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An expeditious method for the selective cyclotrimerization of isocyanates initiated by TDAE

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ABSTRACT

We developed a rapid and green synthesis of various isocyanurates by cyclotrimerization of isocyanates using TDAE (tetrakis(dimethylamino)ethylene). TDAE displays excellent performance in catalytic quantities, affording the corresponding trimer of isocyanates very rapidly, under air and at room temperature in good to excellent yields.

1,3,5-Triazinane-2,4,6-triones or isocyanurates, with their high thermal stability, are used to enhance the physical properties of polyurethanes and coating materials.[1] Incorporation of isocyanurates into the framework of polyurethanes increases thermal and chemical resistance, flame retardation, as well as film-forming characteristics.[2] Isocyanurates are also employed in other areas such as chiral discrimination,[3] selective ion bonding,[4] and drug delivery.[5] Triaryl isocyanurates are often used as activators for the polymerization and postpolymerization of ε-caprolactam in the production of nylons with high melt viscosities.[6]

The general route for the preparation of isocyanurates is the cyclotrimerization of the corresponding isocyanates. A number of reports have been published concerning this method using a variety of different Lewis-basic catalysts, including phosphines,[7] amines,[8] NO,[9] alkoxyallenes,[10] fluoride anions,[11] *p*-toluenesulfinates,[12] carbamate anions,[13] cyanates,[14] and *N*-heterocyclic carbenes.[15] Organometallic catalysts such as lithium amides,[16] alkylzinc amines and alkoxides,[17] tin complexes,[18] palladium(0),[19] copper(II) and nickel(II) halides[9] also allowed the cyclotrimerization of isocyanates. But, many of the known cyclotrimerization procedures suffer from low catalyst activity, diazetidine byproduct formation, lengthy reaction times, product separation difficulties, and the use of toxic solvents.[15,20]

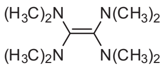

Figure 1. Structure of TDAE.

Therefore, developing catalysts which promote cyclotrimerization selectively is of great importance due to wide application of isocyanurate structure in both industry and academic studies.[1–6]

Tetrakis(dimethylamino)ethylene[21] (Fig. 1) is an electron-rich organic reductant, which reacts with halogenated derivatives to generate an anion under mild conditions via two sequential single electron transfers.

During our investigation of 9-bromofluorene addition to phenyl isocyanate in the presence of TDAE, we discovered that TDAE allowed the cyclotrimerization of isocyanates to their respective isocyanurates. Herein, we report further details about this efficient and straightforward isocyanurate synthesis using commercially available TDAE.

Phenyl isocyanate **1a** was used as a model substrate for the optimization of the cyclotrimerization conditions and the results are summarized in Table 1. We first carried out a reaction using an equimolar amount of TDAE and phenyl isocyanate in anhydrous THF at room temperature. The conversion, monitored by TLC, was complete after 15 min. A complex mixture was obtained and triphenylisocyanurate **2a** was isolated in only 25% yield (entry 1). Using 40 mol % of TDAE resulted in a small decrease of the

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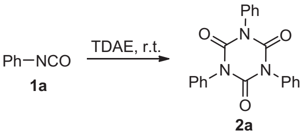
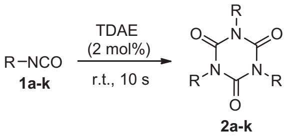
Table 1
Optimization of the cyclotrimerization of phenyl isocyanate initiated by TDAE

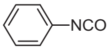
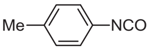
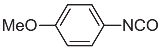
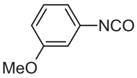
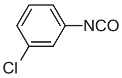
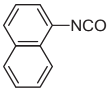
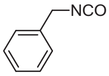
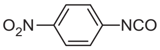
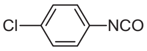
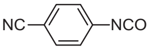
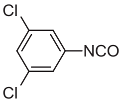


Entry	TDAE (mol %)	Solvent	Time	% Yield[a] **2a**
1	100	THF	15 min	25[b]
2	40	THF	15 min	35[b]
3	15	THF	15 min	69[b]
4	15	Cyclohexane	15 min	63[b]
5	15	*n*-Heptane	15 min	70[b]
6	15	Diethyl ether	15 min	46[b]
7	15	Ethyl acetate	15 min	71[b]
8	15	Ethyl acetate	15 min	69[c]
9	15	None	10 s	67[c]
10	5	None	10 s	80[c]
11	2	None	10 s	81[c]
12	2	Ethyl acetate	15 min	70[c,d]
13	None	None	12 h	16[c]

[a] Isolated yields.
[b] Reactions were performed under nitrogen at room temperature using 2 mL of anhydrous non-degassed solvent.
[c] Reactions were performed under air at room temperature.
[d] Reaction was performed with 0.5 mL of ethyl acetate.

Table 2
Scope of the cyclotrimerization of various isocyanates



Entry	RNCO	Solvent	% Yield[a,b] **2a–k**
1		None	81 **2a**
2		None	95 **2b**
3		None	92 **2c**
4		None	94 **2d**
5		None	91 **2e**
6		None	91 **2f**
7		None	93 **2g**
8		EtOAc	81[c] **2h**
9		EtOAc	76[c] **2i**
10		EtOAc	90[c] **2j**
11		EtOAc	82[c] **2k**

[a] Isolated yields.
[b] Reactions were performed under air at room temperature.
[c] 0.5 mL of EtOAc was used and the reaction was stirred for 15 min.

by-product proportions and allowed **2a** in 35% yield (entry 2). With 15 mol % of TDAE, a dramatic improvement was observed and **2a** was isolated in 69% yield (entry 3). A variety of solvents were screened (entries 4–7) and ethyl acetate gave the best result (71% yield, entry 7). Performing the reaction under air gave a similar yield than under nitrogen (entry 7 vs 8).

Then, we explored the possibility to run the reaction without solvent under air with 15 mol % of TDAE. After 10 s, the mixture became completely solid, so the reaction was stopped. Interestingly, trimer **2a** was isolated in a yield similar to those obtained with ethyl acetate as the solvent (entry 8 vs 9). This encouraging finding prompted us to investigate the influence of TDAE amount under solvent-free conditions and air. Decreasing the amount of TDAE from 15 mol % to 5 mol % resulted in a slight improvement (80% yield, entry 10). No significant effect was observed between 5 mol % and 2 mol % of TDAE (entry 10 vs 11). Using a small amount of ethyl acetate as solvent resulted in a slightly lower yield of trimer **2a** (entry 12). A control experiment without catalyst (entry 13) showed the importance of TDAE to achieve good yields.

So, the method developed here is very simple, fast, and environmentally-friendly as it allowed the formation of the trimer under air at room temperature in only 10 s without solvent. Furthermore, separation of the desired product was achieved by simply triturating and filtering the crushed reaction mixture with cold diethyl ether and water, successively.

With the optimized conditions in hand, we proceeded to investigate the substrate scope of the reaction. The results are shown in Table 2.[22] Under the optimized solvent-free reaction conditions, a variety of liquid isocyanates were converted to the corresponding isocyanurates in very good yields (entry 1–7). Both electron-donating and electron-withdrawing substituents on the aryl group are well tolerated. Interestingly, a benzyl substituent gave also a very good 93% yield of the corresponding isocyanurate **2g** (entry 7).

The reactivity of solid isocyanates was then studied with the optimized conditions. But, our preliminary attempt with nitrophenyl isocyanate, previously powdered in a mortar with a pestle, and 2 mol % of TDAE at room temperature, did not allow the formation of the corresponding isocyanurate **2h**. So, we further investigated the use of a minimum amount of solvent. When 2 mol % of TDAE was added to a solution of nitrophenyl isocyanate in 0.5 mL of ethyl acetate under air, the corresponding trimer **2h** was isolated in 81% yield (entry 8). With these new conditions for solid isocyanates in hand, the scope of the cyclotrimerization using a variety of solid isocyanates was explored and gave good to excellent yields of the corresponding isocyanurates **2i-k** (entry 9–11).

Based on the ability of TDAE to give electrons and on a recent Letter showing that the trimerization of isocyanates can be initiated by an electron,[23] we propose a similar mechanism involving an anion radical intermediate formed by donation of an electron of TDAE to the isocyanate.

In conclusion, commercially available TDAE has been used for the first time to catalyze the cyclotrimerization of a wide range of aryl isocyanates and benzyl isocyanate to isocyanurates in high yield. The important features of our method are: solvent-free conditions with liquid isocyanates, mild reaction conditions under air, very short reaction time, and simple purification procedure.

Acknowledgments

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22. *General procedure for liquid isocyanates* ***2a–g:*** TDAE (9.3 μL; 0.04 mmol; 2 mol %) was added to a vial containing the isocyanate (2 mmol) under air at room temperature with vigorous stirring. The mixture became completely solid after 10 seconds. The crude mixture was then crushed and 6 mL of cold diethyl ether was added followed by 1 minute stirring. After filtering and washing with additional diethyl ether and water, successively, the desired isocyanurate was isolated by simple filtration without further purification.

    General procedure for solid isocyanates ***2h–k:*** To a solution of isocyanate (2 mmol) in EtOAc (0.5 mL) was added TDAE (9.3 μL; 0.04 mmol; 2 mol %) under air at room temperature with vigorous stirring. After 15 min, the solvent was evaporated under reduced pressure. The resulting mixture was then crushed and 2 mL of cold diethyl ether was added followed by 1 min stirring. After filtering and washing with additional diethyl ether and water, the desired isocyanurate was isolated by simple filtration without further purification.

    Analyses for compounds **2a**, **2b**, **2c**, **2e**, **2f**, **2g**, **2h**, **2i**, and **2j** are in agreement with those reported in the literature.[16,24–26]

    1,3,5-tris-(3-Methoxyphenyl)-1,3,5-triazinane-2,4,6-trione ***2d:*** mp 210 °C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.44–7.35$ (m, 3H), 7.02–6.92 (m, 9H), 3.82 (s, 9H); ^{13}C NMR (50 MHz, $CDCl_3$): 160.3, 148.4, 134.4, 129.9, 120.5, 115.4, 114.1, 55.4.

    1,3,5-tris(3,5-Dichlorophenyl)-1,3,5-triazinane-2,4,6-trione ***2k:*** mp 179 °C; ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.51–7.49$ (t, $J = 1.8$ Hz, 3H), 7.31 (d, $J = 1.8$ Hz, 6H); ^{13}C NMR (50 MHz, $CDCl_3$): 147.2, 135.8, 134.3, 130.3, 127.4.

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