

DIELS-ALDER ADDUCTS FROM N-UNSUBSTITUTED TAUTOMERIC 2(1H)-PYRIDONE-2-HYDROXYPYRIDINES;  
5,6-BENZO-2-AZABARRELENONES AND 5,6-BENZO-2-AZABARRELENES

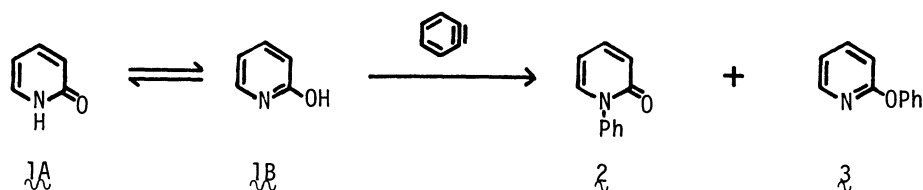
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Diels-Alder reactions of several N-unsubstituted tautomeric 2(1H)-pyridone-2-hydroxypyridines with benzyne were examined and found to afford 5,6-benzo-2-azabarrelenones, which were converted to hitherto unknown 5,6-benzo-2-azabarrelenes.

It is now well established that  $\lambda$  exists largely in the 2(1H)-pyridone tautomeric form  $\lambda^A$  in solution,<sup>1</sup> whereas there is no significant difference in the fundamental stabilities of the tautomers,  $\lambda^A$  and  $\lambda^B$  in the gas phase.<sup>2</sup>

A study of the Diels-Alder reactivity of these compounds with a highly reactive dienophile such as benzyne is of interest because reactions could provide insight into the structure-reactivity relationship of the tautomeric equilibrium. Furthermore, the resulting adducts probably could be converted to hitherto unknown 5,6-benzo-2-azabarrelene derivatives, which seem to be otherwise difficultly accessible and which contain many interesting physical and chemical features for study.

In contrast to the substantial amount of experimental work on the Diels-Alder reaction of N-substituted-2(1H)-pyridones with a variety of dienophile in recent years,<sup>3</sup> little attention has been focussed on similar reactions of N-unsubstituted-2(1H)-pyridones.<sup>4</sup> Earlier attempts at such reactions with benzyne were unsuccessful and resulted only in the formation of N-phenyl-2(1H)-pyridone ( $\lambda$ ) and 2-phenoxy pyridine ( $\lambda$ ) in rather poor yield.<sup>5</sup> Interest in reactions of this type seems to have declined thereafter.



We have studied the Diels-Alder reaction of one series of 4-phenyl substituted-2(1H)-pyridones of ( $4a-e$ ) with benzyne, and found that these compounds in fact underwent the Diels-Alder reaction with ease to give 5,6-benzo-2-azabicyclo[2.2.2]octadien-3-one derivatives (5,6-benzo-2-azabarrelenones), ( $5a-e$ ). Success in this reaction is not only of interest in its own way, but also it opens a convenient route to 5,6-benzo-2-azabarrelenes.

The Diels-Alder reactions of  $4$  with benzyne were carried out according to the procedure reported by Bauer and co-workers.<sup>3a</sup> Work-up and chromatographic separation (alumina, benzene eluent) led to isolation of two products which were identified as  $5a-e$ , and 2-phenoxy pyridines ( $6a-e$ ). Surprisingly, N-phenyl-2(1H)-pyridones were not isolated experimentally. The

structures of the adducts  $\bar{5}$  follow from their spectral properties.<sup>6,7</sup> Further proof for the structures of  $\bar{5}$  were provided by their facile conversion to N-methyl derivatives  $\bar{7}$  on treatment with methyl iodide. These products were also obtained from the reaction of 1-methyl-2(1H)-pyridones ( $\bar{8}$ ), derived from the methylation of  $\bar{4}$ , with benzyne. These reaction sequences are shown below, and the results, including those of methylation of  $\bar{4}$ , are summarized in Table I.

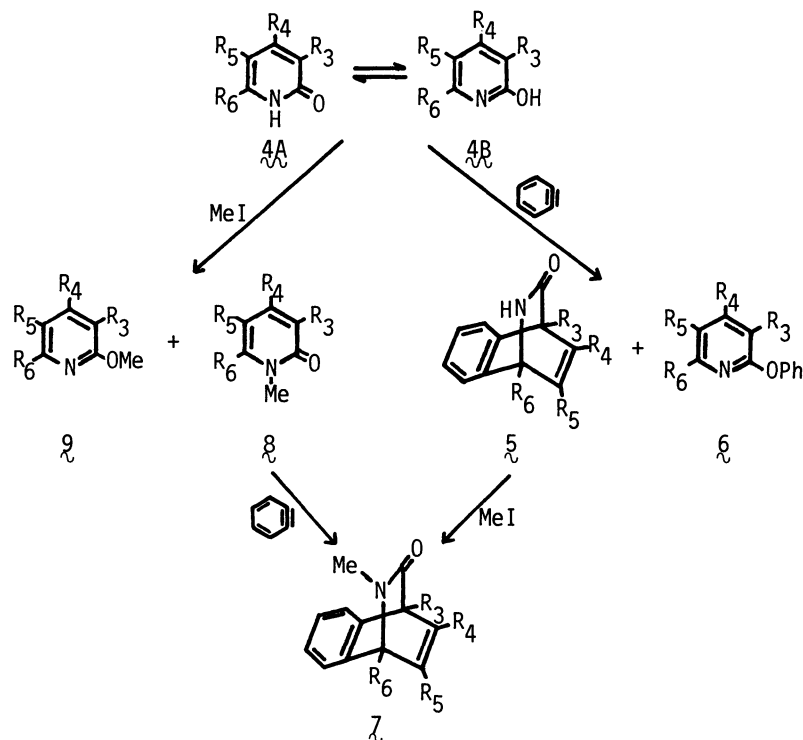


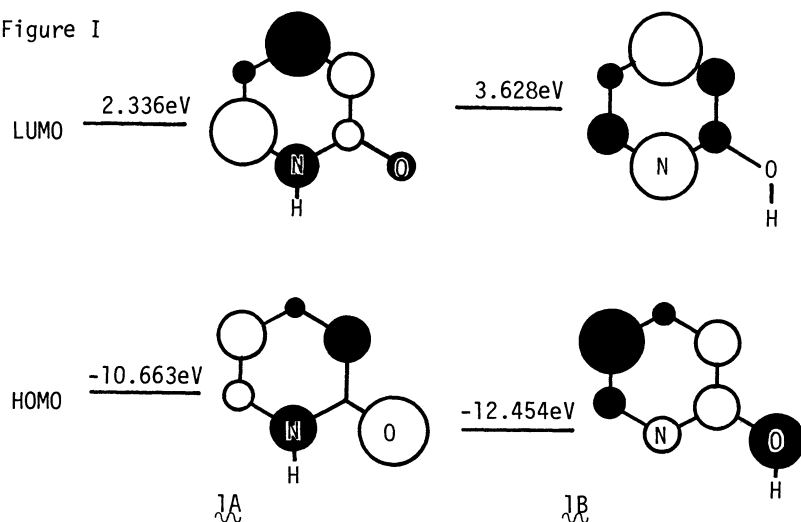
Table I. Product Distributions from Reaction of N-unsubstituted-2(1H)-Pyridones with Benzyne and Methyl Iodide<sup>a</sup>

2(1H)-Pyridones <sup>b</sup>	Substituents	Product Yield <sup>c</sup>		Product Ratios <sup>d</sup>	
		$\bar{5}$	$\bar{6}$	N-Me %	O-Me %
$\bar{1}$	$R_3=R_4=R_5=R_6=H$	0	5.0 <sup>f</sup>	95	5 <sup>g</sup>
$\bar{4a}$	$R_3=R_5=H, R_4=Ph, R_6=Me$	10.6	14.6	90	10
$\bar{4b}$	$R_3=R_6=Me, R_4=Ph, R_5=H$	12.9	8.5	91	9
$\bar{4c}$	$R_3=R_5=R_6=Me, R_4=Ph$	38.0	29.0	75	25
$\bar{4d}$	$R_3=Me, R_4=Ph, R_5\sim R_6=-(CH_2)_4-$	28.6	33.6	87	13
$\bar{4e}$	$R_3=Me, R_4=Ph, R_5\sim R_6=-(CH_2)_3-$	35.0	16.9	89	11

a. Methylations were carried out in DMF/K<sub>2</sub>CO<sub>3</sub> at room temperature with stirring for 24 hrs. b. C. R. Hauser and C. J. Eby, J. Am. Chem. Soc., 79, 728 (1957) c. Isolated yield, not always optimized. d. Determined by <sup>1</sup>H NMR spectra. e. The rest of product was the starting 2(1H)-pyridone; total recovery was about 75-85% in each run. f. Reproduced from ref. 4. g. G. C. Hoptins, J. P. Jonak, H. J. Minnemeyer, and H. Tieckelmann, J. Org. Chem., 32, 4040 (1967)

Introduction of a phenyl substituent to 2-pyridones (**1**) would raise the energies of HOMO and lower those of LUMO so that the Diels-Alder reactivity should be enhanced, assuming that the reaction proceeds along the line derived from a frontier molecular orbital theory. This effect, however, can not explain the noticeable difference in reactivity between **4a-b** and **4c-e**. The common difference of a structural feature of **4c-e** from that of **4a-b** is in presence of the substituent at C<sub>5</sub>. In view of distribution of HOMO coefficients of 2(1H)-pyridone (**1A**) and

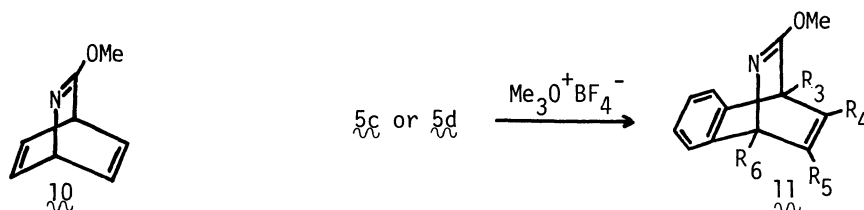
Figure I



2-hydroxypyridine (**1B**) as shown in Figure I, the magnitude of a substituent effect at C<sub>3</sub> and C<sub>5</sub> should be the greatest. Thus, introduction of methyl substituent at C<sub>3</sub> and C<sub>5</sub> would efficiently raise HOMO energy on both forms, (**1A**) and (**1B**).<sup>8</sup> Thus, the reactivities with benzyne should be further enhanced with **4c-e** in accord with the experimental results.

Although 2-azabarrelene has considerable interest from a theoretical and a photochemical point of view, and *ab initio* (STO-3G) calculations<sup>9</sup> predict some stability for 2-azabarrelene as a result of a positive balance between the stabilizing through bond interactions and the destabilizing through space ones, it was not until last year (1980) that 2-azabarrelene (**10**) was synthesized<sup>10</sup> in rather poor overall yield from 2(1H)-pyridone derivative (less than 2% yield). 5,6-Benzo-2-azabarrelenes are still unknown.

The conversion of **5c** into 5,6-benzo-2-azabarrelene (**11**) has been briefly explored. **5c** and **5d** were treated with trimethyloxonium tetrafluoroborate in the ordinary way to afford novel 5,6-benzo-2-azabarrelene (**11**), exclusively, as colorless crystalline products in good yield (70-80%), despite generating an antibicycloaromatic system.<sup>11</sup> The structure of **11** rests on the spectral properties.<sup>12</sup> It should be noted that **11** is quite stable at room temperature, and the mass spectrum shows an intense molecular ion peak, unlike 2-azabarrelene (**5**), (**7**) and (**10**),<sup>10</sup> in which retro Diels-Alder fragmentation easily occurs to exhibit a base peak corresponding to the mass of the naphthalene derivatives.



We hope our results will spark new interest in this area of chemistry, and we are continuing to explore the scope and limitation of these reactions as well as the excited state chemistry of (**11**).

## References

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4. One such reaction with maleimide has been reported to undergo the Diels-Alder reaction; *Japn. Pat. s 50-14698* (1975), L. V. Vetaneli, N. P. Shusherina, A. U. Stepanyants, and E. A. Tarkhanova, *Zh. Org. Khim.*, **13**, 1926 (1977).
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6. All new compounds reported herein gave a satisfactory elemental analysis.
7. Selected spectral data are as follows:  $\text{4c}$  mp 206-208°;  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  1.48 (s, 3H), 1.59 (s, 3H), 1.91 (s, 3H), 7.00-7.55 (m, 9H), 7.66 (s, 1H); IR (KBr): 1675  $\text{cm}^{-1}$ ; MS (70 eV):  $m/e=289$  (4%,  $\text{M}^+$ ), 246 (100%,  $\text{M}^+-\text{HNCO}$ ).  $\text{4d}$  mp 228-230° (EtOH);  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  1.50 (s, 3H), 1.40-2.98 (m, 6H), 6.50-7.55 (m, 10H); IR (KBr): 1670  $\text{cm}^{-1}$ ; MS (70 eV):  $m/e=315$  (2%,  $\text{M}^+$ ), 272 (100%,  $\text{M}^+-\text{HNCO}$ ).
8. This was confirmed by MO calculations supported by CNDO/2 method. We have carried out a number of calculations on various 2(1H)-pyridones and 2-hydroxypyridines. A detailed account of the calculations and the nature of the structure-reactivity relationship associated with the tautomeric properties on those compounds will be provided elsewhere.
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11. M. J. Goldstein and R. Hoffmann, *J. Am. Chem. Soc.*, **93**, 6193 (1971).
12. Spectral data are as follows:  $\text{11c}$  mp 160-161° (EtOH);  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  1.54 (s, 3H), 1.61 (s, 3H), 2.12 (s, 3H), 3.96 (s, 3H), 6.50-7.51 (m, 9H); IR (KBr): 1630  $\text{cm}^{-1}$ ; MS (70 eV):  $m/e=303$  (89%,  $\text{M}^+$ ), 288 (100%,  $\text{M}^+-\text{CH}_3$ ), 246 (37%,  $\text{M}^+-\text{CH}_3\text{OCN}$ ).  $\text{11d}$  mp 142-143° (EtOH);  $^1\text{H NMR}$  ( $\text{CDCl}_3$ )  $\delta$  1.56 (s, 3H), 1.45-2.95 (m, 8H), 3.68 (s, 3H), 6.45-7.55 (m, 9H); IR (KBr) 1630  $\text{cm}^{-1}$ ; MS (70 eV):  $m/e=329$  (100%,  $\text{M}^+$ ), 314 (52%,  $\text{M}^+-\text{CH}_3$ ), 282 (31%,  $\text{M}^+-\text{CH}_3\text{OCN}$ ).

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