

REACTIONS OF ALKYLALUMINUM COMPOUNDS WITH CYCLIC ETHERS

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SUMMARY

Oxetane and its 3,3-dimethyl and 3,3-bis(chloromethyl) derivatives undergo ring-opening reactions with Et_2AlX . When $\text{X}=\text{H}$ or Cl subsequent hydrolysis gives the corresponding propanol or 3-chloropropanol, but when $\text{X}=\text{CN}$ the product isolated was a butyrolactone. At elevated temperature oxetane reacts with triethylaluminum to give 1-propanol and 1-pentanol, but the 3,3-disubstituted oxetanes give only propanols. Friedel-Crafts alkylation accompanies the alkylation and reduction of oxetane when it reacts with triethylaluminum in cumene. At elevated temperatures tetrahydrofuran and tetrahydropyran react with diethylaluminum hydride, giving 1-butanol and 1-pentanol, respectively.

INTRODUCTION

3,3-Bis(chloromethyl)oxetane (BCMO) is an interesting substrate for organometallic reagents. Since BCMO is a strained cyclic ether that contains the neopentyl chloride moiety, reactions at both the carbon-oxygen and the carbon-chlorine bonds are possible. Reactions of 4- to 6-membered cyclic ethers at the carbon-oxygen bond (ring opening), while not numerous, are exemplified by the reductive cleavage of oxetane, tetrahydrofuran (THF) and tetrahydropyran (THP) by diborane¹ and by the cleavage of oxetane and THF by alkyllithiums^{2,3} and Grignard reagents^{2,4,5}. Although BCMO is polymerized by triethylaluminum^{6,7**}, no metathetical reactions of alkylaluminum compounds with 4- to 6-membered cyclic ethers have been reported. Oxiranes, on the other hand, react with diethylaluminum cyanide to give 3-hydroxypropionitriles⁹; trialkylaluminums and dialkylaluminum hydrides effect alkylation and reduction of oxiranes¹⁰. In aromatic solvents, reaction of triethylaluminum and oxirane gives 2-arylethanol, the products of a Friedel-Crafts alkylation¹¹.

Many organic halides, including some related to BCMO, react with triethyl-

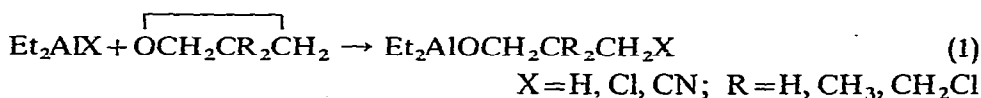
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** This polymerization, reportedly⁶ requiring temperatures upwards of 100°, will in fact proceed at room temperature or below⁸ (for tabulated patent examples see ref. 6). The finding that oxetane and 3,3-dimethyloxetane are readily polymerized by triethylaluminum⁸ shows that these polymerizations do not depend on the generation of aluminum chloride (*cf.* ref. 7).

aluminum at the carbon-chlorine bond. Neopentyl chloride and (2-chloro-1,1-dimethylethyl)benzene react below 100°; the products, all of which have a rearranged carbon skeleton, are those of alkylation, reduction and dehydrohalogenation¹². The present work revealed, however, that BCMO reacts with alkylaluminum compounds nearly exclusively at the carbon-oxygen bond. The reactions of other cyclic ethers with alkylaluminum compounds were subsequently investigated.

RESULTS AND DISCUSSION

The results of this study are summarized in Table 1. We see that diethylaluminum hydride, diethylaluminum chloride and diethylaluminum cyanide react with oxetanes at moderate conditions (< 100°) to give diethylaluminum propoxides [reaction (1)] which upon hydrolysis yield the corresponding propanols*. Good



conversions (usually > 75%) to propanols are obtained when approximately equimolar amounts of oxetane and alkylaluminum are used. Unlike the reactions of Grignard reagents with oxetanes, which give both alkylation and halogenation products^{2,4}, the reactions of oxetanes with the three dialkylaluminum compounds gave no detectable alkylation products.

The reactions of triethylaluminum with oxetanes require temperatures of 100° or higher, and even then excess alkylaluminum is necessary to obtain good conversion. Neither BCMO nor 3,3-dimethyloxetane (DMO) underwent detectable alkylation. Only reduction was observed with DMO [reaction (2a)]; reduction also predominated for BCMO, but accompanying the 2,2-bis(chloromethyl)propanol were varying amounts of 3-chloro-2,2-bis(chloromethyl)propanol. Formation of the latter product requires the transferral of chlorine from one molecule to another. Apparently triethylaluminum reacts to some extent with BCMO at the carbon-chlorine bond, giving diethylaluminum chloride**. The latter can then react with more BCMO as shown in reaction (1).

Unlike BCMO and DMO, oxetane is both reduced [reaction (2a)] and alkylated [reaction (2b)] by triethylaluminum. When cumene is present, a Friedel-

* Although no 4-hydroxy-3,3-bis(chloromethyl)butyronitrile was isolated from the reaction of BCMO and diethylaluminum cyanide, its formation was indicated by IR analysis. The hydroxy nitrile is also a logical precursor of the isolated 3,3-bis(chloromethyl)butyrolactone [reaction (a)]. As suggested by a referee, cyclization could also precede hydrolysis [reaction (b)].



** The fate of the oxetane moiety is not known.

TABLE I
 REACTIONS OF ALKYLALUMINUM COMPOUNDS AND CYCLIC ETHERS

Alkylaluminum compound	Cyclic ether	Al/Ether ratio	Reaction temperature (°C)	% Unchanged ether ^a	Products	% Conversion to product ^d	Identification ^b
Et ₃ Al	BCMO	1	140-160	60	2,2-Bis(chloromethyl)propanol	ca. 30	A
Et ₃ Al	BCMO	2	140-160	< 5	2,2-Bis(chloromethyl)propanol	81	B, C, D
Et ₂ AlCl	BCMO	1	50-100	10	3-Chloro-2,2-bis(chloromethyl)propanol	ca. 1	A
Et ₂ AlCl	BCMO	2	50-100	10	3-Chloro-2,2-bis(chloromethyl)propanol	68	A
Et ₂ AlH	BCMO	1.3 ^c	25-50	4	3-Chloro-2,2-bis(chloromethyl)propanol	81	B, C, D
Et ₂ AlF	BCMO	1.3	50-150		2,2-Bis(chloromethyl)propanol	84	A
Et ₂ AlCN	BCMO	1	25-50		BCMO polymer	77	C
Et ₃ Al	DMO	2.0	140-160		3,3-Bis(chloromethyl)butyrolactone ^d	88	B, C, D
Et ₃ Al	DMO ^f	2.0	150		2,2-Dimethylpropanol		A
Et ₂ AlCl	DMO	1.2	50-100		2,2-Dimethylpropanol ^e	ca. 100	A
Et ₃ Al	Oxetane	2.2	100-150		3-Chloro-2,2-dimethylpropanol	78	B, C
					1-Propanol	55	A
					1-Pentanol	23	A
Et ₃ Al	Oxetane ^f	2.4	100	10	1-Propanol	50	A
					1-Pentanol	23	A
					3-Cumyl-1-propanol (2 isomers)	10	A
Et ₂ AlCl	Oxetane	1.2	25		3-Chloro-1-propanol	73	A
Et ₂ AlH	Oxetane	1.3 ^c	25		1-Propanol	80	A
Et ₂ AlF	Oxetane	1.3	25-50		Oxetane oligomer	57	C
Et ₃ Al	THF	2.2	140-170	100	(No reaction)		
Et ₂ AlCl	THF	1.2	140-170	100	(No reaction)		
Et ₂ AlH	THF	1.3 ^c	140-170	40	1-Butanol ^h	50	A
Et ₂ AlF	THF	1.3	140-170	100	(No reaction)		
Et ₂ AlH	THP	1.3 ^c	190-210	45	1-Pentanol ⁱ	50	A

^a Usually determined by GLC analysis. ^b A, GLC comparison with authentic sample; B, structure conforms with NMR spectrum; C, structure conforms with IR spectrum; D, compound gave satisfactory elemental analysis. ^c Et₂AlH/ether ratio, Et₃Al also present. ^d Other products were present; see Experimental Section. ^e Not determined. ^f Reaction conducted in cumene. ^g No 2,2-dimethyl-1-pentanol or 3-cumyl-2,2-dimethyl-1-propanol could be detected. ^h No 1-hexanol could be detected. ⁱ Reaction accompanied by thermal decomposition of alkylaluminum (grey precipitate).

of 1.4% AlH_3 (15 mole% diethylaluminum hydride). Diethylaluminum hydride was received as a mixture containing 35% of the hydride, 57% triethylaluminum and 7% tri-*n*-butylaluminum.

Reactions were conducted in 225 ml beverage bottles which had been cooled under argon and sealed with buna-N septa (Firestone Tire and Rubber Co.) secured with perforated metal caps*. Solvents and reactants were added with syringes. The reactions were monitored by NMR analysis or by gas-liquid chromatography (GLC). For analysis by GLC small portions of the reaction mixtures were hydrolyzed with 15% sodium hydroxide. Carbowax 20 M and poly *m*-phenyl ether (PMPE) columns were used for the GLC analyses and separations. Mixtures which did not react at room temperature were heated successively at 50°, 100° and 150° for 5 days or longer, as necessary, to effect reaction. Products were characterized and identified by their IR and NMR** spectra (chemical shifts are given in Table 2) and when

TABLE 2
CHEMICAL SHIFTS OF REACTION PRODUCTS^a

Compound	Type of hydrogen				
	OH	CH ₃	CH ₂ Cl	CH ₂ O	CH ₂ C=O
(CH ₂ Cl) ₃ CCH ₂ OH	1.50		3.59	3.67	
CH ₃ (CH ₂ Cl) ₂ CCH ₂ OH	1.56	1.06	3.48	ca. 3.55	
CH ₂ Cl(CH ₃) ₂ CCH ₂ OH	2.28	0.97	3.38 ^b	3.38 ^b	
$\overbrace{\text{OCH}_2\text{C}(\text{CH}_2\text{Cl})_2\text{CH}_2\text{CO}}$			3.68	4.10	2.50

^a Samples were dissolved in carbon tetrachloride. Shifts are given in ppm downfield from tetramethylsilane. ^b Unresolved single signal.

possible by comparison with authentic standards using GLC. Authentic 3-chloro-1-propanol was prepared from oxetane and hydrogen chloride. Authentic 3-cumyl-1-propanols were obtained as the principal products of the aluminum chloride-catalyzed reaction of oxetane and cumene¹⁴. Representative procedures are described below.

Diethylaluminum chloride and BCMO

Addition of BCMO (1.78 ml, 15 mmoles) to a solution of diethylaluminum chloride (3.8 ml, 30 mmoles) in *n*-decane (20 ml, Phillips Petroleum Co.) gave a slight exotherm; the resulting reaction mixture consisted of two immiscible layers. Warming to 50° gave a homogenous system. After diethylaluminum chloride and BCMO had reacted, copious colorless crystals, presumably $\text{Et}_2\text{AlOCH}_2\text{C}(\text{CH}_2\text{Cl})_3$, deposited reversibly on cooling. Following the addition of 5 ml ethyl ether, the reaction mixture was treated at < 0° with 15% sodium hydroxide (20 ml) and gradually warmed to 50°. After extraction with ether and dichloromethane, the organic portions were combined and concentrated to remove the low boiling solvents. 3-Chloro-2,2-bis-

* We thank the Bond Crown Division, Continental Can Co., San Francisco, California, for generous gifts of unlined caps.

** NMR spectra were provided by Dr. P. W. Flanagan, Continental Oil Co., and Mr. W. R. Anderson, Jr., Stanford Research Institute.

(chloromethyl)propanol crystallized readily from the decane. Filtration followed by washing with cold pentane gave colorless needles (2.02 g, 10.6 mmoles, 71%), m.p. 64–66° (lit.¹⁵: 65.5°). (Found: Cl, 55.6%. $C_5H_9Cl_3O$ calcd.: Cl, 55.7%.) GLC analysis before work-up showed 10% unreacted BCMO and 81% conversion to product.

Triethylaluminum and BCMO

A mixture of triethylaluminum (4.1 ml, 30 mmoles) and BCMO (1.78 ml, 15 mmoles) in 20 ml decane showed little reaction after 7 days at 100°, but after 5 days at 150° all BCMO had been converted. After hydrolysis with 15% sodium hydroxide, the decane solution was passed through a silicic acid column, which was then washed with pentane and eluted with dichloromethane. The oil obtained after evaporation of the dichloromethane was dissolved in hexane containing a little ether and then crystallized by cooling with dry ice. Several recrystallizations gave colorless 2,2-bis(chloromethyl)propanol (1.04 g, 6.6 mmoles, 44%) m.p. ca. 20°. (Found: Cl, 45.00. $C_5H_{10}Cl_2O$ calcd.: Cl, 45.20%.) Yields based on reaction mixture analysis were 81% 2,2-bis(chloromethyl)propanol and ca. 1% 3-chloro-2,2-bis(chloromethyl)propanol.

In a preliminary run, triethylaluminum and BCMO (1.1:1 mole ratio) were reacted in cyclohexane 14 days at ca. 150°. Most of the solvent escaped, leaving a viscous, pale yellow liquid. Work-up gave 2,2-bis(chloromethyl)propanol and 3-chloro-2,2-bis(chloromethyl)propanol in a ratio of ca. 2:1**. 3-Chloro-2,2-dimethylpropanol, from the reaction of diethylaluminum chloride and DMO, was also isolated by absorption and elution from silicic acid. Low temperature crystallization from hexane gave deliquescent crystals, m.p. 30°. 3-Chloro-2,2-dimethylpropanol and 2,2-bis(chloromethyl)propanol have been reported¹⁶, but melting points were not given.

Diethylaluminum cyanide and BCMO

Diethylaluminum chloride (2.3 ml, 18 mmoles) and sodium cyanide (0.98 g, 20 mmoles) were stirred 3 days in cumene at 120–130°. Then BCMO (2.33 g, 15 mmoles) was added at 25° and the mixture stirred 4 days at 50°. After hydrolysis with 15% sodium hydroxide and extraction with ether and dichloromethane, the organic portions were combined, concentrated and distilled. The pale yellow gum-like product (1.75 g), boiling at 100–165° (0.2 mm), had a complex IR spectrum with strong absorption (in microns) at 2.8 (O–H), 4.4 ($C\equiv N$) and 5.6 (C=O). The four components observed by GLC analysis had the following relative areas (in order of decreasing retention times on a PMPE column at 220°): A, 100; B, 12; 3-chloro-2,2-bis(chloromethyl)propanol, 5; C, 4. Separation of A by preparative GLC followed by sublimation (50°, 0.2 mm), recrystallization from ether at low temperature and another sublimation gave 3,3-bis(chloromethyl)butyrolactone as a colorless translucent gum which liquefied at 98–100° (Found***: C, 39.46; H, 4.41; Cl, 37.80. $C_6H_8Cl_2O_2$ calcd.: C, 39.40; H, 4.40; Cl, 38.78%.) The glistening platelets which crystallize from ether appeared to be ordinary crystals, but examination at room tem-

* Microanalyses by Galbraith Laboratories, Knoxville, Tenn.

** We thank Mr. A. B. Carcl, Continental Oil Co., for GLC separations.

*** Microanalysis by Stanford University Analytical Laboratory.

perature revealed that they are very plastic and show no discernible optical birefringence. The presence of crystallinity was demonstrated by X-ray diffraction analysis (at 25°); differential thermal analysis revealed an endothermic phase transition (melting) at 98.3°*. Components B and C were not studied further.

Diethylaluminum cyanide was also prepared by the reaction of triethylaluminum and hydrogen cyanide. Subsequent reaction with BCMO gave a product mixture similar to the one of the preceding paragraph, except that no 3-chloro-2,2-bis(chloromethyl)propanol was found.

Diethylaluminum fluoride and BCMO

A reaction mixture containing diethylaluminum fluoride (5.3 ml of a 50% solution in hexane, 19.5 mmoles) and BCMO (1.78 ml, 15 mmoles) in 20 ml decane slowly became cloudy at 25°. After 5 days at 50°, much of the BCMO had disappeared. After 7 days at 150° only a trace of BCMO remained, but no volatile products were detected by GLC analysis. The reaction mixture contained a finely dispersed colorless solid which apparently was unaffected by 15% NaOH used for hydrolysis. Filtration gave 1.5 g product, η_{inh} 0.13 (0.5 g/dl in cyclohexanone at 30°), identified as poly-(BCMO) from IR spectra of films cast from cyclohexanone or dichloromethane solutions.

Similarly, there was obtained from the reaction of diethylaluminum fluoride and oxetane a colorless nonvolatile liquid (57% yield) insoluble in heptane and water, but soluble in methanol and benzene. The IR spectrum was appropriate for an oxetane oligomer [strong absorption at 9 μ (-O-C) and moderate absorption at 2.8 μ (O-H)]. No volatile products were observed.

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* X-ray analysis and differential thermal analysis were performed at SRI by Dr. M. G. Barlow and Dr. C. A. Crutchfield, respectively.