

Optically Active Organoaluminum Based Inclusion Compounds. Synthesis and Characterization of (S) - $(-)$ - α - $[(C_6H_5)CH(CH_3)N(CH_3)_3][Al_2R_6I]$ ($R = CH_3, C_2H_5$)

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Abstract. The optically active quaternary ammonium salt (S) - $(-)$ - α - $[(C_6H_5)CH(CH_3)N(CH_3)_3]I$ reacts with AlR_3 to afford optically active organoaluminum based inclusion compounds, liquid clathrates, of the formula (S) - $(-)$ - α - $[(C_6H_5)CH(CH_3)N(CH_3)_3][Al_2R_6I]$ ($R = CH_3, C_2H_5$). Specific rotation $([\alpha]_D^{25})$ for the $Al(CH_3)_3$ compound was determined to be -13.19° while that for the $Al(C_2H_5)_3$ analog was determined to be -14.30° . There are 13.8 toluene molecules per anionic moiety for the trimethylaluminum based liquid clathrate while there are 15.0 toluene molecules per anion for the corresponding triethylaluminum inclusion compound.

Key words. Aluminum alkyls, liquid clathrate, optical activity.

1. Introduction

The origin of the organoaluminum inclusion compounds known as liquid clathrates [1] may be traced to the reaction of aluminum alkyls with MX moieties ($M =$ alkali metal or tetraalkylammonium ion; $X =$ halide or pseudohalide ion). These reactions were shown to result in 1 : 1 (eq. 1) or 2 : 1 (eq. 2) complexes [2]. Upon interaction with aromatic solvents the 2 : 1 complex affords the desired inclusion compound. These novel organoaluminum species have shown promise in various aspects of host-guest chemistry and have been examined in such processes as aromatic separations and coal liquefaction [1]. Indeed, liquid clathrates represent one of the most exciting recent entries into host-guest chemistry.



Optical resolution remains a significant concern in chemistry. Optical resolution via inclusion compounds has precedence in the literature [3–8]. Herein, we describe the synthesis and characterization of (S) - $(-)$ - α - $[(C_6H_5)CH(CH_3)N(CH_3)_3][Al_2R_6I]$ ($R = CH_3, C_2H_5$) isolated from reaction of the optically active quaternary ammonium salt (S) - $(-)$ - α - $[(C_6H_5)CH(CH_3)N(CH_3)_3]I$ with AlR_3 . These compounds represent the initial report of liquid clathrates possessing optical activity. The inherent significance of these novel materials is traced to the fact that they are potential agents for separating racemic mixtures.

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2. Experimental

Owing to the extreme air- and water-sensitivity of the aluminum alkyls and the resulting optically active compounds, the exclusion of oxygen and moisture from the synthesis and subsequent manipulations was essential. To this end, standard Schlenk techniques were employed in conjunction with an inert atmosphere drybox (Vacuum Atmospheres HE-43 DRi-Lab). Toluene was distilled from sodium/benzophenone under an atmosphere of nitrogen immediately prior to use. Trimethylaluminum, triethylaluminum, (*S*)-(-)- α -methylbenzylamine, and methyl iodide, all purchased from Aldrich Chemical Co., were used as received. NMR data were recorded on a JOEL-FX90Q NMR spectrometer. Specific rotations were recorded on a Horiba Sepa-200 polarimeter.

2.1. PREPARATION OF (*S*)-(-)- α -[(C₆H₅)CH(CH₃)N(CH₃)₃][Al₂R₆] (R = CH₃, C₂H₅)

The preparation of the optically active liquid clathrates may be divided into two distinct tasks: (a) The exhaustive alkylation of an optically active primary amine; and (b) The reaction of the optically active amine salt with aluminum alkyls resulting in the optically active organoaluminum inclusion compounds.

2.2. PREPARATION OF (*S*)-(-)- α -[(C₆H₅)CH(CH₃)N(CH₃)₃]I

In a typical synthesis, (*S*)-(-)- α -methylbenzylamine (5.60 g, 46 mmol) was placed in a flask along with CH₂Cl₂ (50 mL). The flask was cooled in an ice bath. Methyl iodide (13.2 g, 93 mmol) was slowly added with a syringe. The system was stirred overnight. Sodium methoxide (5.10 g, 93 mmol) was added with cooling. At this point, the system was allowed to warm to room temperature and stirred for 24 hr. A second portion of methyl iodide (13.2 g, 93 mmol) was subsequently added, the system was again allowed to stir overnight. The solvent was removed *in vacuo*. The residue was extracted with dry methylene chloride and filtered. The filtrate was concentrated. Ethylacetate was added to the oil. As the solvent slowly evaporated, large, colorless crystals of the (*S*)-(-)- α -[(C₆H₅)CH(CH₃)N(CH₃)₃]I salt formed. Total amount of product collected was 11.40 g (84% yield). ¹H NMR (CDCl₃): δ 1.87 (d, 3H, CH₃), 3.39 (s, 9H, N(CH₃)₃), 5.45 (q, 1H, CH), 7.39–7.36 (d of q, 5H, (C₆H₅)). Melting point: 159–160°C. Specific rotation (CH₂Cl₂): $[\alpha]_D^{25} = -30.58^\circ$.

2.3. PREPARATION OF (*S*)-(-)- α -[(C₆H₅)CH(CH₃)N(CH₃)₃][Al₂(CH₃)₆]·13.8 C₆H₅CH₃

Inside the drybox, a reaction tube was charged with (*S*)-(-)- α -[(C₆H₅)CH(CH₃)N(CH₃)₃]I (5.60 g, 46 mmol), and toluene (20 mL). Trimethylaluminum (0.500 g, 68.8 mmol) was slowly added with a syringe. Reaction was immediate, vigorous, and extremely exothermic. The formation of two distinct liquid layers, the overt indication of liquid clathrate formation, was observed within minutes of reaction. ¹H HMR (CDCl₃): δ -0.65 (s, 9H, Al(CH₃)₃); 1.87 (d, 3H, CH₃); 3.26 (s, 9H, N(CH₃)₃); 5.10 (q, 1H, CH); 7.54 (s, 5H, C₆H₅). Specific rotation (toluene): $[\alpha]_D^{25} = -13.19^\circ$.

2.4. PREPARATION OF (*S*)-(-)- α -[(C₆H₅)CH(CH₃)N(CH₃)₃][Al₂(C₂H₅)₆]·15.0 C₆H₅CH₃

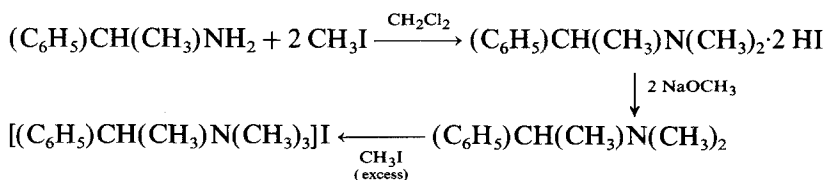
The triethylaluminum-based optically active liquid clathrate (*S*)-(-)- α -[(C₆H₅)CH(CH₃)N(CH₃)₃][Al₂(C₂H₅)₆]I was prepared in a similar fashion to its trimethylaluminum

analog. $^1\text{H NMR}$ (CDCl_3): δ 0.52 (q, 6H, $\text{Al}(\text{CH}_2\text{CH}_3)_3$), 1.57 (t, 9 H, $\text{Al}(\text{CH}_2\text{CH}_3)_3$). Specific rotation (toluene): $[\alpha]_D^{25} = -14.30^\circ$.

3. Results and Discussion

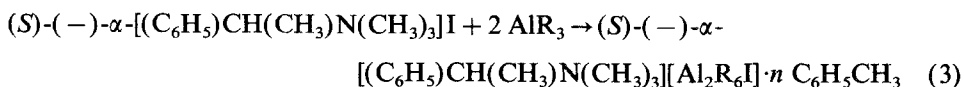
Optical resolution via host-guest compounds has been previously addressed in the literature. For example, cyclodextrins [3–5], choleic acids [6], urea [7], and tri-*o*-thymotide [8] have all been examined with respect to resolving racemic mixtures. As pointed out by Arad-Yellin *et al.* [9], optical resolution via host-guest compounds is attractive, *inter alia*, in that: (a) A given host may accommodate guests that vary widely in functional groups, sizes, and shapes; (b) With a given host, correlations may be drawn concerning the degree of enantiomer specificity and prediction of host and preferred guest chirality; (c) Since host-guest chemistry is based on the fact that “regular” chemical bonds (i.e., covalent, polar, etc.) are neither formed nor broken (between host and guest), many molecules that are very difficult or impossible to resolve may be examined. The work described herein discusses the synthesis and characterization of optically active organoaluminum inclusion compounds.

In addition to alkali metal salts, liquid clathrates are also readily prepared from reaction of AlR_3 with tetraalkylammonium salts. Thus, a convenient preparation route to an optically active liquid clathrate could begin with an optically active amine which is exhaustively alkylated to its quaternary ammonium salt. The optically active quaternary ammonium would subsequently be allowed to react with AlR_3 in an aromatic solvent to afford the desired inclusion compound. The resulting optically active liquid clathrate would be of the formula $\text{M}^*[\text{Al}_2\text{R}_6\text{X}]$. The optically active primary amine (*S*)-(–)- α -methylbenzylamine was chosen to initiate these studies. The exhaustive alkylation of α -methylbenzylamine was accomplished by modifications of the procedure offered by Sommer [10, 11]. The alkylation of α -methylbenzylamine to its iodide salt proved to be a substantial problem as the desired product was often contaminated with byproducts when the procedure of Sommer was employed. The procedure outlined in Scheme I afforded the facile isolation of the pure optically active salt in high yield (85%).



Scheme I

The freshly prepared salt of the optically active amine (*S*)-(–)- α - $[(\text{C}_6\text{H}_5)\text{CH}(\text{CH}_3)\text{N}(\text{CH}_3)_3]\text{I}$ was subsequently reacted with AlR_3 in toluene thus yielding the optically active liquid clathrate as given by (eq. 3).



($\text{R} = \text{CH}_3$ { $n = 13.8$ }, O_2H_5 { $n = 15.0$ })

An important quantity relative to liquid clathrate behavior is the aromatic to anion, A/A_−, ratio. This quantity is defined to be the number of aromatic molecules per anionic

Table I. Specific rotation and A/A data for the optically active salt and optically active liquid clathrates.

Compound	$[\alpha]_D^{25}$	A/A**
(S)-(-)-[(C ₆ H ₅)CH(CH ₃)N(CH ₃) ₃]I	-30.58°*	—
(S)-(-)-α-[(C ₆ H ₅)CH(CH ₃)N(CH ₃) ₃][Al ₂ (CH ₃) ₆]I	-13.19°**	13.8
(S)-(-)-α-(C ₆ H ₅)CH(CH ₃)N(CH ₃) ₃ [Al ₂ (C ₂ H ₅) ₆]I	-14.30°**	15.0

* Solvent: methylene chloride

** Solvent: toluene

unit. The A/A ratio is obtained from NMR integrations of the aromatic resonance relative to the anion resonance. The A/A ratio for the Al(CH₃)₃ and Al(CH₂CH₃)₃ based liquid clathrates was determined to be 13.8 and 15.0, respectively. Relevant data on the optically active liquid clathrates, as well as data on the optically active salt, is given in Table I. It is interesting to note that the specific rotation of the two optically active liquid clathrates have values comparable to each other. This is quite reasonable in that the chiral center is effectively independent of the aluminum alkyl in the compound.

The synthesis of these optically active liquid clathrates will serve as a benchmark as we explore the feasibility of using optically active liquid clathrates in achieving optical resolution.

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