Lithium Dibenzylamide, a Simple, Selective and Highly Efficient Catalyst for Isocyanate Cyclotrimerization to Isocyanurate

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Received 25 April 2011

Abstract: Lithium dibenzylamide catalyzed the rapid and essentially quantitative cyclotrimerization of a variety of isocyanates under mild conditions and could be recycled for six times in high yield.

Key words: lithium amides, catalysis, isocyanates cyclotrimerization, isocyanurates

Aromatic isocyanurates, manufactured by cyclotrimerizing corresponding isocyanates, have been shown to enhance the uses of polyurethanes as coating materials.^{1,2} Polymers, such as polyurethanes incorporated with isocyanurates, can improve their flame retardation characterisfilm-formation, and thermal tics. and chemical resistance.³⁻⁶ Isocyanurates are also used in the synthesis of co-polymer resins to enhance their water-resistance, transparency, and impact resistance.^{7,8} An optically active isocyanurate having peripheral amino acid units served for the chiral recognition of racemic binaphthol.⁹ Trialkyl isocyanurates have been employed in the preparation of flame-retardant laminating materials for electrical devices,¹⁰ and, because of their selective microbial and low mammalian toxicity, are used for drug delivery and release.^{11,12} Triaryl isocyanurates are activators in the continuous anionic co-polymerization of ɛ-caprolactam to nylon-6 possessing low monomer content and high melt viscosities.13

The various industrial and commercial applications of isocyanurates have attracted much attention in developing more effective methods for isocyanate cyclotrimerization. Development of efficient catalysts is crucial. A number of catalysts for isocyanate trimerization have been reported, including phosphines,^{7,8,14} N-heterocyclic carbenes,^{2,15} calcium carbene complexes,^{16,17} amines,¹⁸ NO,¹⁹ fluoride anions,²⁰ alkoxyalkenes,²¹ or *p*-toluenesulfinate,¹³ cyanate²² or carbamate²³ anions. Organometallic catalysts include organotin²⁴ and zirconium²⁵ compounds, organozinc halides and alkoxides,²⁶ copper and nickel halides,¹⁹ rare earth metal complexes^{27,28} and palladium(0) systems.²⁹ Very recently, an electron-rich, sterically hindered proazaphosphatrane was reported as an effective catalyst for the cyclotrimerization of both aryl and alkyl isocyanat. $^{\rm 8}$

In this paper, we report a facile synthetic method for the synthesis of isocyanurates by the cyclotrimerization of an appropriate isocyanate catalyzed by a simple lithium, sodium, or potassium amide.

Our initial objective was to prepare metal complexes containing a k-N,O-chelated ureido ligand from a lithium amide and an isocyanate. In most cases, isocyanurates were obtained as predominant products. This led us to investigate a new kind of catalyst for the cyclotrimerization of an isocyanate to an isocyanurate. Thus, phenyl isocyanate (Table 1) was selected as a model substrate and a variety of lithium amides, as well as Na or K amides or a tertamine were screened as potential catalysts, and the results are summarized in Table 1. Tertiary amine (entry 12) had no catalytic activity for the cyclotrimerization of phenyl isocyanate and lithium primary amides (entries 6 and 7) exhibited very low catalytic activities, but lithium secondary amides, except for lithium bis(trimethylsilyl)amide (entry 3), were very effective. Sodium or potassium dibenzylamide also catalyzed the reaction efficiently (entries 9 and 10). Lithium dibenzylamide at 0.1 mol% loading in diethyl ether in two minutes at room temperature (entry 8) promoted the quantitative cyclotrimerization of phenyl isocyanate to the corresponding isocyanurate; and lithium diethylamide or diisopropylamide catalyzed this reaction under the same conditions to give an isolated product yield of >90% (entries 1 and 2). Lithium bis(trimethylsilyl)amide catalyzed the reaction in only moderate yield, which may have been due to its high steric hindrance. In each case, IR spectral examination of the crude product showed that the isocyanurate was the exclusive product of the reaction, free of any dimer.² The isolation and purification of the product was straightforward, e.g. the insoluble triphenyl isocyanurate was obtained by simply filtering and washing the precipitate from the reaction mixture at the end of the reaction.

In view of the above results, a variety of isocyanate substrates was examined, using lithium dibenzylamide as the catalyst (Table 2). Even though only 0.05 mol% or 0.01 mol% catalyst loadings were employed, phenyl isocyanate was readily cyclotrimerized in two minutes at room temperature in 98% and 96% isolated yields of product, respectively (entry 1). Compared to the reported good cat-

SYNLETT 2011, No. 13, pp 1937–1939 Advanced online publication: 28.06.2011 DOI: 10.1055/s-0030-1260825; Art ID: W09911ST © Georg Thieme Verlag Stuttgart · New York

Table 1 Phenyl Isocyanate Cyclotrimerization Catalyzed by Various Lithium (or Na or K) Amides^a

Ph

PhN=C=O	$\begin{array}{c} \underline{\text{cat. (0.1 mol%)}}\\ \underline{\text{Et}_2\text{O, r.t.}}\\ \text{Ph} \end{array} \begin{array}{c} O \\ N \\ N \\ O \\ Ph \end{array} \begin{array}{c} O \\ Ph \\ O \\ Ph \end{array}$	
Entry	Catalyst	Yield (%) ^b
1	Et ₂ NLi	91 97°
2	<i>i</i> -Pr ₂ NLi	97
3	(Me ₃ Si) ₂ NLi	50 56°
4	pyrrolididolithium	86 90°
5	piperidinatolithium	83 88 ^c
6	Ph(H)NLi	9
7	t-Bu(H)Nli	6
8	Bn ₂ NLi	99
9	Bn ₂ NNa	98
10	Bn ₂ NK	97
11	Ph ₂ NLi	97
12	N,N-dimethylaniline	0
13	none	0

^a Reaction conditions: catalyst (0.1 mol%), phenyl isocyanate (30 mmol, degassed and dried prior to use), Et₂O (30 mL), r.t., 2 min. ^b Isolated yield (average of three runs).

^c Reaction time: 30 min.

alysts such as proazaphosphatrane^{7,8} or N-heterocyclic² carbenes, similar isolated yields with lower catalyst ratio or shorter reaction time were achieved. 4-Chlorophenyl isocyanate, or 4-methylphenyl isocyanate, or 4-methoxyphenyl isocyanate was converted successfully to its respective isocyanurate in two minutes in 98% isolated yield (entries 2–4). Such electron-rich substrates have typically exhibited low reactivities in the isocyanate cyclotrimerization reactions and afforded low isolated yields by using other catalyst systems.^{8,15,21}

Unexpectedly, the alkyl compound cyclohexyl isocyanate was cyclotrimerized to its isocyanurate in only low isolated yield (entry 5); good yield was obtained when sodium dibenzylamide was employed in diethyl ether albeit longer reaction time (30 min) was required.

The high catalytic performance of lithium dibenzylamide encouraged us to test its recyclability in the PhNCO– Et_2O system as summarized in Table 3. Thus, the isolated yield of isocyanurate on the sixth run had only decreased by ca. 10% compared to the initial run.

 Table 2
 Lithium Dibenzylamide Catalyzed Cyclotrimerization of Isocyanates^a

RN=C=O
$$\xrightarrow{\text{lithium dibenzylamide (0.1 mol%)}}{\text{Et}_2\text{O}, r.t., 2 min}$$

			-
Entry	Isocyanates ^b	Product	Yield (%) ^c
1	NCO NCO	1	99 98 ^d 96 ^e
2		2	98(lit. 93) ²¹
3	NCO	3	98(lit. 91) ¹⁵
4	MeO-	4	98(lit. 96) ⁸
5	NCO	5	32 89 ^f (lit. 99) ²

^a Reaction conditions: lithium dibenzylamide (0.1 mol%), isocyanate (30 mmol), Et_2O (30 mL), r.t., 2 min.

^b Isocyanates were degassed and dried prior to use.

^c Isolated yield (average of three runs).

^d A 0.05 mol%-loading of lithium dibenzylamide was used

^e A 0.01 mol%-loading of lithium dibenzylamide was used.

 $^{\rm f}$ A 0.1 mol%-loading of sodium dibenzylamide was used as catalyst, r.t., 30 min.

We propose that the mechanism for the formation of isocyanurate follows a route similar to that for a variety of Lewis base catalyzed reactions (Scheme 1).^{2,7,17,27} However, the formation of isocyanurates, particularly, alkyl isocyanurates catalyzed by previous Lewis bases was typically quite slow (taking many hours) even at elevated temperatures¹⁷ and commonly gave a mixture of both dimerization and trimerization products in low yields.^{2,27} In this system, the stronger Lewis base, sodium dibenzylamide initiated the cyclotrimerization rapidly and in good yield.

 Table 3
 Recyclability of Lithium Dibenzylamide^a

Entry	Cycle	Time (min)	Yield (%) ^b
1	1	2	99
2	2	2	99
3	3	2	97
4	4	2	94
5	5	2	94
6	6	2	89

 a Reaction conditions: lithium dibenzylamide (0.1 mol%), phenyl isocyanate (15 mmol), Et_2O (15 mL), r.t.

^b Isolated yield (average of two runs).





In conclusion, alkaline metal (Li, Na, and K) amides have been used for the first time in cyclotrimerization of isocyanates to isocyanurates.^{30,31} Aryl isocyanate, ArNCO [Ar = Ph, or $4-XC_6H_4$ (X = Cl, Me or MeO)] is rapidly, selectively and essentially quantitatively cyclotrimerized by treating a diethyl ether solution with 0.1 mol% of lithium dibenzylamide, while alkyl isocyanate, $C_6H_{11}NCO$ was converted to the corresponding isocyanurate in good yield by using sodium dibenzylamide as catalyst.

Supporting Information for this article is available online at http://www.thieme-connect.com/ejournals/toc/synlett.

Primary Data for this article are available online at http:// www.thieme-connect.com/ejournals/toc/synlett and can be cited using the following DOI: 10.4125/pd0013th.

Acknowledgment

We thank the NSFC (No. 20572065; 20772074), the SXNSFC (2008011021; 2008012013-2) and the Research Project Supported by Shanxi Scholarship Council of China for financial support.

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- (30) **Representative Procedure:** An oven-dried Schlenk tube under nitrogen was charged with phenyl isocyanate, lithium dibenzylamide (0.1 mol%), and Et_2O (30 mL). The reaction mixture was stirred at r.t. for 2 min. The resulting precipitate was filtered off, washed with Et_2O (3 × 3 mL), and dried under reduced pressure to give the isocyanurate 1,3,5triphenyl-1,3,5-triazinane-2,4,6-trione (1) as a white solid.
- (31) Procedure for Recycling Experiment of Lithium Dibenzylamide: Phenyl isocyanate was added to a solution of lithium dibenzylamide (0.1 mol%) in Et₂O (30 mL) with stirring. The reaction mixture was stirred at r.t. for the allotted time and filtered via a canula filter. The Et₂O filtrate was subjected to a second reaction cycle. This procedure was repeated six times (for details see Table 3).