zenesulfinylmorpholine, 16066-32-3; trimorpholinosulfonium chloride, 64508-84-5.

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Imidazo[1,2-*a*]pyridine 1-Oxide. Synthesis and Chemistry of a Novel Type of *N*-Oxide

Elli S. Hand and William W. Paudler*

Department of Chemistry, The University of Alabama, University, Alabama 35486

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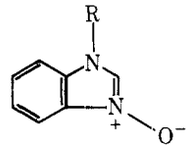
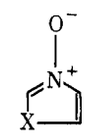
2-Phenylimidazo[1,2-*a*]pyridine 1-oxide, the first *N*-oxide of the polyazaindenes with the oxide function in the π-excessive five-membered ring, has been prepared. In contrast to the π-deficient *N*-oxides, back-bonding of the oxygen appears to be minimal. Some transformations of this compound are described.

The chemistry of π-deficient heterocyclic *N*-oxides has been the subject of numerous studies for many years. In contrast, much less is known about π-excessive heterocyclic *N*-oxides. Among the few representatives of this class of *N*-oxides are compounds of the general types A and B.[1,2] No *N*-oxides

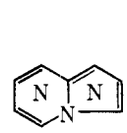


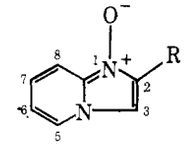
A



B, X = O, S, NR

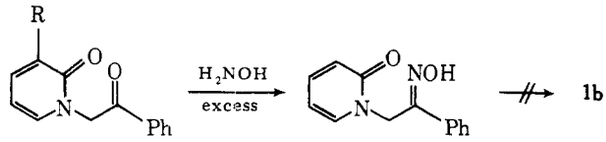
of the π-excessive five-membered ring in the nitrogen-bridged polyazaindenes are known. We now wish to describe the synthesis and some chemical reactions of a member of this class of heterocyclic *N*-oxides, imidazo[1,2-*a*]pyridine 1-oxide (**1b**).





1a, R = H
b, R = Ph

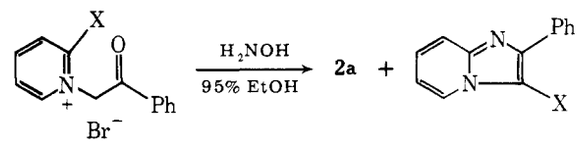
Since earlier work in our laboratory had shown that direct N-oxidation of imidazo[1,2-*a*]pyridines with peracids leads to cleavage of the five-membered ring,[3] we approached the *N*-oxide synthesis by indirect intramolecular cyclizations. When compound **2a**, obtained either by alkylation of 2-pyridone[4] or preferably by base hydrolysis of the pyridinium salts **4** (X = Cl, Br), is treated with hydroxylamine under acidic or neutral conditions, the reactions stop at the oxime stage, high yields of *syn*- and *anti*-oximes **3** being formed. The mixtures, largely the undesired anti isomer with respect to the phenyl substituent,[5] are stable at the melting point and thus not thermally convertible to the *N*-oxide **1b**.



2a, R = H

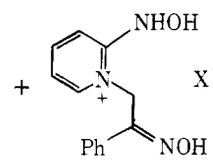
3 syn + anti

An attempt to prepare compound **1b** by reaction of the pyridinium salt **4** with hydroxylamine in 95% ethanol also gave



4a, X = Cl
b, X = Br

5, X = H
6a, X = Br
b, X = Cl



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none of the desired product, but rather a mixture containing the pyridone **2a** (55%) and compounds **5** (8%) and **6a** and **6b** (3%). Another component had IR and mass spectral properties consistent with structure **7**. The formation of the imidazo[1,2-*a*]pyridines **5**, **6a**, and **6b** suggests that cyclization to the *N*-oxide **1b** may indeed have occurred, but that this compound is not stable under the reaction conditions. Further, formation of the pyridone **2a** implicates hydroxylamine in the hydrolysis of the pyridinium salt **4**, either as a general base catalyst or as a nucleophile.[6]

The reaction was therefore repeated under strictly anhydrous conditions in the presence of the hydroxylamine hydrochloride. Under these reaction conditions, the product

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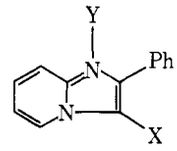
Table I. ^{1}H NMR Chemical Shifts (δ, ppm) of Imidazo[1,2-*a*]pyridines[a]

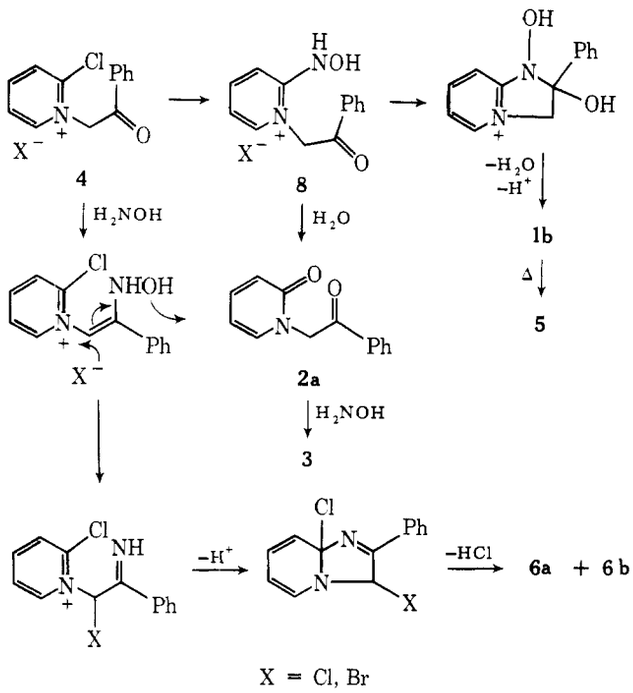


1b, X = H; Y = O
5, X = H; Y = nil
6a, X = Br; Y = nil
b, X = Cl; Y = nil
c, X = I; Y = nil
10,[b] X = H; Y = nil (Ph = H)
11a,[c] X = H; Y = OCH_3
13a, X = Br; Y = O

Compd	H-3	H-5	H-6	H-7	H-8	C_6H_5 o	C_6H_5 m,p
			Me_2SO-d_6				
5	8.44	8.56	6.92	7.27	7.62	8.02	7.48
1b	~8.40	~8.42	7.00	7.30	7.75	~8.42	7.49
10·HCl[b]	8.28, 8.53	9.07	7.56	~8.03	~8.03		
11a[d]	8.86	9.03	~7.69	8.18	8.36	7.96	~7.69
1b·TFAA[e]	8.72	8.89	~7.52	~8.02	~8.02	~8.02	~7.62
5·TFAA[e]	8.86	8.96	~7.60	~8.03	~8.03	~8.03	~7.60
13a·HBr		8.91	~7.75	~8.14	~8.14	~7.75	~7.75
			$CDCl_3$				
5[d]	7.88	8.13	6.78	7.16	7.66	8.00	~7.42
1b	7.69	8.02	6.78	7.15	7.86	8.26	7.40
11a[d]	9.36	9.66	~7.59	~8.18	~8.18	7.96	~7.59
13a		~8.10	7.00	7.28	7.98	~8.10	7.54
6a[f]		~8.16	6.90	7.24	7.63	~8.16	7.47
6b		~8.09	6.90	7.24	7.64	8.18	7.45
6c		8.23	6.94	7.26	7.65	8.01	7.48

[a] Solutions were 0.25 *m* unless otherwise stated. Chemical shift assignments are based on the splitting patterns, integrated areas, and analogy to those of other similar compounds. H-3 is a singlet; H-5, a doublet often showing further fine splitting ($J_{5,6} \sim 6$, $J_{5,8}$ 0–1 Hz); H-6, a triplet ($J_{6,7} \sim 6$ Hz); H-8, a doublet ($J_{7,8} \sim 9$ Hz). In the protonated compounds the signals of H-7 and H-8 overlap; for these and other overlapping signals the center of the multiplet is given. [b] The unsubstituted imidazo[1,2-*a*]pyridine. [c] Iodide salt. [d] 0.14 *m* solutions. [e] An excess of trifluoroacetic acid was added to the solutions. [f] 0.30 *m* solution.

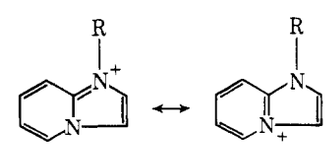
Scheme I



distribution is drastically altered, and the desired *N*-oxide **1b** is formed in up to 65% yield. Variable amounts of the oximes **3** are also formed. Although other *N*-oxides have been prepared from both oximes and hydroxylamines,[1] the formation of compound **1b** is best rationalized as shown in Scheme I. Attack of hydroxylamine can in principle occur either at the carbonyl carbon to yield the oximes or afford the hydroxylamine derivative **8** by nucleophilic displacement of the chlorine in compound **4**. The hydroxylamine derivative **8** can cyclize or hydrolyze in the manner indicated above. The former affords the *N*-oxide **1b**, while the latter yields the pyridone **2a**, which can be converted to the oximes **3**. Initial attack by hydroxylamine at the carbonyl carbon of compound **4** affords the intermediate which can be transformed in the indicated manner to yield the 3-halo derivatives **6a** and **6b**.

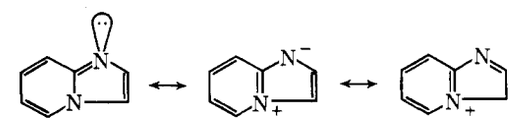
The mass spectrum of the yellow, hygroscopic *N*-oxide **1b** shows facile loss of an oxygen atom, while the remainder of the spectrum is essentially the same as the fragmentation pattern observed for 2-phenylimidazo[1,2-*a*]pyridine (**5**).

The ^{1}H NMR spectrum (in Me_2SO-d_6 or $CDCl_3$, cf. Table I) of the *N*-oxide is rather unique in that only the ortho hydrogens of the 2-phenyl substituent are strongly affected by the presence of the *N*-oxide (deshielded by about 0.40 ppm). This is contrary to the effect that either N-1 protonation or methylation has upon all of the proton chemical shifts (deshielding by 0.4–0.7 ppm) in nonoxygenated imidazo[1,2-*a*]-pyridines. The latter was shown by us to be due to resonance contributors to the ground state of the type shown in **9**.[7] The



9, R = H, CH_3

absence of such chemical shift changes in the *N*-oxide implies that the ground-state contributors in the free base **10** are not



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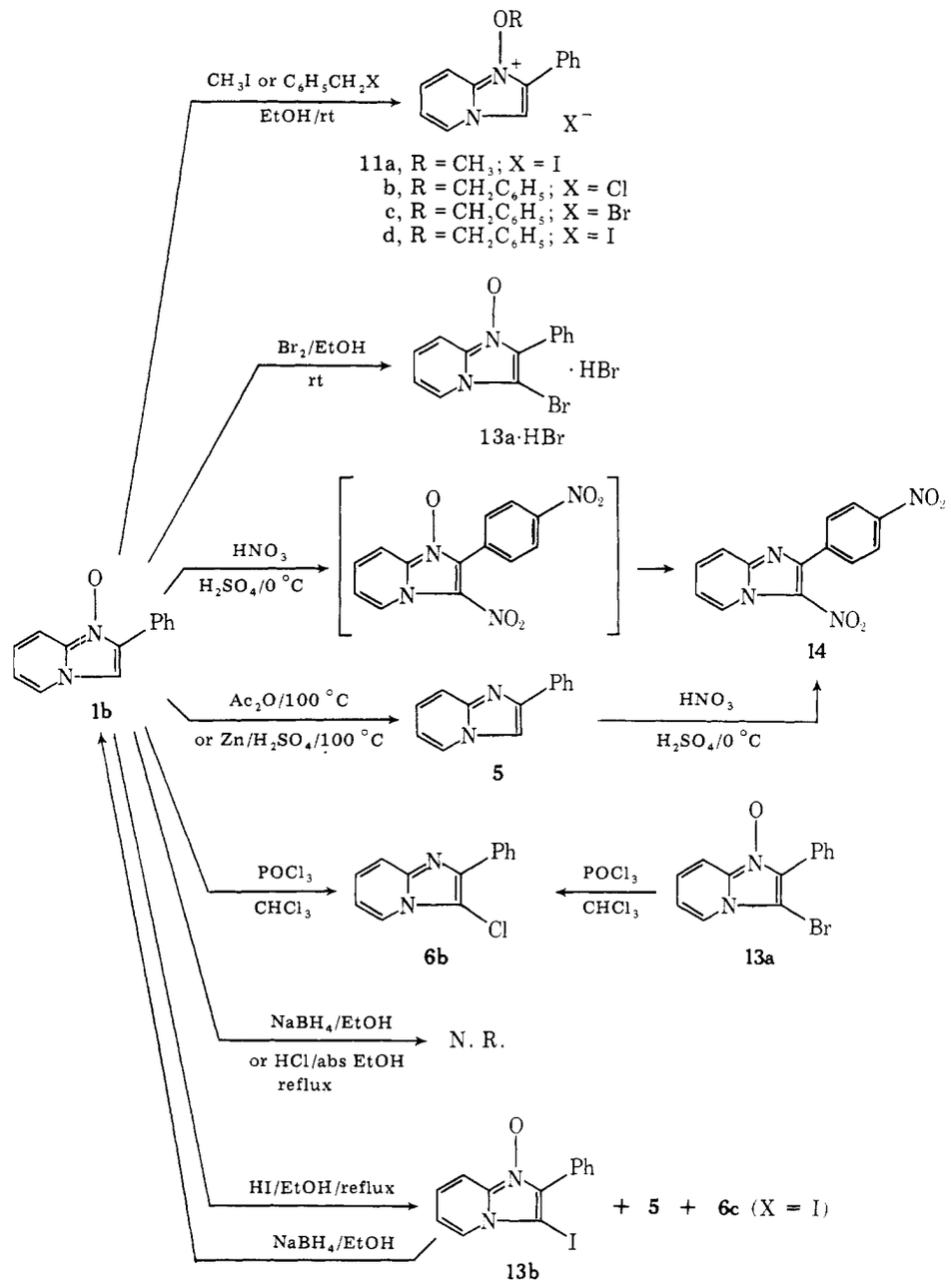
Scheme II



significantly effected by N-1 oxidation. This, in turn, suggests little back-donation by oxygen in the π-excessive *N*-oxide and points to the fact that the lone pair of electrons on N-1 of the free base is not involved in the resonance structures. However, in the methylated *N*-oxide **11a** (cf. Scheme II) the changes in the chemical shifts of all of the ring protons do parallel those observed when imidazo[1,2-*a*]pyridine is N-1 methylated (**9**, R = CH_3). This clearly implies the similarity in the ground-state contributing structures of the alkoxy (**11a**) and alkyl (**9**, R = CH_3) quaternary salts.

The above considerations lead to the prediction that the presence of the *N*-oxide function will not greatly alter the reactivity of the imidazo[1,2-*a*]pyridine system.

Some Reactions of the *N*-Oxide 1b. (1) Formation of a hemipicrate, $(C_{13}H_{10}N_2O)_2 \cdot C_6H_3N_3O_7 \cdot H_2O$ (**12**), parallels the basic salt formation $(Het^+ \text{-} O^-)_2 \cdot HX$ frequently encountered in π-deficient heteroaromatic *N*-oxides.[1]

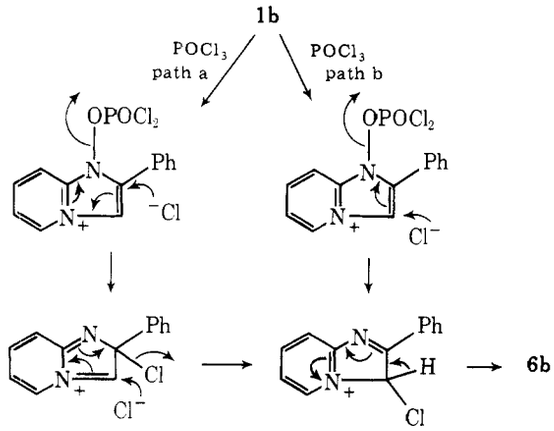
(2) The *N*-oxide **1b** is readily alkylated at room temperature by alkyl halides, in the order of reactivity $PhCH_2I > PhCH_2Br > CH_3I > PhCH_2Cl$, to give compounds **11a–d**. All of these compounds are sensitive to heat and the methiodide, especially, is sensitive to light.

(3) As with nonoxygenated imidazo[1,2-*a*]pyridines, facile electrophilic substitution occurs at the 3 position. Thus, bromination gives the 3-bromo *N*-oxide **13a**. Nitration takes place at both the 3 position and para in the phenyl substituent; the ultimate product, the deoxygenated compound **14**, may well be formed from the dinitro *N*-oxide during the workup procedure. Nitration of 2-phenylimidazo[1,2-*a*]pyridine (**5**) affords the same dinitro compound.

(4) The "classical" acetic anhydride reaction of π-deficient *N*-oxide chemistry, when applied to the *N*-oxide **1b**, yields at least seven components, of which only the deoxygenated material, compound **5** (25%), could be isolated. Since the *N*-oxide, on standing for several weeks or on brief heating at its melting point, becomes contaminated with the free base **5**, we envision the above reaction to be a thermal deoxygenation.

In contrast to this observation, 1-methylbenzimidazole 3-oxides[8] as well as 1-methylpyrazole 2-oxide[9] react with

Scheme III

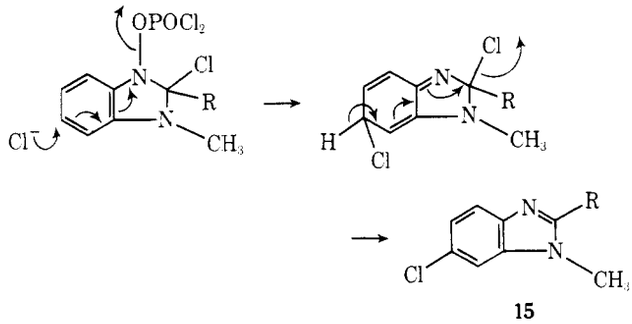


acetic anhydride to afford products analogous to those obtained in π-deficient N-oxides.

(5) Reaction of the N-oxide **1b** with $POCl_3$ affords a high yield (70%) of the deoxygenated 3-chloro derivative **6b,** along with traces of the deoxygenated compound **5** and polychloro compounds. In a control experiment, the parent compound **5** was shown to be unaffected by $POCl_3$.

The formation of this 3-chloro derivative can be rationalized by either of the following sequences (Scheme III). While path b is more direct, path a is more likely in view of our earlier work,[10] involving the reaction of 3-halo imidazo[1,2-*a*]pyridines with *tert*-butyl hypochlorite, where *nucleophilic* substitution at position 2 occurs when N-1 is substituted with a facile negative leaving group. When the 3-bromo-2-phenyl N-oxide **13a** is treated with $POCl_3$, deoxygenation *and* halogen exchange lead to 3-chloro-2-phenylimidazo[1,2-*a*]pyridine (**6b**) in 54% yield. Mechanisms similar to those delineated above account for this reaction.

The reaction of $POCl_3$ with 1-methylbenzimidazole 3-oxide[8] affords the deoxygenated 2-chloro derivative when C-2 is unsubstituted, while the 6-chloro derivative **15** is obtained



when the 2 position is blocked. It is of interest to comment that the formation of these 6-chloro compounds can be explained in a manner akin to path a above.

(6) Attempted reduction of the N-oxide **1b** with $NaBH_4$ in ethanol failed. In fact, 3-iodo-2-phenylimidazo[1,2-*a*]pyridine 1-oxide (**13b**) can be dehalogenated to the N-oxide **1b** with $NaBH_4$. Since the nonoxygenated iodo compound (**6c,** X = I) is also dehalogenated by this reagent,[11] the reactivity of the substituent is presumably unaffected by the presence of the N-oxide function. Under more vigorous conditions, zinc dust in the presence of acid, the deoxygenated compound **5** is rapidly formed (70% yield).

(7) Prolonged heating of the N-oxide **1b** with hydrogen iodide in ethanol leads to the gradual formation of the deoxygenated compound **5,** as well as the 3-iodo N-oxide **13b,** and its deoxygenated derivative (**6c,** X = I). Here, also, deoxygenation is most reasonably explained by thermal decomposition.

Introduction of iodine in the 3 position is envisioned to take place by electrophilic substitution, the necessary iodine being formed by air oxidation of iodide.

When the N-oxide **1b** is treated with refluxing ethanolic hydrogen chloride for 2 h, no decomposition product (**5**) can be detected by TLC. The protonated N-oxide thus appears to be more stable than the nonprotonated species.

Some aspects of the chemistry of the 1-alkoxy derivatives as well as the syntheses of related polyazaindene N-oxides will be the subjects of forthcoming publications.

Experimental Section

Woelm neutral alumina, Brockmann grade 3, was used for chromatography. Solutions were dried over anhydrous Na_2SO_4. Melting points are uncorrected. ^1H NMR spectra were recorded with a Varian HA-100 spectrometer. Mass spectra were obtained with a Hitachi Perkin-Elmer RMU-6M instrument equipped with a solid sample injector; ionizing voltage was 73 eV. IR spectra were recorded of Nujol mulls with a Beckman AccuLab 1 instrument. Elemental analyses were determined by either the Analytical Services Laboratory of the University of Alabama Chemistry Department or Atlantic Microlab, Inc., Atlanta, Ga.

1-Phenacyl-2(1*H*)-pyridone (2a). (1) A mixture of 2-pyridone (2.0 g, 21 mmol) and phenacyl bromide (4.0 g, 20 mmol) was kept at its melting point for 3 h.[12] The cooled mixture was treated with hot H_2O and the brown solid was filtered. Fractional crystallizations from EtOAc or EtOH gave only impure product. Chromatography of the material in the mother liquors gave with 50% $C_6H_6/CHCl_3$ compounds **2b** (1.7%) and **2a,** mp 150.5–153 °C [after sublimation, 150 °C (0.02 Torr)] (lit.[13] mp 154.5 °C), total yield 30–40%. Compound **2b,** extracted into hexane, crystallized from very small amounts of MeOH: mp 123–125 °C; mass spectrum mol wt 291 and 293; ^1H NMR (δ, $CDCl_3$) 5.40 (s, CH_2), 6.10 (t, H-5), 7.2–8.04 (remaining protons).[14]

Anal. Calcd for $C_{13}H_{10}NO_2Br$: C, 53.42; H, 3.42; N, 4.79; Br, 27.40. Found: C, 53.44; H, 3.44; N, 4.88; Br, 27.29.

(2) Compound **2a** is best prepared by treating the salt **4a** with NaOH[13] (70% yield): ^1H NMR (δ, $CDCl_3$) 5.40 (s, CH_2), 6.23 (t, H-5), 6.62 (d, H-3), 7.2–8.1 (remaining protons).

2-Chloro-1-phenacylpyridinium Bromide (4a). This material had mp 170–170.5 °C (lit.[13] mp 179 °C for the monohydrate) and after drying for 2 h at 100–110 °C in vacuo did not retain H_2O of crystallization.

Anal. Calcd for $C_{13}H_{11}NOClBr$: C, 49.92; H, 3.52; N, 4.48; halide, 36.96. Found: C, 49.79; H, 3.52; N, 4.41; halide, 37.00.

2-Bromo-1-phenacylpyridinium Bromide (4b). Heating of 2-bromopyridine (9.5 g, 60 mmol) with phenacyl bromide (12 g, 60 mmol) at 120 °C for 20 min, cooling slightly, adding 25 mL of toluene, then heating at 100 °C for 2 days, filtering, and triturating with C_6H_6 and Et_2O gave compound **4b** (X = Br) in 83% yield. It crystallized from EtOH as sturdy rhombs, mp 178.5 °C.

Anal. Calcd for $C_{13}H_{11}NOBr_2$: C, 43.70; H, 3.08; N, 3.92; Br, 44.82. Found: C, 43.69; H, 3.10; N, 3.87; Br, 44.89.

Oximes of 1-Phenacyl-2(1*H*)-pyridone (3). (1) To an aqueous solution (3 mL) of H_2NOH·HCl (0.54 g, 7.7 mmol) neutralized with 10% NaOH (pH 7) were added compound **2a** (0.33 g, 1.55 mmol) and absolute EtOH (20 mL). When, after refluxing the resulting solution for 1.5 h, much starting material remained (TLC), another portion of neutralized H_2NOH·HCl (1.08 g) was added and heating was continued for 22 h. Some separated solid was filtered and rinsed with EtOH. The filtrate was treated with H_2O (20 mL) and concentrated (to 20 mL) when crystals (0.30 g, 85%, mp 161–175 °C) separated. This solid was a 1:5 syn/anti mixture of the oximes **3:** ^1H NMR (δ, Me_2SO-d_6) 5.22 and 4.97 (s, 5:1, CH_2), 11.87 and 11.17 (s, 5:1, OH), 6.15 (t, H-5), 6.22 (d, H-3), 7.2–7.6 (remaining protons). Crystallization from absolute EtOH did not appreciably change the isomer ratio, but raised the melting point to 175–185 °C.

Anal. Calcd for $C_{13}H_{12}N_2O_2$: C, 68.42; H, 5.26; N, 12.78. Found: C, 68.41; H, 5.45; N, 12.16.

Although this mixture turned brown on heating just above its melting point for 30 min, no change was detectable by ^1H NMR spectroscopy.

(2) When a solution of compound **2a** (0.33 g) and H_2NOH·HCl (0.54 g) in EtOH (25 mL) was refluxed for 1.5 h, no starting material remained (TLC). Evaporation to dryness and addition of H_2O (20 mL) to the residue gave the oximes **3,** mp 164–168 °C (0.30 g), as predominantly the anti isomer.

Reaction of the Salts 4 with Hydroxylamine. (1) An aqueous solution (10 mL) of H_2NOH·HCl (1.4 g, 20 mmol) was treated with

NaOH to pH 7 and added to a warm, aqueous solution (60 mL) of compound **4a** (3.1 g, 10 mmol). The solution became deep yellow, a gas was liberated, pH became ~5, and a gum that could not be induced to crystallize separated. After 30 min the mixture was extracted with 5 × 10 mL of $CHCl_3$. The $CHCl_3$ layers were dried and stripped of solvent to give a mixture from which compounds **6a** (and **6b**) (80 mg, 3%), **5**, and **2a** were isolated by chromatography, eluting with C_6H_6, 10% $CHCl_3/C_6H_6$, and 10% $CHCl_3/C_6H_6$, respectively. The aqueous layer (now pH 3) was neutralized with aqueous NaOH and extracted with 5 × 10 mL of $CHCl_3$. The extracts were dried and stripped of solvent to give a residue from which a solid (25 mg), tentatively assigned structure **7**, separated on addition of $CHCl_3$. The $CHCl_3$-soluble portion (0.66 g) on chromatography gave small amounts of compounds **5** (70 mg, 8% total) and **2a** (120 mg, 55% total).

Compound **6a** was identified by IR and ^1H NMR spectral comparisons with an authentic sample (see below). Its picrate showed the same strange melting behavior as, and no depression on admixture with, the authentic material (see below). Its mass spectrum, however, also contained peaks attributable to **6b** (~15%) (other chloro- and bromoimidazo[1,2-*a*]pyridines cannot be separated by chromatography). Compound **5**, after crystallization from hexane, had the same melting point, IR, and ^1H NMR as an authentic sample (see below). Compound **2a**, after crystallization from C_6H_6/hexane and EtOAc, had mp 153–153.7 °C and the same spectral properties as the authentic material (see above). Compound **7**, mp ~172 °C dec, had an IR spectrum quite different from those of the oximes **3** and the pyridone **2a**, but strongly reminiscent of those of the pyridinium salts **4**; the carbonyl absorption of **4** (at 1680 cm^{-1}) was absent, and broad bands were present at 2700–3400 cm^{-1}. Its mass spectrum showed *m/e* peaks at 227 (cation **7** -OH), 209, and 193.

(2) **Anhydrous Conditions: 2-Phenylimidazo[1,2-*a*]pyridine 1-Oxide (1b).** The starting materials were dried at 80 °C in vacuo for 6 h. A mixture of $H_2NOH{\cdot}HCl$ (1.4 g, 21 mmol) and compound **4b** (X = Br) (1.07 g, 3.0 mmol) in dry EtOH (50 mL) was heated with stirring at 80 °C for 5 h; reaction vessels were dried at 120 °C and protected with a Drierite-filled tube. The solvent was evaporated and the residue extracted with 3 × 10 mL of $CHCl_3$ from which a semisolid mixture was obtained that was fractionated by chromatography into the colorless compounds **6a** and **6b** (1.2%), **5** (1.7%), **2a** (6.8%) eluted as above, and the waxy, yellow, hygroscopic compound **1b** (0.41 g, 65%), mp 100–115 °C, eluted with 2% absolute EtOH/$CHCl_3$. The $CHCl_3$-insoluble residue, on treatment with H_2O, gave the insoluble oximes **3** (13%).

Changing the reaction conditions to 5 times the amount of salt **4b**, 5–10 times $H_2NOH{\cdot}HCl$, and 1.5–3 times EtOH lowered the yield of *N*-oxide **1b** to 30–40%. Lowering the temperature to 55 °C resulted in a 7% yield of *N*-oxide.

The *N*-oxide **1b**, when dry, is soluble in C_6H_6 and $CHCl_3$. After crystallization from C_6H_6, it has mp 117–118 °C, resolidifies partially, and is melted again by 162 °C; after cooling it then has mp ~158–168 °C (darkens). On exposure to (moist) air it becomes gummy. ^1H NMR spectra, concentration dependent, are the same of non- and recrystallized material. On standing several weeks some of the compound became deoxygenated (TLC).

The *picrate* **12**, formed by adding a hot absolute EtOH solution (3 mL) of picric acid (40 mg, 0.17 mmol) to a hot absolute EtOH solution (2 mL) of compound **1b** (40 mg, 0.18 mmol), crystallized from absolute EtOH as fine yellow needles, mp 201 °C dec.

Anal. Calcd for $(C_{13}H_{10}N_2O)_2{\cdot}H_2O{\cdot}C_6H_3N_3O_7$: C, 57.57; H, 3.75; N, 14.69. Found: C, 57.37; H, 3.55; N, 14.82.

The colorless *methiodide* **11a** rapidly turns yellow on exposure to light. Its preparation and purification were thus carried out in foil-wrapped vessels and as little light as possible. After standing 19 h a solution of compound **1b** (0.20 g, 0.95 mmol) and CH_3I (1 mL) in absolute EtOH (4 mL) was concentrated and EtOAc (ca. 5 mL) was added to the hot solution to the point of turbidity. Rapid cooling gave a colorless solid (75%) which was purified by dissolution in a little hot absolute EtOH and addition of EtOAc as above, and then had mp 146 °C dec.

Anal. Calcd for $C_{14}H_{13}N_2OI$: C, 47.73; H, 3.69; N, 7.95; I, 36.08. Found: C, 47.78; H, 3.73; N, 7.95; I, 35.97.

1-Benzyloxyimidazo[1,2-*a*]pyridinium Halides (11b–d). All manipulations were carried out in dimmed light. Exposure to heat was kept to a minimum, since the compounds are heat sensitive. Each colorless compound was prepared by treating the *N*-oxide **1b** (100 mg) in absolute EtOH (3 mL) with a ca. sixfold excess of benzyl halide.[15] Since with benzyl chloride much *N*-oxide remained after 5 h (TLC), the solution was left to stand for 6 days. With benzyl bromide, reaction was complete after ~10 min. All were worked up by concentrating the warmed solutions in a stream of N_2, adding EtOAc until the product separated as an oil, and scratching to induce crystallization. The *chloride* **11b**, mp 143–145 °C dec (67%), dissolved in a little hot absolute EtOH, reprecipitated with warm EtOAc, and rapidly cooled, had mp 135–145 °C dec.

Anal. Calcd for $C_{20}H_{17}N_2OCl{\cdot}H_2O$: C, 67.70; H, 5.36; N, 7.90. Found: C, 67.21; H, 5.45; N, 8.37.

The *bromide* **11c**, mp 170–172 °C dec (softens ~118 °C), was analyzed directly.

Anal. Calcd for $C_{20}H_{17}N_2OBr{\cdot}H_2O$: C, 60.15; H, 4.76; N, 7.02. Found: C, 60.74; H, 4.60; N, 7.21.

The *iodide* **11d** (93%), rapidly recrystallized from absolute EtOH, had mp 167 °C dec.

Anal. Calcd for $C_{20}H_{17}N_2OI$: C, 56.07; H, 3.97; N, 6.54. Found: C, 56.46; H, 4.04; N, 6.57.

Mass spectra showed only the peaks due to the *N*-oxide **1b** and the respective benzyl halides.

3-Bromo-2-phenylimidazo[1,2-*a*]pyridine 1-Oxide Hydrobromide (13a·HBr). To a solution of *N*-oxide **1b** (0.20 g, 0.95 mmol) in absolute EtOH (5 mL) was added dropwise an absolute ethanolic solution (3 mL) of Br_2 (0.30 g, 1.8 mmol). After 24 h the colorless solid was filtered. Concentration of the filtrate (to 4 mL) gave a second crop (0.31 g, 88% total), mp 210 °C dec (depends on rate of heating). The material crystallizes from absolute EtOH as either plates or needles.

Anal. Calcd for $C_{13}H_{10}N_2OBr_2$: C, 42.16; H, 2.70; N, 7.57; Br, 43.24. Found: C, 42.17; H, 2.76; N, 7.54; Br, 43.14.

The free base was obtained by mixing $NaHCO_3$ (28 mg, 0.33 mmol), H_2O (1 mL), compound **13a·HBr** (80 mg, 0.22 mmol), and EtOH (4 mL), evaporating to dryness in vacuo, and extracting the residue with $CHCl_3$. Evaporation of $CHCl_3$ gave yellow needles, mp 185–186 °C dec. The yellow solid **13a** (as well as the yellow mother liquor) obtained by recrystallization from dry C_6H_6 turned colorless on rinsing with (moist) ether and then had mp 135–138 °C. The color change is reversed when the compound is boiled with C_6H_6. An analytical sample of solid **13a**·H_2O was dried at 60 °C in vacuo for 4 h: mass spectrum, mol wt 288 and 290.

Anal. Calcd for $C_{13}H_9N_2OBr{\cdot}H_2O$: C, 50.81; H, 3.58; N, 9.12; Br, 26.06. Found: C, 50.69; H, 3.59; N, 9.02; Br, 25.93.

3-Nitro-2-(*p*-nitrophenyl)imidazo[1,2-*a*]pyridine (14). (1) To a stirred, cold (0 °C), orange solution of compound **1b** (0.10 g, 0.95 mmol) in concentrated H_2SO_4 (0.75 mL) was added dropwise concentrated HNO_3 (~0.5 mL), whereupon it turned deep red. After 15 min it was poured on ice and partially neutralized with aqueous 20% NaOH (pH 2) to give orange and colorless crystals, mp 220 °C dec (gradual darkening ≳140 °C) (70 mg, ~50%). On crystallization from absolute EtOH the colored material dissolved more readily than the colorless one, a light tan powder separating on cooling. The powder turned orange overnight and was then crystallized three times from acetone to give pale yellow needles: mp 262 °C dec (gradual darkening ≳200 °C); mass spectrum, mol wt 284; IR 850 cm^{-1} (para-substituted phenyl).

Anal. Calcd for $C_{13}H_8N_4O_4$: C, 54.93; H, 2.82; N, 19.72. Found: C, 54.75; H, 2.90; N, 19.64.

Its mass and IR spectra are the same as those of the dinitro compound prepared from compound **5** as described next.

(2) Compound **5** (0.12 g, 0.62 mmol) was treated as above to give a water-insoluble material (0.17 g, ~100%), mp 242–255 °C dec, that was recrystallized from acetone to give pale yellow needles: mp 263 °C dec (90 mg); ^1H NMR (δ, TFAA) 9.95 (d, H-5), 7.98 (t, H-6), 8.38 (overlap, H-7, 8), 8.15 (d, H_o), 8.62 (d, H_m). The material in the mother liquor was predominantly the mononitration product, 3-nitro-2-phenylimidazo[1,2-*a*]pyridine, according to its ^1H NMR spectrum (TFAA).

Treatment of the *N*-Oxide 1b with Acetic Anhydride. A solution of compound **1b** (0.10 g, 0.48 mmol) in acetic anhydride (0.5 mL) was heated at 100 °C for 22 h, when TLC indicated the presence of compounds **5**, **1b**, and at least six other components. The black solution was poured on ice, treated with aqueous 20% NaOH, and extracted with 4 × 5 mL of $CHCl_3$. The extracts were dried and subjected to chromatography to give compound **5** (20 mg, 25%), small amounts of the other components, and starting material **1b** (15 mg), eluted with 50% $C_6H_6/CHCl_3$ and 2% absolute EtOH/$CHCl_3$, respectively.

Treatment of the *N*-Oxide 1b with Phosphorus Oxychloride. To compound **1b** (0.20 g, 0.95 mmol) in $CHCl_3$ (2 mL) was added dropwise freshly distilled $POCl_3$ (1.5 mL). The solution was refluxed for 75 min. Evaporation in a stream of N_2 and in vacuo gave a thick brown oil that was treated with ice and aqueous 10% NaOH until the pH remained ca. 9. The mixture was extracted with 5 × 8 mL of $CHCl_3$; the extracts were dried, filtered, stripped of solvent, and

fractionated by chromatography with C_6H_6 into polychloro compounds (mass spectrum <5%) and compounds **6b**, mp 119–120.5 °C (70%), and **5** (~5%). After sublimation [115 °C (0.02 Torr)] compound **6b** had mp 120–122 °C, mass spectrum, mol wt 230 and 228.

Anal. Calcd for $C_{13}H_9N_2Cl$: C, 68.27; H, 3.94; N, 12.25. Found: C, 68.20; H, 3.97; N, 12.23.

Treatment of 2-Phenylimidazo[1,2-a]pyridine (5) with Phosphorus Oxychloride. When carried out as above, this reaction gave at the base treatment stage a solid which was filtered. Crystallization from hexane afforded pure starting material **5** (TLC and mixture melting point, 85% recovery).

Treatment of 3-Bromo-2-phenylimidazo[1,2-a]pyridine 1-Oxide (13a) with Phosphorus Oxychloride. On gently warming a mixture of the HBr salt of **13a** (0.30 g, 0.81 mmol), $NaHCO_3$ (0.13 g, 1.5 mmol), H_2O (3 mL), and EtOH (10 mL), solution was not achieved. The solvents were evaporated in vacuo and the dry residue was extracted with 3 × 10 mL of hot $CHCl_3$ to give the anhydrous free base **13a**. When $POCl_3$ was added as above, the solution turned red. It was heated and worked up as above by the $CHCl_3$ extraction method. The products were separated by chromatography with 50% hexane/C_6H_6. Mass spectra of early fractions indicated the presence of penta-, tetra-, tri-, and dihalo compounds. The last (30 mg, 14%) was primarily a dichloro compound, 3,8-dichloroimidazo[1,2-a]pyridine (mass spectrum) which decomposed on attempted crystallization from hexane: ^1H NMR (δ, $CDCl_3$) 8.05 (d, H-5), 6.85 (t, H-6), 7.32 (d, H-7), 8.20 (m, H_o), 7.55 (m, H_m, H_p). Later fractions gave the 3-chloro-2-phenyl compound **6b** (100 mg, 54%).

Treatment of the N-Oxide 1b with Sodium Borohydride. When a solution of compound **1b** (0.21 g, 1 mmol) in EtOH (3 mL), treated with $NaBH_4$ (12.5 mg, 0.33 mmol) in EtOH (5 mL), was left to stand 30 min, only starting material was detectable by TLC. The solution was then heated on the steam bath for 1 h, left to stand overnight, filtered, and evaporated to dryness in vacuo to give starting material (0.20 g, 95% recovery; ^1H NMR).

Reaction of N-Oxide 1b with Zinc. After refluxing a stirred mixture of compound **1b** (0.17 g, 0.81 mmol), Zn dust (0.50 g, 7.6 mmol), and aqueous 5% H_2SO_4 (10 mL) for 30 min, no further starting material remained (TLC). A solid was filtered and rinsed with H_2O. When the filtrates were treated with aqueous 20% NaOH, a copious white precipitate was obtained that did not dissolve at pH 11–12. It was filtered, washed with H_2O, dried in vacuo and extracted with hot hexane to give compound **5** (90 mg). The aqueous filtrates, treated with dilute H_2SO_4 to pH 9, were extracted with 3 × 10 mL of $CHCl_3$. Extracted material was recrystallized from hexane to give a second crop of compound **5** (20 mg, 70% total).

Treatment of the N-Oxide 1b with Hydrogen Iodide. A solution of compound **1b** (50 mg) and aqueous 48% HI (0.2 mL) in absolute EtOH (3 mL) was refluxed. After 2 h, trace amounts of compound **5** had formed (TLC). I_2 was detectable with moistened starch paper. After 3 days, TLC indicated the presence of large amounts of compounds **5** and **6c** and small amounts of starting material and its iodination product **13b**, confirmed by mass spectra. After evaporating the solvent, dilution with ice/H_2O, and addition of 2.5 N NaOH to pH 10, the mixture was extracted with 3 × 5 mL of $CHCl_3$. The extracts were dried and stripped of solvent to give 71 mg of the four-component mixture.

Treatment of Compounds 6c and 13b with Sodium Borohydride. The above mixture was dissolved in absolute EtOH and treated with $NaBH_4$ (6 mg). TLC showed the presence of only the nonhalogenated compounds **5** and **1b** after 20 min. The solution was evaporated to dryness and the residue separated by chromatography into compounds **5** (30 mg, eluted with 50% $C_6H_6/CHCl_3$) and **1b** (15 mg, eluted with 2% absolute EtOH/$CHCl_3$).

Treatment of 3-Bromo- and 3-Chloro-2-phenylimidazo[1,2-a]pyridines (6a and 6b) with Sodium Borohydride. When a mixture of halo compounds **6a** and **6b** (from H_2NOH reaction with the salt **4**) was treated as above with $NaBH_4$ (tenfold molar excess), no dehalogenated material (**5**) could be detected by TLC. Workup as above gave a residue with mass spectrum identical with that of the starting material.

2-Phenylimidazo[1,2-a]pyridine (5). When a mixture of phenacyl bromide (2.0 g, 10 mmol) and 2-aminopyridine (1.0 g, 10 mmol) was heated, a vigorous reaction ensued.[17] After this subsided, the melt was kept at 80–100 °C for 2 h. It was dissolved in absolute EtOH (10 mL). Since addition of Et_2O gave an oil that could not be induced to crystallize, the supernatant was decanted, and the oil was treated with ice and aqueous 20% NaOH to pH 8. The separated oil was extracted with 3 × 15 mL of $CHCl_3$ and fractionated by chromatography into compound **5**, mp 130–131 °C (1.0 g, 60%, eluted with 50% $C_6H_6/CHCl_3$), and starting material (0.15 g, eluted with $CHCl_3$). Compound **5** crystallized from hexane as needles, mp 133–133.5 °C (lit.[16] mp 135 °C and lit.[17] mp 140 °C), mass spectrum, mol wt 194.

3-Bromo-2-phenylimidazo[1,2-a]pyridine (6a). To a stirred solution of compound **5** (0.19 g, 1 mmol) in absolute EtOH (5 mL) was added dropwise a solution of Br_2 (0.19 g, 1.2 mmol) in absolute EtOH (6 mL). When the Br_2 color no longer faded, addition was stopped, and the mixture was stirred an additional 5 min. The colorless, precipitated solid, **6a**·HBr, was filtered and rinsed with EtOH and Et_2O. Concentration of the filtrate gave a second crop (0.31 g total, 89%). Crystallization from EtOH gave needles, mp 249–250 °C dec.

Anal. Calcd for $C_{13}H_{10}N_2Br_2$: C, 44.07; H, 2.82; N, 7.91; Br, 45.20. Found: C, 44.05; H, 2.86; N, 7.90; Br, 45.09.

The free base, obtained by treating an aqueous solution of compound **6a**·HBr with aqueous 10% NaOH, followed by extraction with $CHCl_3$, was purified by sublimation [60 °C (0.02 Torr)] and had mp 63–64.5 °C (lit.[18] mp 83–85 °C and mp[19] 88–90 °C), mass spectrum, mol wt 272 and 274.

Anal. Calcd for $C_{13}H_9N_2Br$: C, 57.14; H, 3.30; N, 10.26; Br, 29.30. Found: C, 57.11; H, 3.37; N, 10.19; Br, 29.31.

The picrate, prepared by treating the free base **6a** (0.1 g, 0.36 mmol) in hot EtOH (5 mL) with picric acid (90 mg, 0.4 mmol) in hot EtOH (5 mL), crystallized as needles, partial melting ~140 °C, resolidifying, melting 151–152.5 °C, the same after crystallization from EtOH. Its ^1H NMR spectrum showed the presence of EtOH.

Anal. Calcd for $C_{13}H_9N_2Br \cdot C_6H_3N_3O_7 \cdot 0.75C_2H_5OH$: C, 45.85; H, 3.08; N, 13.05. Found: C, 46.39; H, 3.20; N, 13.45.

3-Iodo-2-phenylimidazo[1,2-a]pyridine (6c). An absolute EtOH solution (2 mL) of compound **5** (0.10 g, 0.5 mmol), treated with I_2 (0.20 g, 0.8 mmol) in absolute EtOH (3 mL), after standing 3 days deposited purplish-brown needles, mp 77 °C dec (0.24 g), of a mixture of compounds **6c**·HI and **6c**·HI_3. When this mixture was left to stand in aqueous dilute NaOH, it gradually changed to a colorless solid (**6c**, 67%) that was crystallized from hexane and then had mp 166 °C, mass spectrum, mol wt 320.

Anal. Calcd for $C_{13}H_9N_2I$: C, 48.75; H, 2.82; N, 8.75. Found: C, 48.84; H, 2.84; N, 8.63.

Registry No.—**1b**, 64413-99-6; **2a**, 952-75-0; **2b**, 64413-95-2; *syn*-**3**, 64413-94-1; *anti*-**3**, 64425-84-9; **4a**, 6273-90-1; **4b**, 7146-43-2; **5**, 4105-21-9; **6a**, 4044-95-5; **6a** HBr, 64413-93-0; **6a** picrate, 64413-92-9; **6b**, 64413-91-8; **6c**, 64413-90-7; **6c** HI, 64413-89-4; **6c** HI_3, 64440-83-1; **7**, 64413-88-3; **10** HCl, 34167-64-1; **11a**, 64413-87-2; **11b**, 64413-86-1; **11c**, 64425-85-0; **11d**, 64414-01-3; **12**, 64414-00-2; **13a**, 64413-98-5; **13a** HBr, 64413-97-4; **14**, 22244-94-6; phenacyl bromide, 70-11-1; 2-pyridone, 142-08-5; 2-bromopyridine, 109-04-6; hydroxylamine hydrochloride, 5470-11-1; picric acid, 88-89-1; methyl iodide, 74-88-4; acetic anhydride, 108-24-7; phosphorus oxychloride, 10025-87-3; 3,8-dichloroimidazo[1,2-a]pyridine, 64413-96-3.

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