ 	$i\text{-C}_4\text{H}_9$	0.375	toluene (4)	70	3	$\text{CH}_3\text{CHOHCH}_3$ (84)
10	$\text{C}_6\text{H}_5\text{CH}-\text{CH}_2$ 	$i\text{-C}_4\text{H}_9$	0.375	toluene (3)	25	1	$\text{C}_6\text{H}_5\text{CH}_2\text{CH}_2\text{OH}$, (69) $\text{C}_6\text{H}_5\text{CHOHCH}_3$ (27)
11	$n\text{-C}_3\text{H}_7\text{COOH}$	$\text{CH}_2\text{CH}(\text{C}_2\text{H}_5)\text{C}_4\text{H}_9$	1.125	hexane (6.5)	reflux	2.5	$n\text{-C}_4\text{H}_9\text{OH}$ (92)
12	$n\text{-C}_5\text{H}_{11}\text{COOH}$	$i\text{-C}_3\text{H}_7$	0.825	toluene (4)	85	2	$n\text{-C}_6\text{H}_{13}\text{OH}$ (≥99)
13	$\text{C}_6\text{H}_5\text{COOH}$	$i\text{-C}_4\text{H}_9$	1	toluene (4)	80	2	$\text{C}_6\text{H}_5\text{CH}_2\text{OH}$ (68)
14	$n\text{-C}_3\text{H}_7\text{COOC}_2\text{H}_5$	C_6H_{11}	0.75	benzene (6.5)	20	1	$n\text{-C}_4\text{H}_9\text{OH}$ (≥99)
15	$n\text{-C}_5\text{H}_{11}\text{COOC}_2\text{H}_5$	$i\text{-C}_3\text{H}_7$	0.55	toluene (3)	25	1	$n\text{-C}_6\text{H}_{13}\text{OH}$ (92)

16	$(CH_2)_5CHCOOC_2H_5$	$CH_2CH(C_2H_5)C_4H_9$	0.75	toluene (5)	20	1	$(CH_2)_5CHCH_2OH$ (≥99)
17	$C_6H_5COOC_2H_5$	i-C ₄ H ₉	1.1	toluene (3)	60	0.25	$C_6H_5CH_2OH$ (≥99)
18	$C_5H_4NCOOC_2H_5$	i-C ₄ H ₉	0.55	toluene (1)	80	0.5	$C_5H_4NCH_2OH$ (78)
19	$O(CH_2)_3CO$	i-C ₄ H ₉	0.75	toluene (3)	20	1	$HO(CH_2)_4OH$ (≥99)
20	n-C ₅ H ₁₁ COCl	i-C ₄ H ₉	0.625	toluene (4)	80	0.5	n-C ₆ H ₁₃ OH (≥99)
21	C_6H_5COCl	i-C ₄ H ₉	0.625	toluene (3)	25	1	$C_6H_5CH_2OH$ (≥99)
22	$C_6H_5CH=CHCOCl$	i-C ₃ H ₇	0.55	toluene (3)	25	1	$C_6H_5CH=CHCH_2OH$ (≥99)
23	$C_6H_5CH=CHCOCl$	i-C ₄ H ₉	1.25	toluene (6)	100	5	$C_6H_5(CH_2)_3OH$ (62)
24	$(CH_3CH_2CO)_2O$	C ₆ H ₁₁	1.87	benzene (12.5)	reflux	2.5	n-C ₃ H ₇ OH (≥99)
25	$[(CH_3)_3CCO]_2O$	i-C ₃ H ₇	1.1	toluene (4)	80	2	$(CH_3)_3COCH_2OH$ (91)
26	$(C_6H_5CO)_2O$	i-C ₃ H ₇	1.1	toluene (4)	100	3	$C_6H_5CH_2OH$ (92)
27	$C_6H_5CONH_2$	i-C ₄ H ₉	1.5	benzene (4)	reflux	3	$C_6H_5CH_2NH_2$ (62)
28	$CH_3CONHC_6H_5$	i-C ₄ H ₉	1.1	benzene (4)	reflux	4	$CH_3CH_2NHC_6H_5$ (93)
29	$NH(CH_2)_5CO$	i-C ₄ H ₉	0.9	toluene (4)	80	2	$(CH_2)_6NH$ (70)
30	$C_6H_5CH=NOH$	i-C ₄ H ₉	1	toluene (4)	90	3	$C_6H_5CH_2NH_2$ (43)
31	$C_6H_5CH_2CN$	i-C ₄ H ₉	1	toluene (5)	reflux	3	$C_6H_5(CH_2)_2NH_2$ (36)
32	n-C ₅ H ₁₁ Br	C ₆ H ₁₁	0.375	toluene (3)	90	18	n-C ₅ H ₁₂ (65)
33	$C_6H_5CH_2Cl$	C ₆ H ₁₁	0.375	benzene (3.5)	reflux	4	$C_6H_5CH_3$ (55)

^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 ₂ H ₂	NaAlH ₂ (OR) ₂ ^b	CaAlH ₂ (OR) ₂ ^c	Al(<i>i</i> -Bu) ₂ H	LiBH ₄	LiBEt ₃ H	NaBH ₄	LiAl(O- <i>t</i> -Bu) ₃ H
RCHO → RCH ₂ OH	+	+	+	+	+	+	+	+	+
R ₂ CO → R ₂ CHOH	+	+	+	+	+	+	+	+	+
RCOOH → RCH ₂ OH	+	+	+	+	— ^d	—	—	— ^f	—
RCOOR' → RCH ₂ OH	+	+	+	+	— ^d	+	+	—	—
(RCO ₂) ₂ O → RCH ₂ OH	+	+	+	+	+	+	+	+	— ^d
RCOCl → RCH ₂ OH	+	+	+	+	+	+	+	+	— ^d
RCON → RCH ₂ NH ₂	+	+	+	+	+	—	— ^e	— ^g	—
RCN → RCH ₂ NH ₂	+	+	+	+	— ^d	—	— ^e	—	—
 → 	+	+	+	+	+	+	+	—	—
Rhal → RH	+	+	+	+	—	—	+	—	—
 → 	—	—	—	—	+	—	— ^e	—	—

^a + indicates that the reduction reaction occurs as described; — indicates that this reduction does not take place. ^b OR is OCH₂CH₂OCH₃. ^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 LiBH₄ [3]. ^f Very slow reduction to RCH₂OH can be achieved in some cases. ^g RCN is formed from RCONH₂. ^h Non-activated olefin.

Reduction reactions

Typical procedures are as follows.

A. Reduction of pivalic anhydride. A toluene solution (3.8 ml) of $\text{Ca}[\text{AlH}_2(\text{O}-i\text{-C}_3\text{H}_7)_2]_2 \cdot \text{THF}$ (5.5 mmol) was added dropwise to a stirred and cooled solution of $[(\text{CH}_3)_3\text{CCO}]_2\text{O}$ (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 $\text{Ca}[\text{AlH}_2(\text{O}-i\text{-C}_4\text{H}_9)_2]_2 \cdot \text{THF}$ (5.5 mmol) was added dropwise to a stirred and cooled solution of $\text{CH}_3\text{CONHC}_6\text{H}_5$ (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 $\text{Ca}[\text{AlH}_2(\text{O}-i\text{-C}_4\text{H}_9)_2]_2 \cdot \text{THF}$ (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.

Acknowledgements

Thanks are due to ANIC for financial support and to the ASSORENI management for permitting publication.

References

- 1 S. Cucinella, G. Dozzi and G. Del Piero, *J. Organometal. Chem.*, 224 (1982) 1.
- 2 G. Dozzi, S. Cucinella and M. Bruzzzone, *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.