

Chapter 4

Generation of Organic Isocyanates from Amines, Carbon Dioxide, and Electrophilic Dehydrating Agents

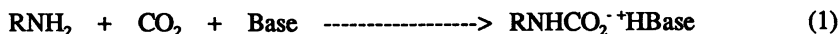
Use of *o*-Sulfobenzoic Acid Anhydride

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Isocyanates are produced on the billions of pounds scale annually and are generated almost exclusively via phosgenation technology. The reaction of an amine with phosgene has several drawbacks, including the high toxicity of phosgene and the generation of HCl. The use of carbon dioxide as a phosgene replacement has been explored, and conditions for the highly selective synthesis of isocyanates from carbamate anions (generated from amines and carbon dioxide) have been found using various "dehydrating agents". One of the goals is not only to eliminate the use of phosgene in the production of isocyanates but also to eliminate salt waste. The initial results will be presented along these lines by the use of recyclable dehydrating agents.

In previous accounts the use of electrophilic dehydrating agents in the direct generation of isocyanates from amines and carbon dioxide has been discussed, equations 1-2 (1-3).

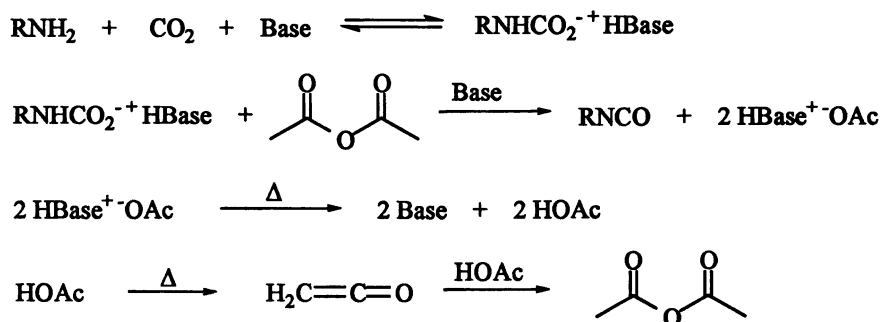


This chemistry was shown to proceed with the highest selectivities and yields using phosphorus containing electrophiles (POCl_3 , PCl_3 and P_4O_{10}). Although this provided a relatively low cost, mild route to new materials, a large amount of salt waste was generated. Subsequently the use of non-halide and potentially low to no waste reagents capable of achieving the same high selectivities and yields of isocyanates (4) has been explored.

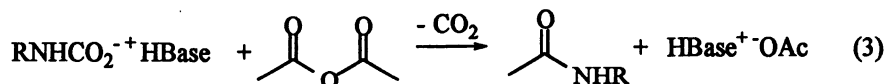
Introduction

From the outset of this research the use of organic anhydrides as dehydrating agents (i.e., acetic anhydride) was investigated with the idea of a “no waste” process for the generation of isocyanates via “dehydration” of carbamates (see Scheme I).

Scheme I



Although isocyanates were generated, the use of acetic anhydride, unfortunately, showed selectivities which were not of practical use (competitive generation of amide, see equation 3).



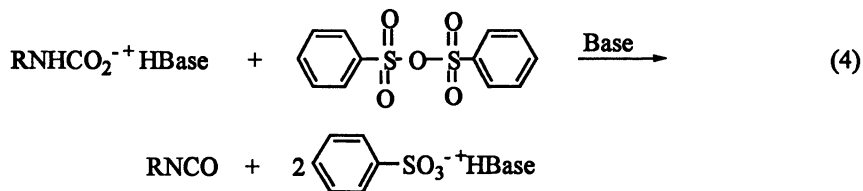
Previous results clearly suggested that the leaving group ability on the anhydride plays an important role in the generation of isocyanates (see Table I).

Table I. “Dehydration” of Amines to Isocyanates Using Organic Anhydrides

RNH ₂	Anhydride	Base	%NCO
octyl-NH ₂	acetic	CyTEG	40
octyl-NH ₂	acetic	NEt ₃	2
octyl-NH ₂	benzoic	CyTEG	65
octyl-NH ₂	benzoic	NEt ₃	22
octyl-NH ₂	trifluoroacetic	CyTEG	95
octyl-NH ₂	trifluoroacetic	NEt ₃	35

All reactions were run in acetonitrile under 80 psig carbon dioxide at 0°C (CyTEG = N-cyclohexyl-N',N',N'',N''-tetraethylguanidine).

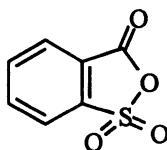
The ability of an acetate group to act as a leaving group has been well established to be relatively poor in comparison to the excellent leaving group ability of the alkyl (aryl) sulfonates. Use of a sulfonate leaving group in the anhydrides gave excellent yields and selectivities of isocyanates (i.e., benzenesulfonic acid anhydride gave essentially quantitative yields of isocyanates under mild conditions), equation 4.



Unlike acetic anhydride, benzene sulfonic acid anhydride can not be generated from the parent acid via a thermal dehydration. This regeneration of anhydride is a critical step in a waste free process. Therefore, a dehydrating agent capable of high selectivity toward isocyanate generation and one which showed the ability toward thermal regeneration was sought.

Results and Discussion

Based on its availability and structural nature, investigation of the “dehydrating” power of *o*-sulfobenzoic acid anhydride (I) was carried out. The parent acid may be readily available as an intermediate in the synthesis of saccharin (5). The cyclic nature of this anhydride along with its half sulfonic/ half benzoic composition hinted to us that it may prove to be a suitable compound for the present isocyanate technology.



I

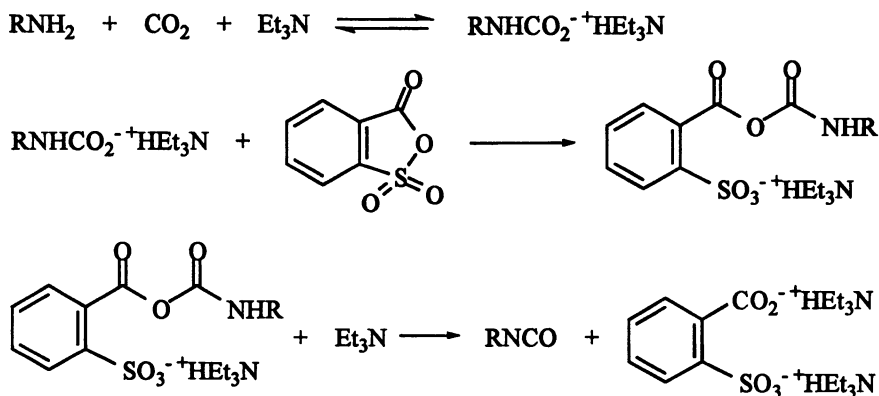
The results of the use of this anhydride in model reactions is summarized in Table II below. This reagent gave rise to high yields and selectivities of isocyanates under mild conditions.

Table II. Conversion of Amines to Isocyanates Using *o*-Sulfobenzoyl Chloride

RNH ₂	%NCO
n-octyl-NH ₂	95
cyclohexyl-NH ₂	100
triaminononane	83-92
HMD	70-80

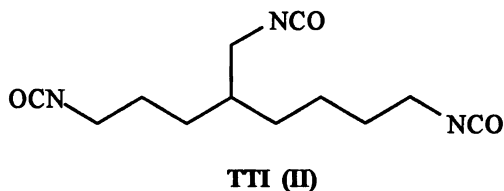
All reactions run in acetonitrile using an excess of triethylamine as base under 80 psig carbon dioxide pressure at -10°C (triaminononane = 4-aminomethyl-1,8-octanediamine, HMD = 1,6-diaminohexane).

Ideally, the reaction proceeds as shown in Scheme II depicted below.

Scheme II

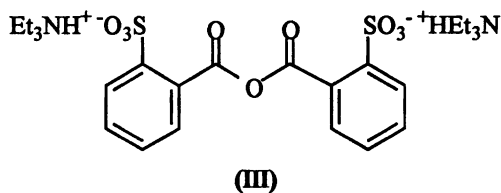
This reaction is thought to proceed via nucleophilic attack of the carbamate anion at the anhydride giving rise to a mixed anhydride which then undergoes base induced elimination to the corresponding isocyanate. The assumption that the intermediate is that resulting from nucleophilic attack at the carboxylic carbonyl rather than the sulfonyl site is based on literature precedence (6).

Extension of the use of this reagent to the synthesis of TTI (triaminononane tris-isocyanate) was investigated.

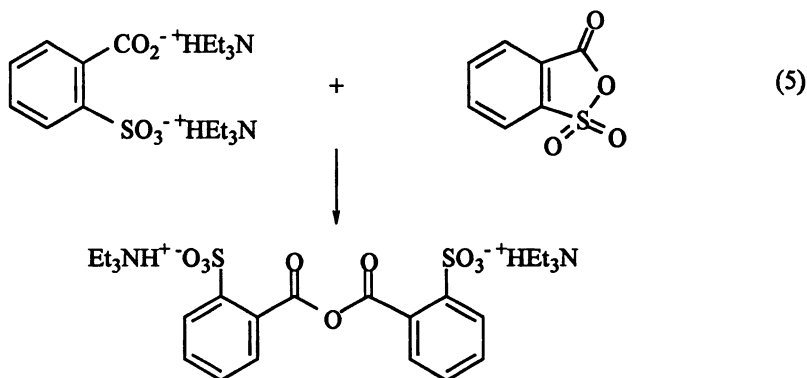


The results for the reaction of triaminononane - tris carbamate with *o*-sulfobenzoic acid anhydride gave high yields of TTI (TAN triisocyanate)(7-8). This isocyanate has been evaluated as a low viscosity, low vapor pressure crosslinking agent in coating applications (9).

In the synthesis of this isocyanate using the above mentioned "dehydration" technology it was observed that an increase in isocyanate yield with an increase of one to two equivalents of anhydride (per reactive nitrogen) was found which was somewhat surprising. Insight into the cause of this result was gained by identifying the by-product of the reaction. Interestingly, it is the linear anhydride (III) which is the result of this dehydration reaction and not the sulfonate/benzoate as expected.

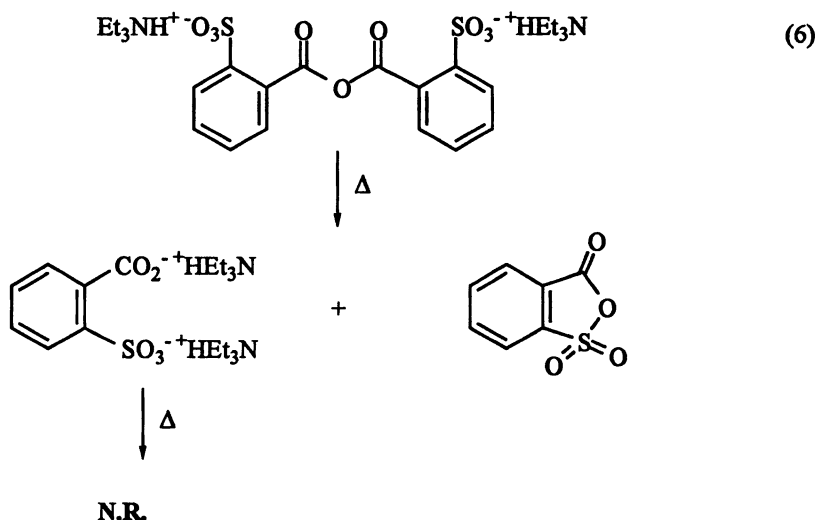


A reasonable explanation for the formation of the substituted benzoic acid anhydride from this reaction lies in competitive nucleophilic attack of generated carboxylate on the *o*-sulfobenzoic acid anhydride as shown below (10) in equation 5.



Independent confirmation of the plausibility of this reaction was demonstrated by the addition of an equal molar amount of the dianion of *o*-sulfobenzoic acid to the anhydride giving the same linear benzoic anhydride. This result points out that attack of the carboxylate is competitive with carbamate attack on the cyclic anhydride. The generation of linear anhydride does not appear to affect the production of isocyanate.

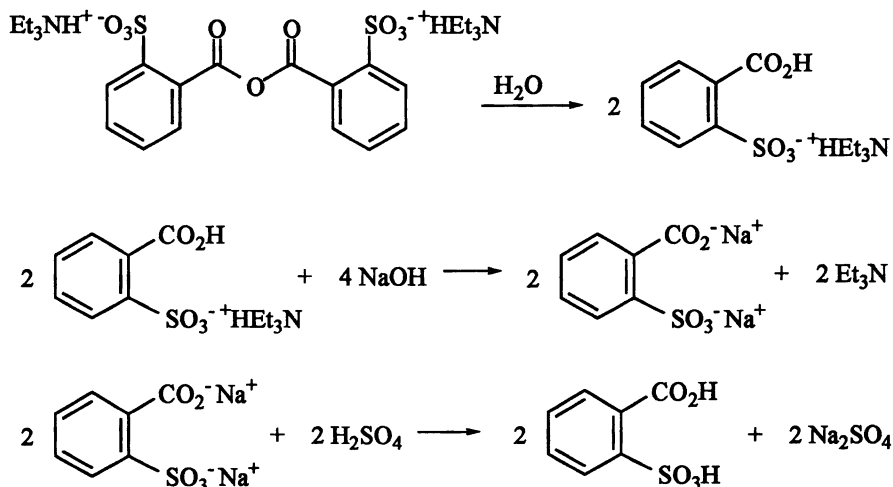
Thermal Reaction of Linear Anhydride. The most desirable and simplest scenario for regeneration of *o*-sulfobenzoic acid anhydride is the thermal cracking of the salt obtained, followed by thermal dehydration to the anhydride. Attempts to thermally effect this conversion have not been successful. Heating the linear anhydride in the solid state under a nitrogen purge generates one equivalent of *o*-sulfobenzoic acid anhydride and one equivalent of the sulfonate/benzoate as shown in equation 6. This is the reverse reaction of that observed for the formation of anhydride.



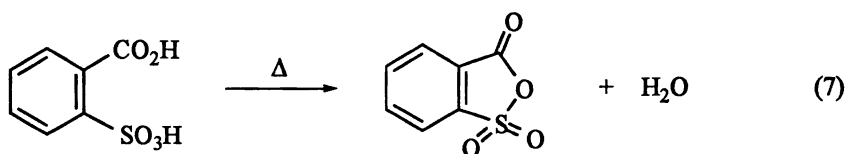
The anhydride sublimes out of the reaction leaving a heavy oil which was identified by IR. This result is consistent with the thermal gravimetric results obtained from the same linear anhydride. Continued heating of the remaining salt does not lead to any productive chemistry.

Conversion of Linear Anhydride to *o*-Sulfobenzoic Acid Anhydride. Critical to the successful use of *o*-sulfobenzoic acid anhydride as a dehydrating agent for the production of isocyanates is the ability to recycle the anhydride. Since direct conversion from the isolated by-product appears to be unlikely, another pathway must be demonstrated. A reasonable route is shown below in Scheme III, and progress in each of the steps shown has been made.

Scheme III

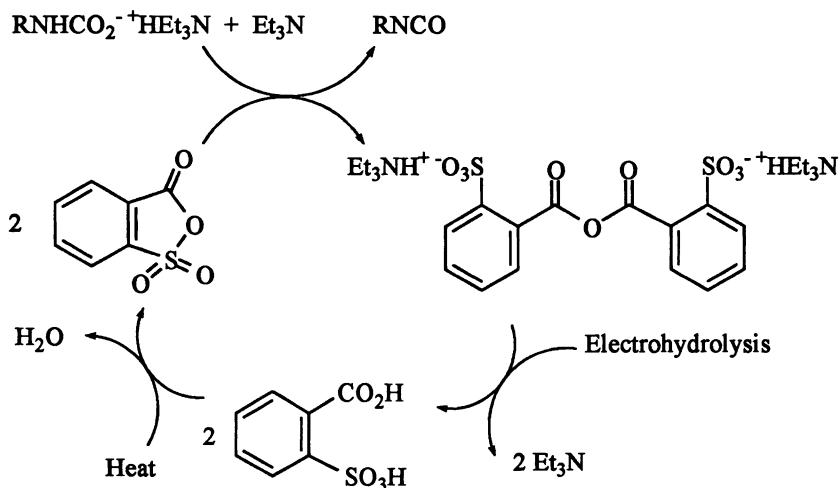


This route involves hydrolysis of the linear anhydride into the mono-triethylammonium salt followed by neutralization with caustic soda (or calcium hydroxide) to liberate the triethylamine giving the sodium salt of *o*-sulfobenzic acid. This salt is then converted to the free acid via protonation by sulfuric acid (or on an ion exchange column, regeneration of the ion exchange resin involves addition of a strong acid such as sulfuric acid). The free acid is then dehydrated thermally (driven by a physical removal of generated water) to *o*-sulfobenzic acid anhydride (11) as shown in equation 7.



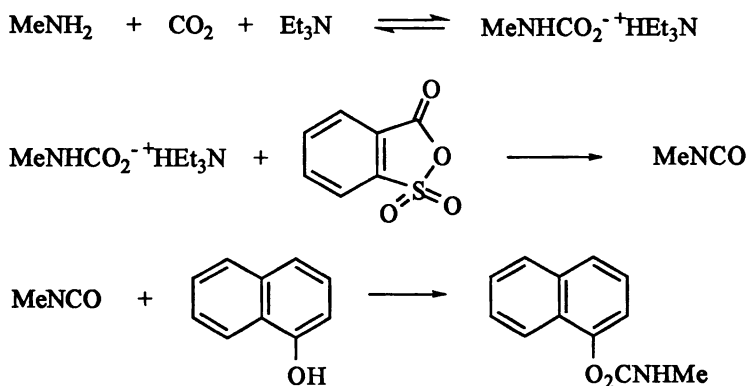
The above results show that a recyclable dehydrating agent for the high conversion of amines to isocyanates using carbon dioxide can be used; however, the use of sodium hydroxide (or calcium hydroxide) in the recycle of anhydride and for the recovery of triethylamine gives rise to salt by-product (sodium or calcium sulfate). To circumvent this salt generation one can envision a process that utilizes a "salt splitting" step (electrohydrolysis) (12). Use of this technology would create a process whereby we could generate isocyanates from amines and carbon dioxide with water as the sole by-product (see Scheme IV below).

Scheme IV



***In situ* trapping of isocyanate.** The mild conditions of the “dehydration” reaction using *o*-sulfobenzoic acid anhydride provided an opportunity to look at generating isocyanates *in situ* followed by immediate conversion of the isocyanate into urethane materials. This method may prove to be valuable for the generation of materials based on toxic, volatile isocyanates (i.e. methyl isocyanate). An example is shown below in Scheme V(13) which shows the formation of 1-naphthyl N-methylcarbamate (common insecticide).

Scheme V



Experimental

Hexamethylene diisocyanate. Into a 3-neck round bottomed flask was charged 2.0 g (17 mmol) hexamethylenediamine, 15 mL triethyl amine (109 mmol), 0.262 g (1.7 mmol) biphenyl as G.C. internal standard and 100 mL acetonitrile. The three-neck flask was fitted with an overhead stirrer, a CO₂ gas inlet, a thermocouple and a dryice condenser. Into the dryice condenser was added a dryice/*m*-xylene slush bath (-48°C). Carbon dioxide was added subsurface to the reaction mixture at room temperature giving rise to a heterogeneous solution. Over 90 min. the reaction mixture was cooled to 0°C and then to -20°C (*o*-xylene/dryice bath). Once equilibration was established at -20°C *o*-sulfobenzoic acid anhydride (12.5 g, 68 mmol) was added as a solid slowly over a 30 min period. Aliquots were taken periodically and were quenched by the addition of toluene/aq. HCl followed by analysis by G.C. (78%).

1-Naphthyl N-methylcarbamate. Into a Fischer-Porter bottle was charged 2 g methyl ammonium methyl carbamate (19 mmol - 38 mmol methylamine equivalent; generated from methyl amine and carbon dioxide), 16 g triethylamine (158 mmol) and 75 mL CH₃CN. This was attached to a pressure head and 60 psig carbon dioxide was added above the reaction mixture giving rise to an exothermic reaction. Into a second Fischer-Porter bottle was added 13.9 g *o*-sulfobenzoic acid anhydride in 40 mL CH₃CN. After one hour both solutions were cooled to ca. -14 °C using an ice/salt bath. The solution of the anhydride was added all at once to the carbamate solution (exothermic reaction). The ice/salt bath was removed and after 15 min a solution of 8.14 g 1-naphthol (56 mmol) in 40 mL CH₃CN was added to the reaction mixture. The crude reaction was allowed to stir at room temperature for 18 h after which time the pressure was released and the crude mixture was poured into 500 mL 0.5 M aq. HCl. The resulting precipitate was collected by filtration, washed with water and air dried giving 5.68 g (75%) of 1-naphthyl N-methylcarbamate.

Conclusions

A suitable "dehydrating" agent for the highly selective conversion of amines and carbon dioxide into their corresponding isocyanates has been described which eliminates the use of the toxic reagent phosgene. The use of *o*-sulfobenzoic acid anhydride as the dehydrating agent has also provided a process which recycles the dehydrating agent, thereby potentially eliminating large amounts of salt waste. This technology has also allowed the generation of novel isocyanate materials of interest to the coatings industry, in particular the isocyanate derived from 4-aminomethyl-1,8-diaminooctane (triaminononane), TTI. The use of this particular reagent has also led to a method for the *in situ* trapping of volatile isocyanates (methylisocyanate) which precludes the need for isolation of these toxic reagents.

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