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NOVEL CATALYSIS OF o-NITROPHENYL CARBONATES BY p-DIMETHYLAMINOPYRIDINE

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Summary Transesterification reactions of o-nitrophenyl carbonates have been found to be greatly facilitated by use of p-dialkylaminopyridines as catalysts. A 20-fold rate increase is observed using 0.01 eq. of p-dimethylaminopyridine in place of 2.00 eq of triethylamine. Such rate enhancement is not observed with p-nitrophenyl carbonates 2.00 eq of Et_3N causes reaction to occur 8.5 times faster than 0.01 eq of DMAP. DMAP catalyzed reactions of o-nitrophenyl carbonate have been used to prepare aromatic carbonates at 0° in high yields, and avoid the necessity of using 2 equiv. of base.

Carboxylic acid esters of o- and p-nitrophenol, 2,4-dinitrophenol, and 2,4,6-trinitrophenol have been used as activated substrates for transesterification or peptide synthesis for a number of years.[1] We are currently interested in transesterification reactions of aromatic carbonates, and thus were interested in these activated substrates. The carbonates of p-nitrophenol and 2,4-dinitrophenol have been used to prepare urethanes,[2] and in peptide synthesis.[3] The known reactions of these carbonates use a full equivalent of base, and ultimately form an amide bond (either a urethane or an amide).

Our first attempts to form symmetric carbonates from reaction of o- or p-nitrophenyl carbonate with phenol and catalytic base failed. Initial attack of phenoxide affords the nitrophenoxide anion, which precipitates from solution.

Reaction to form diphenyl carbonate occurs when 2 equivalents of triethylamine are used. Reaction of p-nitrophenyl carbonate with two moles phenol and two moles of Et_3N at 0° in CH_2Cl_2 yields diphenyl carbonate quantitatively, affording about a 50% yield in 4 hours. However, ortho nitrophenyl carbonate (o-NPC) reacts at less than half the rate, under the same conditions only 20% diphenyl carbonate is formed in 4 hours (see Figure 1).

In order to try to enhance the reactivity of the nitrophenyl carbonates, we used dimethylaminopyridine (DMAP) as the catalyst. DMAP is a strongly nucleophilic amine, although it is less basic than Et_3N.[4] In acylation of alcohols and hydrolysis of esters, rate enhancements of $\sim 10^4$ are typically seen using DMAP rather than pyridine.[4] When we used 2 eq of Et_3N and 0 01 eq of DMAP as the catalyst, only a slight rate enhancement was noted with p-nitrophenyl carbonate (see Figure 1).[5] However, o-NPC was activated to a large extent a 100% yield of diphenyl carbonate was obtained in 3 hours at 0°!

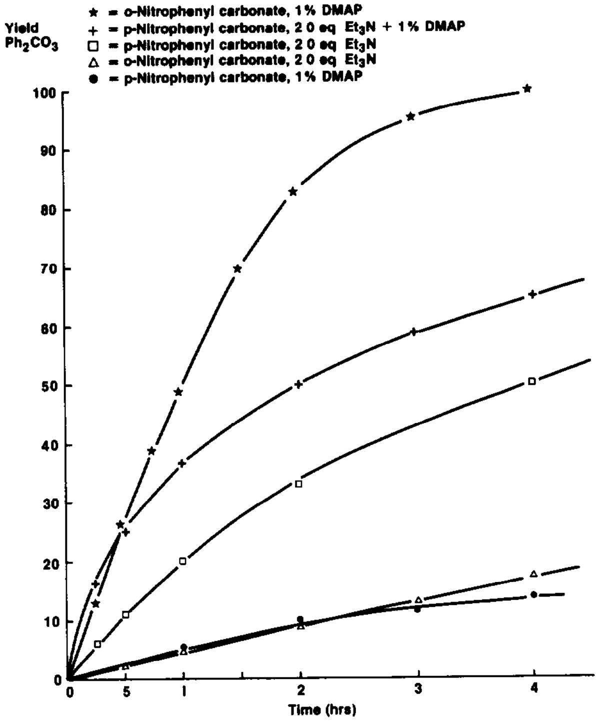


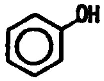
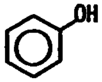
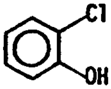
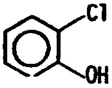
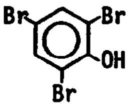
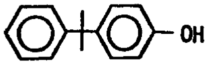
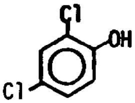
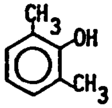
Figure 1 **Preparation of Diphenyl Carbonate from Nitrophenyl Carbonates at 0° in CH_2Cl_2**

We were pleasantly surprised to find that reactions of o-NPC with phenols catalyzed by DMAP do *not* require a stoichiometric amount of base. *No decrease in rate or yield* are observed in reactions using *1% DMAP* if no Et_3N is used. This is not the case using *para*-nitrophenyl carbonate, the reaction rate drops by a factor of 17 if no Et_3N is used. Use of o-NPC with DMAP thus allows a fast, clean reaction to form aromatic carbonates at ambient temperature. Typical results are summarized in Table I. The reaction is so thermodynamically favorable that even activated carbonates (o-chlorophenyl, 2,4-dichlorophenyl) are formed in quantitative yield at 25°.

Selection of the proper catalyst is crucial to the reaction. Only strongly nucleophilic bases are effective at low temperatures. We found that a nucleophile rather than a Bronsted base is required for catalysis. DMAP acts by attacking the carbonyl group to form an activated acyl ammonium ion,[4] which is in turn attacked by the phenol to afford products (Scheme 1). Triethylamine does not form an activated carbonyl, and is dependent on an acid-base equilibrium to form phenoxide ion, which is the attacking species.

TABLE I

Formation of Aromatic Carbonates from Nitrophenyl Carbonates[a]

Phenol	Substrate[b]	Time (hr)	Aromatic Carbonate Yield[c]
	o-NPC	2	100
	p-NPC	48	52[d]
	o-NPC	2	99.5
	p-NPC	48	23[e]
	o-NPC	8	95[f]
	o-NPC	2	97[f]
	o-NPC	20	92
	o-NPC	24	17[g]

[a] Reaction in CH_2Cl_2 at 25° using 1 mole % DMAP.

[b] o-NPC = o-nitrophenyl carbonate; p-NPC = p-nitrophenyl carbonate.

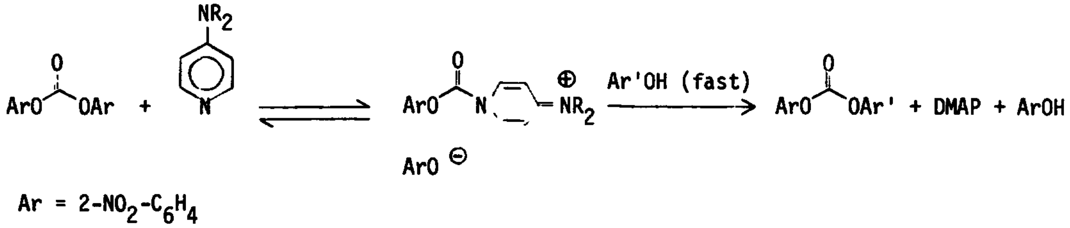
[c] vpc yield unless noted.

[d] 44% mixed carbonate and 4% S.M. were also obtained.

[e] 58% mixed carbonate and 19% S.M. were also obtained.

[f] Isolated yield.

[g] 83% mixed carbonate was also obtained.



SCHEME 1

The dissimilarity in the effects of DMAP catalysis in the reactions of ortho- and para-nitrophenyl carbonates is striking. Whereas 2 equivalents of triethylamine cause p-nitrophenyl carbonate to react about twice as fast as o-NPC, use of 1.0 mole % DMAP causes o-NPC to react 42 times faster than the para isomer. Furthermore, addition of 2.0 eq of Et_3N to a reaction of o-NPC catalyzed by 1.0% DMAP causes no increase in rate, similar addition to a p-nitrophenyl carbonate reaction affords a 17-fold rate increase. Clearly, reaction of o-NPC with DMAP occurs by a different mechanism than reaction of p-nitrophenyl carbonate with Et_3N. A likely explanation is a stabilization of the tetrahedral intermediate carrying delocalized positive charge by the adjacent ortho-nitro group (Figure 2). Evidence for this hypothesis is that only tertiary amines which can form delocalized acyl ammonium salts (DMAP, DBU, DBN, N-methyl imidazole, and 4-pyrrolidinopyridine) are effective catalysts. Further details will be published in a forthcoming report.

We are currently exploring the utility of DMAP catalysis in the reactions of o-nitrophenyl esters. Preliminary results indicate that DMAP also effectively catalyzes reactions of ortho-nitrophenyl esters in the formation of esters and amides.

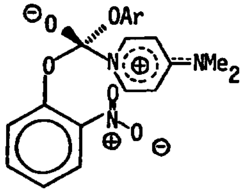


Figure 2

References

1. Numerous examples are available; see (a) T. Widland, B. Heinke, K. Vogeler, Ann. 655, 189 (1962), R. Glattard, M. Matter, Helv., 46, 795 (1963), (b) F. H. C. Stewart, Chem. Ind., (1967) 1960, (c) M. Bodanszky, V. du Vigneaud, Biochem. Prep., 9, 110 (1963), (d) M. Bodanszky, K. W. Funk, M. L. Fink, J Org. Chem., 38, 3656 (1973); (e) M. Bodanszky, M. Kondo, C. Y. Lin, G. F. Sigler, ibid., 39, 444 (1974).
2. (a) E. P. Nesynor, P. S. Pel'kis, Zh. Obshch, Khim., 32, 4004 (1962); (b) A. Dultsch, O. Ferno, Swed. 128, 292 (1950).
3. R. Glatthard and M. Matter, Helv. Chim. Acta, 46, 795 (1963).
4. G. Hofle, W. Steglich, H. Vorbruggen, Angew. Chemie., Int. Ed. Eng., 17, 569 (1978), and references cited therein. pKa pyridine = 5.29, pKa DMAP = 9.70; pKa Et_3N = 10.65.
5. Hofle, et al. (Reference 4) state that DMAP does not enhance reactivity of p-nitrophenyl esters.

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