and alcohols[15]) raises the question that solvated electrons may be involved in reduction reactions by metals in basic solvents. It is recognized that such reactions may be driven to completion because basic atoms in the solvent molecules complex with metal ions. Now it is likely that ionization of metals is facilitated in all these media by electron solvation, the mean lifetimes of the solvated electrons changing among the different solvents, and that the reducing species is the solvated electron.

The utility of HMPA as a medium for Birch[16] reductions is under investigation.

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(16) A. J. Birch, *Quart. Rev.* (London), **4**, 69 (1950); H. S. Smith, "Organic Reactions in Liquid Ammonia," Interscience Publishers, Inc., New York, N. Y., 1963, pp. 151–279.

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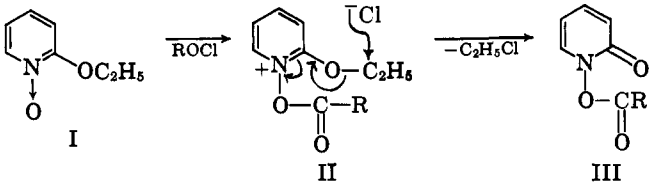
A New Class of Activated Esters. The 1-Acyloxy-2(1H)-pyridones[1]

Sir:

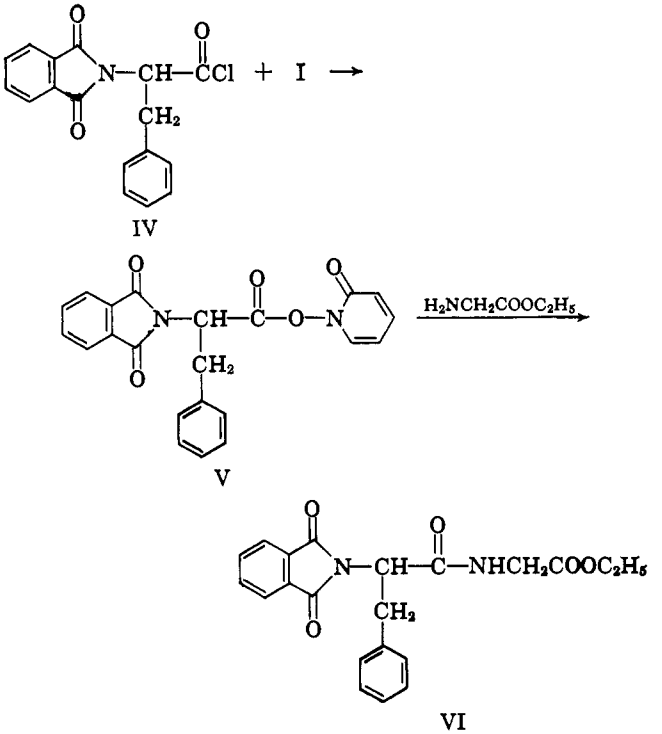
Electrophilic attack of acyl halides on 2-ethoxypyridine 1-oxide (I) has been found to proceed exothermally with the evolution of ethyl chloride to produce 1-acyloxy-2(1H)-pyridones (III) in excellent yields. The reaction undoubtedly involves a mechanistic pathway of the type illustrated in structure II.[2] For example, slow addition of I to acetyl chloride at room temperature resulted in an immediate evolution of gas and produced in 86% yield 1-acetoxy-2(1H)-pyridone (III, R = CH_3), m.p. 93–94°,[3] ν^{Nujol} 1800 and 1655 cm.$^{-1}$



(ester and amide carbonyls, respectively).[4] Similarly, benzoyl chloride afforded 1-benzoyloxy-2(1H)-pyridone (III, R = C_6H_5), m.p. 140°,[3] ν^{Nujol} 1780 and 1670 cm.$^{-1}$, in 93% yield.[6]

It is now well documented[7] that increased reactivity in nucleophilic reactions involving carbonyl groups is paralleled by a marked shift of the infrared absorption of the carbonyl bands toward shorter wave lengths. The infrared data relating to the ester carbonyls of III most strikingly indicate that these substances must be activated esters. This has been found to be the case. Thus, dissolution of the acetyl derivative in a minimum quantity of purified water at room temperature resulted in the quantitative deposition of colorless crystals of 1-hydroxy-2(1H)-pyridone. With *n*-butyl alcohol and *n*-butylamine extremely facile transfer of acetyl from III (R = CH_3) was also observed.

The high reactivity of the 1-acyloxy-2(1H)-pyridones can also be applied to the construction of peptide units. For example, reaction of phthaloyl-L-phenylalanyl chloride (IV)[8] with I afforded a quantitative yield of the



activated ester V which, in turn, was readily condensed with glycine ethyl ester to give a 79.7% yield (from IV) of optically pure phthaloyl-L-phenylalanylglycine ethyl ester (VI), $[\alpha]^{29}D$ −145° (in EtOH). Consequently, carboxyl activation of amino acids *via* 1-hydroxy-2(1H)-pyridone esters appears suitable for the synthesis of peptides and could find application in those cases where liberation of the elements of hydrogen chloride is not desirable. Furthermore, esters of type III are particularly attractive because of their very high reactivity, their high crystallinity, and especially because of the high water solubility of the N-hydroxy-2(1H)-pyridone by-product.[9]

(1) Unsaturated Heterocyclic Systems, part XIV. For part XIII, see L. A. Paquette, and L. D. Wise, *J. Am. Chem. Soc.*, in press.

(2) This mechanism is formally analogous to that by which 2-ethoxypyridine is converted by alkyl halides into 1-alkyl-2(1H)-pyridones; see L. A. Paquette and N. A. Nelson, *J. Org. Chem.*, **27**, 1085 (1962).

(3) Satisfactory analyses were obtained for all new compounds.

(4) Preparation of III (R = CH_3) by an unequivocal route was achieved by acetylating 1-hydroxy-2(1H)-pyridone[5] with acetic anhydride.

(5) G. T. Newbold and F. S. Spring, *J. Chem. Soc.*, 1864 (1948).

(6) A wide variety of other acyl halides has also been employed with equal success.

(7) H. A. Staab, *Angew. Chem. Intern. Ed. Engl.*, **1**, 351 (1961).

(8) J. C. Sheehan, D. W. Chapman, and R. W. Roth, *J. Am. Chem. Soc.*, **74**, 3822 (1952), report $[\alpha]^{29.5}D$ −146° for VI.

(9) It should be noted that the 1-acyloxy-2(1H)-pyridones represent the latest class of activated esters based upon hydroxylamine which have been recently studied: (a) esters of N-hydroxyphthalimide: G. H. L. Nefkens and G. I. Tesser, *ibid.*, **83**, 1263 (1961); G. H. L. Nefkens, G. I. Tesser, and R. J. F. Nivard, *Rec. trav. chim.*, **81**, 683 (1962); (b) esters of N-hydroxysuccinimide: G. W. Anderson, J. E. Zimmerman, and F. M. Callahan, *J. Am. Chem. Soc.*, **85**, 3039 (1963); **86**, 1839 (1964); (c) esters of oximes: G. Losse, A. Baeth, and K. Schatz, *Ann.*, **677**, 185 (1964).

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