

sion about an amide linkage and torsion about the N-O bond.

On the one hand, the observation of barriers to rotation in **2** and **3** makes the suggestion that torsional barriers may account for the observed nonequivalence in other hydroxylamine derivatives seem reasonable. On the other hand, it may be argued<sup>18</sup> that the magnitude of the barriers observed for **2** and **3** suggests that the somewhat higher barriers observed for trialkylhydroxylamines derive from another hindered conformational interchange, namely nitrogen inversion. However, we note that torsional barriers as well as inversion barriers seem to be subject to substituent effects. In particular the torsional barriers in *N,N*-(dialkyl)trichloromethanesulfenamides are lowered by about 3 kcal/mol when the two alkyl groups are replaced by the diacyl succinimide ring.<sup>14d</sup> If the replacement of the *N*-alkyl groups by the pyridone ring were to result in a comparable lowering of the N-O torsional barrier we would expect the torsional barriers in trialkylhydroxylamines to be about 11–12 kcal/mol, which is very close to the barriers observed. Because of these, as yet poorly understood, substituent effects on torsional barriers we do not believe that comparisons of this sort offer convincing evidence concerning the nature of the rate-determining step in topomerization of trialkylhydroxylamines in the absence of confirming evidence.

We do not believe that it is possible, at this time, to definitively assign the barriers to topomerization in trialkylhydroxylamines to either slow inversion or slow rotation. The evidence accumulated thus far seems to indicate that both inversion and rotation barriers are substantial in compounds containing N-O single bonds. Given the probability that substituents and solvents can affect the shape of the conformational energy surface it seems possible that subtle changes in structure and medium should be capable of shifting from a torsional transition state for topomerization to an inversional one or vice versa.

### Experimental Section

Elemental analyses were performed by Midwest Microlab, Inc. Nmr spectra were measured on a Varian A-60A spectrometer, in toluene-*d*<sub>6</sub> solution. Temperatures were calibrated using methanol spectra as described in the Varian manual. Melting points were measured on a Thomas-Hoover melting point apparatus. *N*-Benzyloxy-*N*-methylaniline (**3**) was prepared as described in the literature.<sup>22</sup> Both *N*-isopropoxy-2(1*H*)-pyridones were prepared in a manner similar to that described by Paquette.<sup>23</sup>

***N*-Isopropoxy-2(1*H*)-pyridone (2a).**—Pyridone **2a** was synthesized from 2-ethoxypyridine *N*-oxide<sup>24</sup> by treatment of the latter with excess 2-bromopropane and heating under reflux for 4 days. The mixture was distilled under reduced pressure and a fraction boiling at 69–72° (0.2 mm) was collected (80%). This material was shown by its nmr spectrum to be a 5:2 mixture of **2a** and *N*-ethoxy-2(1*H*)-pyridone which resulted from rearrangement of the starting material. Chromatography of 0.30 g of distillate on 25 g of silica gel (3:1 hexane-acetone eluent) afforded 0.20 g of pure **2a**.

*Anal.* Calcd for C<sub>8</sub>H<sub>11</sub>NO<sub>2</sub>: C, 62.73; H, 7.24; N, 9.14. Found: C, 62.28; H, 7.52; N, 8.98.

**2-Chloro-6-ethoxypyridine *N*-Oxide (4).**—2-Chloro-6-ethoxypyridine *N*-oxide (**4**) was synthesized from commercial 2-chloro-6-ethoxypyridine by hydrogen peroxide-trifluoroacetic acid ox-

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

idation, using a procedure described for the oxidation of substituted pyridines.<sup>25</sup> The crude oxide was purified by chromatography on alumina (chloroform eluent), and then crystallized from a benzene-hexane mixture, mp 93.5–95°.

*Anal.* Calcd for C<sub>7</sub>H<sub>8</sub>ClNO<sub>2</sub>: C, 48.43; H, 4.65; Cl, 20.42; N, 8.07. Found: C, 48.21; H, 4.72; Cl, 20.26; N, 8.03.

***N*-Isopropoxy-6-chloro-2(1*H*)-pyridone (2b).**—Oxide **4**, (0.5 g) was dissolved in 10 ml of 2-bromopropane, and the mixture was refluxed for 24 hr. The excess alkyl bromide was removed under vacuum, and chromatography of the remaining dark oil on 25 g of silica gel (3:1 hexane-acetone eluent) afforded 0.10 g of **2b**.

*Anal.* Calcd for C<sub>8</sub>H<sub>10</sub>ClNO<sub>2</sub>: C, 51.21; H, 5.37; N, 7.47. Found: C, 51.45; H, 5.60; N, 7.49.

**Registry No.**—**2a**, 32846-47-2; **2b**, 32846-48-3; **4**, 32846-49-4.

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## A Comparison of the Electronic Effects of Substituents Bonded to Annular Nitrogen and Carbon Atoms

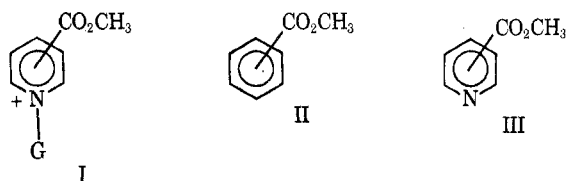
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Much is known about the electronic effects exerted by meta and para substituents bonded to carbon.<sup>2</sup> By comparison, very little is known about the electronic effects exerted by the same groups bonded to an annular nitrogen atom.<sup>3</sup>

We have determined the rates of hydroxide ion catalyzed hydrolysis of esters **I** where the *N* substituents, CH<sub>3</sub>O, CH<sub>3</sub>, and O<sup>-</sup>, are meta and para to the reactive center.<sup>4</sup> Comparison of our results with those for esters **II**<sup>5</sup> provides an insight into the ability of a positively charged annular nitrogen atom to transmit resonance and inductive effects.



Kinetic studies were carried out using a pH-Stat. In the case of the para *N*-methyl ester, the hydroxide ion concentration was varied by a factor of 8 and the second-order rate constant, *k*<sub>2</sub>, was found to be given

(1) On leave from LaTrobe University, Melbourne, Australia.

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(4) Results for hydrolysis in 70% ethanol-water of **I** (G = O<sup>-</sup>) and **III** have been reported by P. R. Falkner and D. Harrison: *J. Chem. Soc.*, 1171 (1960). Hydrolysis is considerably faster in water.

(5) Results for oxide ion esters **II** can be predicted using substituent constants reported by J. Hine, *J. Amer. Chem. Soc.*, **82**, 4877 (1960).

TABLE I  
CONDITIONS AND RESULTS OF THE HYDROXIDE ION CATALYZED HYDROLYSIS OF META AND  
PARA *N*-SUBSTITUTED ESTERS IN WATER AT 25.0° AND 0.5 *M* IONIC STRENGTH<sup>a</sup>

G	Registry no.	pH	$k_2, M^{-1} \text{ min}^{-1}$	$k_{rel}$	$k_p/k_m$
<i>p</i> -O <sup>-</sup>	3783-38-8	9.7-10.1	$5.8 \times 10^2$	1.0	0.67
<i>m</i> -O <sup>-</sup>	15905-18-7	9.7-10.0	$8.6 \times 10^2$	1.5	
<i>p</i> -CH <sub>3</sub>	7630-02-6	7.5-8.4	$3.2 \times 10^4$	55.0	9.1
<i>m</i> -CH <sub>3</sub>	4685-10-3	9.1-9.3	$3.5 \times 10^3$	6.0	
<i>p</i> -CH <sub>3</sub> O	32812-78-5	8.0-8.4	$4.2 \times 10^4$	72.0	4.5
<i>m</i> -CH <sub>3</sub> O	32785-04-9	8.7-9.0	$9.4 \times 10^3$	16.0	
<i>b</i>	2459-09-8	10.4-10.5	$2.2 \times 10^2$	0.38	4.5
<i>c</i>	93-60-7	10.9-11.0	$4.9 \times 10^1$	0.084	

<sup>a</sup> pOH = 14.30 - pH. <sup>b</sup> Methyl 4-pyridinecarboxylate. <sup>c</sup> Methyl 3-pyridinecarboxylate.

by  $k/[\text{OH}^-]$ , where  $k$  is the observed pseudo-first-order constant. This means that the hydrolysis of the ester is catalyzed only by hydroxide ion under the conditions employed.<sup>6</sup> The  $k_2$  values given in Table I represent the average of two experiments at the indicated pH; the average deviation is <10%. Nmr experiments employing a phosphate buffer solution of the para *N*-methoxy ester showed that only ester hydrolysis takes place; no side products were detected.<sup>7</sup>

In order to obtain a measure of the activating effect of the positive charge in I, the hydrolysis of meta and para methyl pyridinecarboxylates (III) also was studied (Table I).<sup>4</sup> Comparison with the results for the *N*-methyl esters indicates that the positive charge increases reactivity by a factor of about 100. The para ester is more reactive than the meta ester in both types of compounds, suggesting activation of the para positions by a resonance effect.

The results for I indicate that there is a 72-fold spread in reactivity with the para *N*-oxide ester being the least and the para *N*-methoxy compound being the most reactive. The nature of the electronic effects of the *N* substituents is revealed by a comparison of the positional rate constants. It is assumed that the electronic effects of the substituents are superimposed on the effects of the annular nitrogen atom and the positive charge. Relative to the *N*-methyl compound, the methoxy group activates while the oxide substituent deactivates meta positions in both I and II, indicating the presence of inductive effects. A methoxy group is activating relative to a methyl group in para positions of I but the opposite order is found in II. This result clearly indicates that the resonance effect of the methoxy group is less important in the heterocyclic series. A similar conclusion has been advanced concerning the importance of resonance effects in *N*-alkoxy pyridinium ions on the basis of ground state infrared studies.<sup>8</sup> That resonance effects do operate in I is seen by the para/meta ratio which decreases in the order CH<sub>3</sub>, CH<sub>3</sub>O, and O<sup>-</sup>. A reduced resonance effect for an uncharged group on a positively charged annular nitrogen atom is readily understandable. Electron delocalization by such a process places a positive charge on the group and this is inhibited electrostatically by the adjacent positive charge on the nitrogen atom.

It is clear that the electronic effects of substituents on a positively charged annular nitrogen atom can be quite different from those on an annular carbon atom.

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### Experimental Section

**Compounds.**—*N*-methyl esters were prepared from the esters and methyl iodide in methanol and were recrystallized from ethanol: 1-methyl-3-carboxymethylpyridinium iodide, mp 130° (lit.<sup>9</sup> mp 129.5-130.2°); 1-methyl-4-carboxymethylpyridinium iodide, mp 180-181° (lit.<sup>10</sup> mp 179°). *N*-oxide esters were prepared by *N* oxidation of the esters using H<sub>2</sub>O<sub>2</sub>-CH<sub>3</sub>CO<sub>2</sub>H: 3-carboxymethylpyridine 1-oxide, mp 101-102° (lit.<sup>10</sup> mp 101-102°); 4-carboxymethylpyridine 1-oxide, mp 115-117° (lit.<sup>10</sup> mp 118-119°). *N*-methoxy esters were prepared from the *N*-oxide esters using dimethyl sulfate by minor variations of a method used to prepare similar compounds.<sup>7</sup> These compounds were isolated as perchlorate salts. Ether aided precipitation of the perchlorate salts, though initial precipitation was induced only at -70° in the case of 1-methoxy-4-carboxymethylpyridinium perchlorate, mp 71-72° (ethanol). *Anal.* Calcd for C<sub>8</sub>H<sub>10</sub>ClNO<sub>7</sub>: C, 35.9; H, 3.7; O, 41.9. Found: C, 35.8; H, 3.8; O, 41.6. 1-Methoxy-3-carboxymethylpyridinium perchlorate had mp 88-89° (ethanol). *Anal.* Found: C, 36.1; H, 3.8; O, 41.7.

**Rates of Ester Hydrolysis.**—Reactions were followed using a Radiometer TTT-1c titrator operating in the pH-Stat mode. Reaction mixtures consisted of ester and 0.5 *M* KCl. Complete reaction represented the addition of ~0.45 ml of 0.1 *M* KOH to 25 ml (initial) of the reaction mixture. Constant temperature (25.0°) was maintained by circulation of water about the titration cell. Pseudo-first-order rate plots were obtained by the Guggenheim method;<sup>11</sup> they were linear over 2-3 half-lives.

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## Organic Mass Spectrometry. I. Retro-1,3-dipolar Cycloaddition Reaction Induced by Electron Impact

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The mechanistic interrelation between the two important electrocyclic reactions, Diels-Alder and the 1,3-dipolar cycloaddition, is of current interest.<sup>1</sup> Although it is well established that both reactions are

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