Monatshefte für Chemie 137, 1591–1595 (2006)
DOI 10.1007/s00706-006-0553-6

Monatshefte für Chemie
Chemical Monthly
Printed in Austria

Short Communication

The Performance of Phthalimide-*N*-oxyl Anion

Mohammad G. Dekamin[1,*], **Firouz M. Moghaddam**[2], **Hamdollah Saeidian**[2], and **Shadpour Mallakpour**[3]

[1] Organic Chemistry Research Laboratory, College of Chemistry, Iran University of Science and Technology, Tehran, Iran
[2] Department of Chemistry, Sharif University of Technology, Tehran, Iran
[3] Organic Polymer Chemistry Research Laboratory, College of Chemistry, Isfahan University of Technology, Isfahan, Iran

Received May 20, 2006; accepted June 8, 2006
Published online November 30, 2006 © Springer-Verlag 2006

Summary. Alkali metal salts of phthalimide-*N*-oxyl, including Li, Na, and K were prepared and applied as novel selective catalysts to promote the cyclotrimerization of aryl and alkyl isocyanates. This paper is addressing these salts as a new class of organic nucleophilic catalysts.

Keywords. Nucleophilic organocatalyst; Isocyanates; Potassium phthalimide-*N*-oxyl; Heterocycles.

Introduction

Designing of new specific catalysts and exploring their catalytic activity has caused profound effects in optimizing the efficiency of a wide range of organic transformations [1]. Development of such catalysts has resulted in more economical and environmentally friendly chemistry through replacing nonselective, unstable, toxic, or flammable catalysts [1, 2]. In this context, nucleophilic organocatalysts have achieved an outstanding place to promote many important organic reactions in recent years [1]. Among these catalytic systems, stable N-heterocyclic carbenes [3, 4] and proazaphosphatrane or its derivatives [5, 6] could be mentioned, which were developed in the recent two decades as phosphine mimics or counterparts.

Cyclotrimerization of isocyanates is one of the reactions which have been investigated with regard to efficient nucleophilic organocatalysts at the threshold of their application in organic synthesis [7, 8]. Isocyanates are very useful and

* Corresponding author. E-mail: mdekamin@iust.ac.ir

reactive substrates undergoing different reactions including conversion to carbodiimide, allophonate, urea, trimer, and dimer. Therefore, developing of catalysts which promote cyclotrimerization selectively is of great importance owing to its application in polymer industry [9, 10]. This arises from the significant effects of isocyanurate structure on the properties of the resulting polymers such as polyurethanes or polyureas [10, 11]. On the other hand, the resulting aromatic isocyanurate structure has unique properties such as rigidity, high symmetry, and low-toxicity, which have led recently to its applications in selective ion bonding, chiral discrimination, and medicinal chemistry [11, 12].

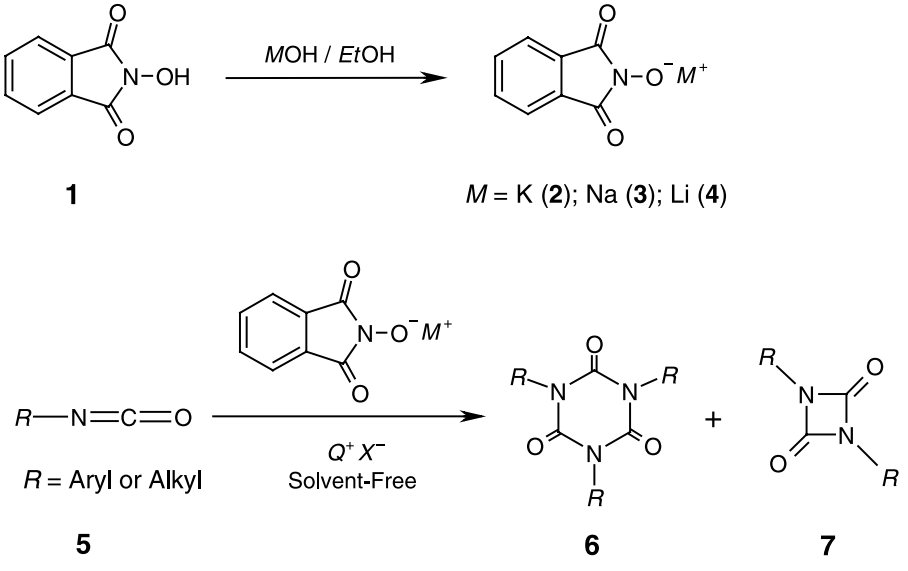
A part of our ongoing research is directed toward new readily available organic [11] and inorganic [13] nucleophilic catalysts for cyclotrimerization of aryl and alkyl isocyanates. Here we wish to report the first use of phthalimide-*N*-oxyl alkali-metal salts as selective nucleophilic organocatalysts for the cyclotrimerization of aryl and alkyl isocyanates under mild and solvent-free conditions.

Results and Discussions

Since *N*-hydroxyphthalimide (**1**) has a pK_a of 6.1, alkali-metal salts of **1**, including the potassium (**2**), sodium (**3**), and lithium (**4**) salts, could be readily prepared by adding **1** to a saturated solution of their corresponding hydroxides in *Et*OH (Scheme 1). Quantitative yields were obtained in all cases (*cf.* Ref. [14]).

The catalyst **2** demonstrated proper activity and solubility for the cyclization of phenyl isocyanate (**5a**), as model compound, under solvent-free conditions (Scheme 1).

Thus, upon heating a mixture of **5a** with only 0.05 mol% of **2**, 95% of the cyclotrimerization product, 1,3,5-triphenyl-1,3,5-triazine-2,4,6(1*H*,3*H*,5*H*)-trione (triphenyl isocyanurate, **6a**) [11], was selectively obtained at 70°C within 17 min.



Scheme 1

To optimize the reaction conditions, various factors, such as the effect of different mol% of the catalyst, temperature, and safer non-reactive solvent [8] were investigated.

Applying higher mol% of **2** decreased the required reaction time while a trace amount of dimer **7a**, as the kinetically controlled product, was formed at >0.2 mol% [7, 8]. The reaction time was also decreased by applying higher temperatures which in turn prefer formation of trimer, as the thermodynamically controlled product. On the other hand, the desired product **6a** was obtained within fewer minutes by using an equivalent amount of a tetraalkylammonium halide (*QX*) at 70°C. Formation of the dimer or substantial loss of yield was not observed under this situation. Therefore, diverse *QX*s, in terms of both halide and ammonium part size, were also investigated. Accordingly, tetraethylammonium bromide (*TEAB*) showed proper activity with slightly improving the yield. These results led us to perform the reaction at ambient temperature. In this situation a quantitative yield of the product was obtained. The significant advantage of the solvent-free conditions was noticed when the reaction was performed in dry toluene in the presence of *TEAB*. Under this situation, a lower yield and prolonged reaction time was observed. Also, **3** and **4** as counterparts of **2**, but with tighter cations were investigated at the optimized condition. These salts displayed their catalytic activity only in the presence of *QX*.

Other aryl isocyanates at optimized reaction condition (0.1 mol% **2**, 70°C) behaved properly. The applied temperature facilitated the reaction of solid substrates under solvent-free conditions (*e.g.* **5d** and **5e**, which melt below this temperature; Table 1).

Although, the so far introduced catalysts generally promote cyclization of phenyl isocyanate they do not efficiently catalyze the reaction of alkyl isocyanates displaying steric hindrance or even aryl isocyanates containing electron releasing groups. Therefore, exploring more effective catalysts for this purpose is a matter of challenge yet [8, 11]. In our hands, 4-methoxyphenyl isocyanate (**5b**) at optimal reaction conditions produced 86% of its corresponding isocyanurate **6b** within 17 min. 1-Naphthyl isocyanate (**5c**), which reacted by previous protocols after a rather long time, afforded 80% of its trimer **6c** in just 78 min [11]. On the other

Table 1. Cyclotrimerization of aryl and alkyl isocyanates at optimized conditions

Entry	Substrate	*R*	Time/min	Trimer	Isolated yield/%[a]
1	**5a**	Phenyl	7	**6a**	97
2	**5b**	4-Methoxyphenyl	17	**6b**	86
3	**5c**	1-Naphthyl	78	**6c**	80
4	**5d**	4-Chlorophenyl	6	**6d**	93
5	**5e**	3,4-Dichlorophenyl	4	**6e**	97
6[b]	**5f**	Ethyl	150	**6f**	82
7	**5g**	Butyl	240	**6g**	78
8	**5h**	Cyclohexyl	240	**6h**	48

[a] Average of at least two runs; [b] reaction was run at 50°C, below substrate boiling point

hand, aryl isocyanates containing electron withdrawing substituents, such as **5d** and **5e**, displayed even shorter reaction times. In general, the yields for cyclization of aryl isocyanates are good to quantitative. Alkyl isocyantes which could be cyclized only by a few catalysts afforded their respective isocyanurates in good yields using the novel catalyst system. However, the required reaction time is longer than for aryl isocyanates (Table 1, entries 6–8). It is noteworthy that the lower reactivity of cyclohexyl isocyanate (**5h**) seems to be related to its steric hindrance [8, 11a] as compared to **5f** or **5g**. Furthermore, it should be noted that preparation and storage of the catalyst is very convenient comparing to other catalysts [7, 8].

In conclusion, the catalytic performance of the alkali metal salts **2**–**4** as readily prepared and stored organonucleophilic catalysts for the cyclotrimerization of isocyanates was investigated for the first time. The catalytic performance of **2** is superior or comparable to the most efficient catalytic systems introduced so far. An easy and solvent-free route to prepare diverse and challenging isocyanurates at high to quantitative yields is thus established.

Experimental

All yields refer to the isolated ones based on an average of at least two runs. All reactions were protected from air moisture using a $CaCl_2$ tube. FT IR spectra were recorded as KBr pellets on a Nicolet Magna 550 spectrometer. A Bruker DRX-500 Avance (500 MHz) spectrometer was used to record the ^{1}H NMR spectra. All NMR spectra were determined in $CDCl_3$ or acetone-d_6 at ambient temperature. Chemical shifts (δ) were expressed in ppm relative to *TMS* ($\delta = 0.00$) and *J* values are given in Hz. GC-MS spectra were recorded on a HP 6890-HP 5973. Melting points were determined on a Büchi B540 apparatus. Analytical TLC was carried out using Fluka 0.2 mm silica gel 60 F-254 Al-plates. All substrates were purchased from Fluka or Merck and used as received except **5b**. This latter was synthesized according to Ref. [11]. After distillation, it was stored under dry condition. Dry ether was freshly distilled over Na and benzophenone.

*General Procedure for Preparation of Phthalimide-N-oxyl Salts **2–4***

To 1.00 g **1** (6.13 mol) dissolved in 20 cm^3 absolute *Et*OH an equivalent amount of KOH, NaOH, or LiOH was added. The mixture was refluxed, cooled, and the obtained precipitate was filtered. It was then washed with additional 10 cm^3 absolute *Et*OH. The yields were quantitative and the salts were dried under vacuum for 2 h at 70°C prior to use. ^{1}H NMR (500 MHz, D_2O): $\delta = 7.45$–7.31 (m, 4H); IR (KBr): $\bar{\nu} = 3057$, 1756, 1662, 1179, 1022, 992, 691 cm^{-1}.

General Procedure for Cyclotrimerization of Isocyanates

The procedure was identical to the one described in Refs. [11, 13] using 0.1 mol% **2** at 70°C. All of the products **6a**–**6h** are known and their physical constants and spectroscopic data were in agreement with their structures as described in Refs. [7, 8, 11].

Acknowledgements

M.G.D. gratefully acknowledges the Research Council of Iran University of Science and Technology (IUST), Iran, for financial support of this research.

References

[1] a) Grasa GA, Guvelli T, Singh R, Nolan SP (2003) J Org Chem **68**: 2812; b) Singh R, Kissling RM, Letellier M, Nolan SP (2004) J Org Chem **69**: 209
[2] Anastas PT, Bartlett LB, Kirchhof MM, Williamson TC (2000) Catal Today **55**: 11
[3] Arduengo AJ, Harlow RL, Kline M (1991) J Am Chem Soc **113**: 361
[4] For reviews see: a) Nair V, Bindu S, Sreekumar V (2004) Angew Chem Int Ed **43**: 5130; b) Enders D, Balensiefer T (2004) Acc Chem Res **37**: 534; c) Bourissou D, Guerret O, Gabbaï FP, Bertrand G (2000) Chem Rev **100**: 39
[5] Lensink C, Xi SK, Daniels LM, Verkade JG (1989) J Am Chem Soc **111**: 3478
[6] For reviews see: a) Verkade JG (2003) Top Curr Chem **233**: 1; b) Verkade JG, Kisanga PB (2004) Aldrichimica Acta **37**: 3
[7] Duong HA, Cross MJ, Louie J (2004) Org Lett **6**: 4679
[8] Tang JS, Mohan T, Verkade JG (1994) J Org Chem **59**: 4931
[9] Schwetlick K, Noack R (1995) J Chem Soc Perkin Trans 2, 395
[10] Wegener G, Brandt M, Duda L, Hofmann J, Klesczewski B, Koch D, Kumpf RJ, Orzesek H, Pirkl HG, Six, C, Steinlein C, Weisbeck, M (2001) Appl Cat A: Gen **221**: 303; b) Gite, VV, Mahulikar, PP, Hundiwale DG, Kapadi, UR (2004) J Sci Ind Res **63**: 348
[11] a) Matloubi Moghaddam F, Dekamin MG, Koozehgari G (2005) Lett Org Chem **2**: 734; b) Matloubi Moghaddam F, Koozehgiri G, Dekamin MG (2004) Monatsh Chem **135**: 849
[12] Guo Z, Wu D, Zhu YF, Tucci FC, Pontillo J, Saunders J, Xie Q, Struthersb RS, Chen C (2005) Bioorg Med Chem Lett **15**: 3685
[13] a) Dekamin MG, Mallakpour S, Ghassemi M (2005) Synth Commun **35**: 427; b) Dekamin MG, Mallakpour S, Ghassemi M (2005) J Chem Res 177
[14] a) Jencks WP, Carriuolo J (1960) J Am Chem Soc **82**: 1778; b) Roderick W, Brown WG (1957) J Am Chem Soc **79**: 5196