Tetrahedron Letters, Vol. 33, No. 6, pp. 733-736, 1992 Printed in Great Britain

N-CYANOIMIDES: REACTIVITY STUDIES WITH AMINE NUCLEOPHILES

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ABSTRACT: N-Cyanoimides are useful precursors to N-alkyl or N-aryl imides. Treatment of aromatic N-cyanoimides such as N-cyanophthalimide (1) with primary amines provides N-substituted imides directly, while aliphatic N-cyanoimides afford diamide intermediates which can be converted to N-substituted imides upon heating.

The synthesis of N-substituted imides by thermal or chemical dehydration of amide-acids is a well known and industrially important process². The precursory amide-acids, often referred to as "amic acids", are the condensation products of cyclic anhydrides with primary amines. While relatively simple, this imide forming process requires either the addition of dehydrating reagents or the application of heat, often in excess of 200 °C. In polymer related applications the evolution of water as a by-product is also a problem and under many circumstances requires careful monitoring of the cure conditions.^{2c}

The desire to avoid such problems has been a driving force for investigating the use of activated imides as precursors for N-substituted imides. For example, N-(carboethoxy)-N'-phenylphthalimide has been shown to yield phthaloylamino acids when treated with amino acids under mild conditions.³ The reaction with aniline, however, yielded N-phenylphthalimide, N-(carboethoxy)-N'-phenylphthalamide, or an isoindolin-3-one derivative depending on the pH or temperature of the reaction.^{4a} The latter two can be converted to the imide by heating in the range of 150-180 °C. N,N'-Bis(carboethoxy)pyromellitimide has been treated with aromatic diamines to yield a polyamide, but again the application of high temperatures was required for the imidization step.^{4b} Replacement of the carboethoxy group in both of the previous examples with a benzenesulfonyl group has been shown to increase the rate of the initial condensation, and to lower the imidization temperature to as low as 80 °C or even room temperature when in the presence of a basic catalyst.⁵

We have investigated the feasibility of using N-cyanoimides as precursors of N-alkyl or Naryl imides. We felt that the nitrile group might similarly activate imides towards transimidization and would provide cyanamide instead of benzenesulfonamide or ethyl carbamate as a leaving group.

In our initial model study we found that treatment of N-cyanophthalimide $(1)^6$ with aniline at room temperature did not yield the expected intermediate diamide 2, but instead afforded Nphenylphthalimide (3) directly.⁷ If one follows this reaction by ¹H NMR, one observes the clean conversion of 1 to 3. No other products, except cyanamide, are observed.⁸ This would imply that the initial condensation is slow compared to the loss of cyanamide in the cyclization. A control reaction using phthalic anhydride in place of 1 gave the corresponding amide-acid as expected.



As expected, the relative rate of reaction can be controlled by the nucleophilicity of the amine. As shown below a 2:1 mixture of N-cyanophthalimide and an aromatic diamine were combined in THF a allowed to stir at 50 °C for the length of time given in Table 1. The resulting diimide products were then isolated by simple filtration.



In the case of 4-aminophenyl ether, the reaction is rapid and complete in just a few hours, but for electron poor diamines such as 4-aminophenyl sulfone, the reaction is quite slow.

Table 1: Reaction of N-Cyanophthalimide (1) with Aromatic Amines			
	Ar	Rxn Time	Yield
4		18 h	70 %
5		48 h	35 %
6		24 h	66 %

In the contrasting case of simple cyclic N-cyanoimides such as N-cyanosuccinimide $(7)^9$ or N-cyanoglutarimide (10),¹⁰ it is possible to isolate the acyclic diamide products such as 8 and 11. As shown below, treatment of 7 with either butylamine or aniline provides the diamides 8a and 8b respectively.



Analysis of 8a by differential scanning calorimetry (DSC) reveals a well defined melting endotherm at 120 °C, followed by an exothermic reaction, exotherm maximum at 125 °C. A second scan exhibited no residual reactivity up to 200 °C. An additional sample, about 50 mg, of 8a was heated to 150 °C for 10 minutes. Analysis of the resulting dark mixture suggests a blend mostly containing N-butylsuccinimide (9) and unreacted 8a. Presumably cyanamide was eliminated during the cyclization, but because of its thermal instability, this was not conclusively proven. Thermal analysis of compound 8b exhibited only an exotherm at about 180 °C, cyclization taking place immediately upon melting. Using high temperature NMR techniques (150 °C, deuterated nitrobenzene), the rapid conversion of 8b to N-phenylsuccinimide was observed.

A similar situation was found for N-cyanoglutarimide (10). As shown below, treatment of 10 with either n-butylamine or aniline provides the diamides 11a and 11b respectively. Thermal analysis of both diamides reveals an endothermic melting transition followed by an exothermic reaction. For 11a the melting endotherm maximum was 71 °C, with an exothermic maximum of 130 °C, and for 11b the endo- and exotherms were at 120 °C and 143 °C.



The case of the bicyclic N-cyanoimide 13 is less clear cut.⁶ It was found that treatment of 13 with aniline provided a 3:1 mixture of the diamide 14 and the imide 15.



These studies clearly demonstrate the feasibility of using aromatic and aliphatic Ncyanoimides as anhydride equivalents in the preparation of substituted imide and, ultimately, polyimides. Differences in the reactivity of aromatic and aliphatic N-cyanoimides and amine nucleophiles were observed and would offer different utility.

Further, compared to its benzenesulfonyl analog,⁵ N-cyanophthalimide (1) offers at least two advantages. First, being more water soluble than benzenesulfonamide, the cyanamide produced by the reaction of 1 with a primary amine can be completely removed by an aqueous wash, thus simplifying imide isolation. Second, in the preparation of polyimide/epoxy blended adhesives, cyanamide released from a polyfunctional N-cyanoimide functions as an active curing agent for the epoxy resin component and not as an inert plasticizer in the resulting polymer matrix.^{6a}

References and Notes

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- 7. A procedure for the conversion of 1 to 3 is as follows. To a solution of N-cyanophthalimide (1.00 g, 5.8 mmol) in 40 mL of THF was added aniline (1.00 mL, 10.9 mmol). The solution was allowed to stir overnight, transferred to a separatory funnel and partitioned between EtOAc and 2 N hydrochloric acid. The organic phase was dried (MgSO₄) and concentrated to afford 1.03 g (80%) of 3. This material was spectroscopically identical to an authentic sample of 3.
- 8. A mixture of N-cyanophthalimide in deuterated DMSO and a 20 fold excess of freshly distilled aniline was monitored by ¹H NMR until more than 90% of the starting N-cyanoimide had been consumed. No signals other than those derived from the starting materials and the expected products, N-phenylphthalimide and cyanamide were observed.
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- 10. A procedure for the preparation of N-cyanoglutarimide (10) is as follows. To a solution of glutaryl dichloride (26.30 g, 156 mmol) in 100 mL of THF, cooled using an ice/salt bath, was added a solution of cyanamide (12.00 g, 285 mmol) in 100 mL of THF over a 20 minute period. The ice bath was removed and the mixture was allowed to stir for 5 h. The slurry was partitioned between 2 N hydrochloric acid and a 1:1 mixture of ethyl acetate/hexanes. The organic phase was dried (MgSO₄) and concentrated to afford 12.34 g of a pink solid. The crude product was recrystallized from 50 mL of ethyl acetate to afford 9.43 g (44%) of light pink flakes, mp 127-129 °C: IR (KBr) 2264, 1771, 1743, 1730; ¹H NMR (200 MHz, DMSO) ∂ 1.96 (quintet, 2 J = 6.5 Hz), 2.74 (t, 4, J = 6.5 Hz); ¹³C NMR (50 MHz, DMSO) ∂ 170.39, 104.01, 31.24, 15.47; GC/MS *m/e* (relative intensity) 138 (56.3), 110 (16.4), 70 (34.1), 69 (10.3), 68 (16.2), 55 (25.2), 42 (100).