Aromaticity in Heterocyclic Systems. IV. Substitution Reactions of Imidazo[1,2-a]pyridine and Related Methyl Derivatives[1]

JOHN P. PAOLINI AND ROLAND K. ROBINS[2]

Department of Chemistry, Arizona State University, Tempe, Arizona, and Department of Chemistry, University of Utah, Salt Lake City, Utah

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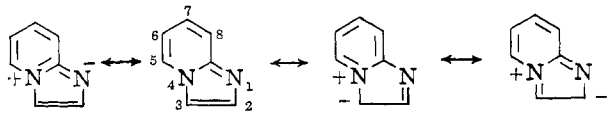
Electrophilic substitution of imidazo[1,2-a]pyridine has been studied for the first time. Chlorination, bromination, and nitration of imidazo[1,2-a]pyridine (I) has been shown to yield the corresponding 3-chloro-, 3-bromo-, and 3-nitroimidazo[1,2-a]pyridine, respectively. Bromination of 2-methylimidazo[1,2-a]pyridine gave the 3-bromo derivative or 2-dibromomethyl-3-bromoimidazo[1,2-a]pyridine (VI) depending on the reaction conditions. 2-Chloroimidazo[1,2-a]pyridine (XI) was nitrated to give 2-chloro-3-nitroimidazo[1,2-a]pyridine (XII). Chlorination of XI gave 2,3-dichloroimidazo[1,2-a]pyridine (XIV). When the 3-position was blocked by a methyl group, bromination occurred at position 5 to yield 5-bromo-3-methylimidazo[1,2-a]pyridine (VIII). These and other structural assignments were made possible by a careful study of the p.m.r. spectra of various known imidazo[1,2-a]pyridines and the new compounds prepared in the present work. These data support the contention that imidazo[1,2-a]pyridine (I) is a condensed aromatic system with ten delocalized π electrons.

Mosby[3a] states that the most important resonance contributing structures of imidazo[1,2-a]pyridine (I) are Ia and Ib. On this basis, electrophilic attack should occur most readily at position 3. One can equally as well write the resonance contributing structure Ic which would predict electrophilic substitution at position 2. Other resonance forms can be drawn with a positive charge at N-4 and a negative charge at positions 5 or 7.



Ia I Ib Ic

One can draw a similar number of transition states for electrophilic substitution which could be stabilized by a positive charge at N-4. Recent π-electron density calculations for imidazo[1,2-a]pyridine (I) have been made[3b] which predict position 3 most susceptible toward electrophilic substitution.

There are very few known examples of electrophilic substitution in the imidazo[1,2-a]pyridine ring[4-6] and no known examples studied with I or its simple monomethyl derivatives. The present work was undertaken in an effort to study the orientation course of selected substitution reactions with imidazo[1,2-a]-pyridine and related methyl derivatives.

Treatment of imidazo[1,2-a]pyridine (I) with N-chlorosuccinimide (NCS) in chloroform resulted in the formation of a monochloroimidazo[1,2-a]pyridine (II). This compound proved to be different from the known 2-chloro-, 5-chloro-, and 7-chloroimidazo[1,2-a]pyridines.[7] The p.m.r. spectrum of II in deuteriochloroform (Figure 1) revealed that the region of the 2-, 3-, and 8-protons integrates for only two protons and that the band is an unsymmetrical doublet. These data indicate that the compound must be either 3-chloroimidazo[1,2-a]pyridine or 8-chloroimidazo[1,2-a]pyridine. The p.m.r. spectrum of 2-chloroimidazo-[1,2-a]pyridine[7] (Figure 2) is very similar to that of II in the same solvent. This established II as the 3 isomer since the splitting pattern in the pyridine ring is apparently unaltered as would be expected if a proton were present at position 8. For instance, in the p.m.r. spectrum of 8-methylimidazo[1,2-a]pyridine,[3,7b] H-7 appears as an unsymmetrical doublet owing to the absence of H-8. In all cases where the pyridine portion of the ring is unsubstituted, H-6 and H-7 appear as triplets, each peak exhibiting secondary splitting.[3b,7] When imidazo[1,2-a]pyridine was treated with N-bromosuccinimide, or with bromine in aqueous alkali,[8a]

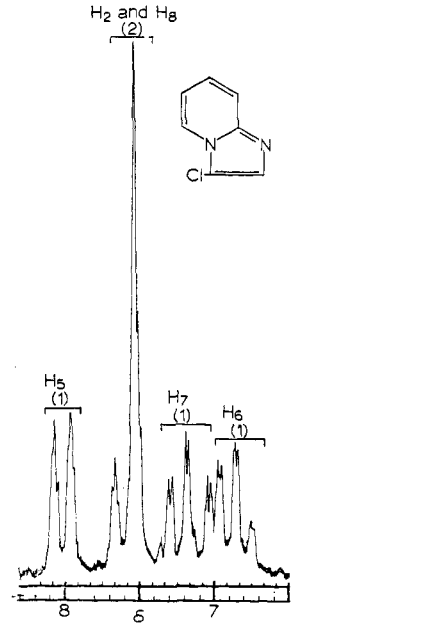


Figure 1.—The p.m.r. spectrum of II in deuteriochloroform (internal standard, TMS).

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(2) To whom correspondence should be addressed at the University of Utah.

(3) (a) W. L. Mosby "Heterocyclic Systems with Bridgehead Nitrogen Atoms," A. Weissberger, Ed., Interscience Publishers, Inc., New York, N. Y., 1961, p. 460; (b) W. W. Paudler and H. L. Blewitt, *Tetrahedron*, **21**, 353 (1965).

(4) V. K. Matveev, *Izv. Akad Nauk. SSSR, Otd. Math. Estes Nauk*, 1005 (1936).

(5) Y. L. Goldfarb and M. S. Kondakova, *J. Gen. Chem. USSR*, **10**, 1055 (1940).

(6) M. S. Kondakova and Y. L. Goldfarb, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 523 (1946).

(7) J. P. Paolini and R. K. Robins, *J. Heterocyclic Chem.*, **2**, 53 (1965).

(8) (a) Nearly all of the early halogenations on imidazo[1,2-a]pyridine and the related methylimidazo[1,2-a]pyridine derivatives studied in our laboratory were executed with NaOBr or NaOCl. These reaction conditions in all cases gave products identical with those later obtained *via* N-chloro- or N-bromosuccinimide. NCS and NBS gave better yields and offered simpler work-up procedures. In view of these results the nuclear halogenation studies are viewed as electrophilic substitution rather than free-radical reactions. (b) A. E. Tschitschibabin, *Ber.*, **58**, 1704 (1925).

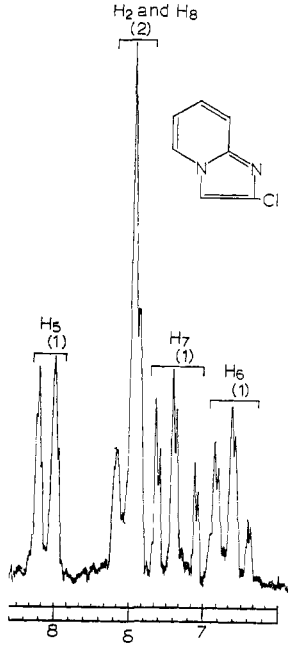
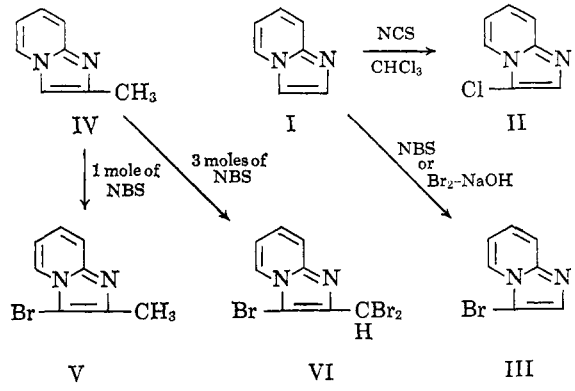


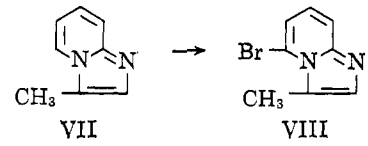
Figure 2.—The p.m.r. spectrum of 2-chloroimidazo[1,2-*a*]pyridine in deuteriochloroform (internal standard, TMS).

3-bromoimidazo[1,2-*a*]pyridine (III) was similarly obtained. The location of the bromo group was made by reference to the similarity of the p.m.r. spectrum to that obtained for II in the same solvent ($CDCl_3$). When the p.m.r. spectrum of III was determined in trifluoroacetic acid, a very sharp singlet (1H) was noted at δ 7.4, which offered additional proof that substitution had indeed occurred in the imidazole ring. (See Scheme I.)

SCHEME I

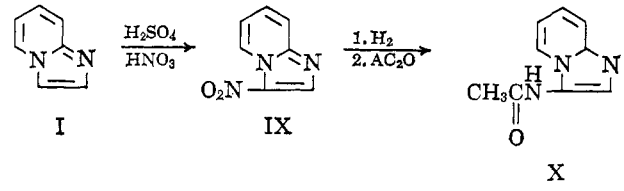


Treatment of 2-methylimidazo[1,2*a*]pyridine[8b] (IV) with 1 mole of N-bromosuccinimide (NBS) yielded a bromo derivative which exhibited a sharp singlet (3H) at δ 2.43 revealing that the methyl group was not attacked. The usual region of the 2-, 3-, and 8-protons shows two multiplets integrating for one proton (H-8) (see Figure 3); thus this compound was designated as 2-methyl-3-bromoimidazo[1,2-*a*]pyridine (V). The absorption due to H-5, H-6, and H-7 was readily assigned and the presence of H-8 was indicated by the splitting pattern of H-7 as previously discussed. When 3 moles of N-bromosuccinimide was used, a tribromo derivative (VI) was obtained. The p.m.r. spectrum of VI contained no methyl peak. The spectrum in $CDCl_3$ is otherwise very similar to that for 2,3-dimethylimidazo[1,2-*a*]pyridine.[7] A sharp singlet at δ 5.93 was assigned to the proton of the dibromomethyl group. The reaction of 3-methylimidazo-[1,2-*a*]pyridine[9] (VII) with N-bromosuccinimide gave a bromo derivative (Figure 4) (VIII) which exhibited



no absorption in the 5-proton region. A sharp singlet integrating for three protons occurs at δ 2.57, showing that the methyl group had not been attacked. The absence of the 5-proton at low field and the presence of the doublet exhibited by H-6 clearly allow the assignment of VIII as 5-bromo-3-methylimidazo[1,2-*a*]-pyridine.

Imidazo[1,2-*a*]pyridine (I) was readily nitrated with concentrated nitric acid in the presence of sulfuric acid to give 3-nitroimidazo[1,2-*a*]pyridine (IX) in good yield. 3-Nitroimidazo[1,2-*a*]pyridine (IX) proved to be a solid, m.p. 203–204° which was light sensitive but was relatively stable when stored in the dark. Reduction of IX followed by acetylation gave the known 3-N-acetylaminoimidazo[1,2-*a*]pyridine[10] which established position 3 as the position of nitration.



2-Chloroimidazo[1,2-*a*]pyridine[7] (XI), when treated with nitric acid, formed 2-chloro-3-nitroimidazo[1,2-*a*]pyridine (XII). A comparison of the p.m.r. spectra of 3-nitroimidazo[1,2-*a*]pyridine and XII established the position of nitration at position 3, since XII possesses a spectrum very similar to that of 3-nitroimidazo[1,2-*a*]pyridine (IX) with the exception of the missing singlet at δ 8.64 (H-2). It is of interest that the 3-nitro group placed H-5 downfield to approximately δ 9.4.

Treatment of 2-chloroimidazo[1,2-*a*]pyridine (XI) with nitrous acid, followed by basic hydrolysis, led to the formation of 3-oximinoimidazo[1,2-*a*]pyridone-2 (XVII). This compound has previously been synthesized by Tschitschibabin[11] who obtained it by nitrosation of imidazo[1,2-*a*]pyridone-2 (XIII). (See Scheme II).

When XI was treated with N-chlorosuccinimide, 2,3-dichloroimidazo[1,2-*a*]pyridine (XIV) was obtained. The p.m.r. spectrum of this compound (Figure 5) shows splitting patterns characteristic of 2,3-disubstituted imidazo[1,2-*a*]pyridines such as 2,3-dimethylimidazo[1,2-*a*]pyridine.[3b,7] 2,3-Dichlorimidazo-[1,2-*a*]pyridine was resistant to hydrolysis in 1 *N* hydrochloric acid and 1 *N* sodium hydroxide at 65° for 1 hr. 2,3-Dichloroimidazo[1,2-*a*]pyridine was unreactive toward aqueous dimethylamine at steam-bath temperature. 2-Chloro-3-nitroimidazo[1,2-*a*]pyr-

(9) R. Adams and J. S. Dix, *J. Am. Chem. Soc.*, **80**, 4618 (1958).
(10) N. W. Bristow, P. T. Charton, D. A. Peak, and W. F. Short, *J. Chem. Soc.*, 616 (1954).
(11) A. E. Tschitschibabin, *Ber.*, **57**, 1381 (1924).

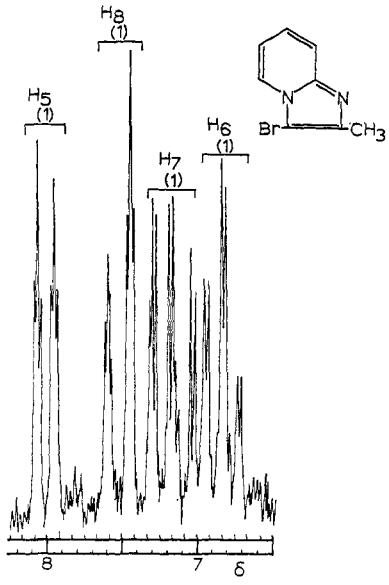
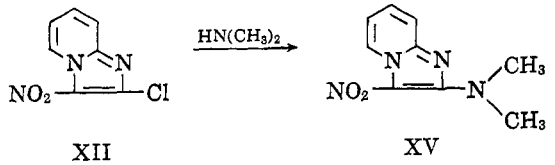


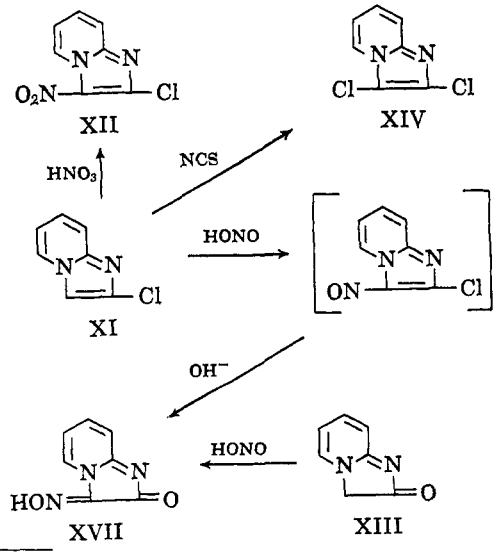
Figure 3.—The p.m.r. spectrum of V in deuteriochloroform (internal standard, TMS).

idine, however, was found susceptible to nucleophilic displacement by dimethylamine to give 2-dimethylamino-3-nitroimidazo[1,2-a]pyridine (XV).



Imidazo[1,2-a]pyridine (I) readily formed a Mannich base when treated with formaldehyde and dimethylamine.[12] This compound is assigned the structure 3-(dimethylaminomethyl)imidazo[1,2-a]pyridine (XVI) based on the p.m.r. spectra and analogous electrophilic substitution reactions. In deuteriochloroform the downfield spectrum of XVI is virtually identical with that for the 3-chloro derivative II. In trifluoroacetic acid a sharp singlet is evident at δ 7.5 owing to H-2.

SCHEME II



(12) After this work was submitted for publication, J. G. Lombardino [*J. Org. Chem.*, **30**, 2403 (1965)] reported this reaction and assigned the same structure to XVI by comparison of the p.m.r. spectra with that of the 2-methyl derivative.

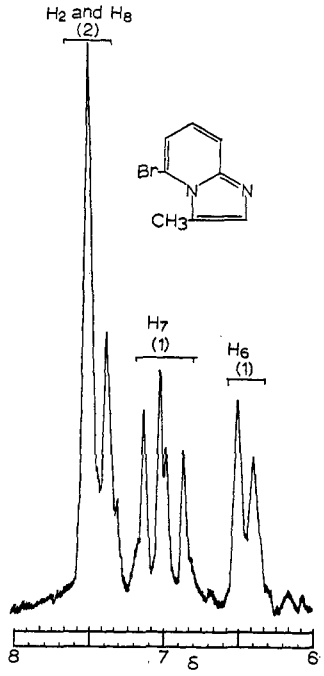


Figure 4.—The p.m.r. spectrum of VIII in deuteriochloroform (internal standard, TMS).

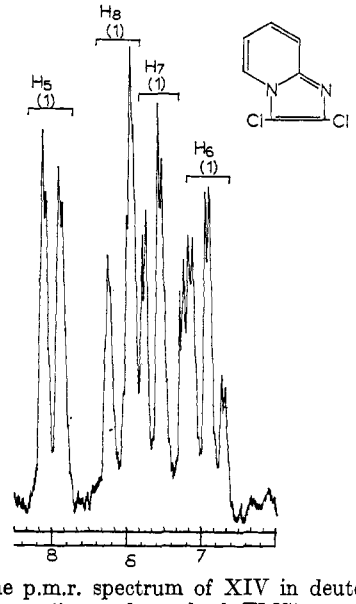


Figure 5.—The p.m.r. spectrum of XIV in deuteriochloroform (internal standard, TMS).

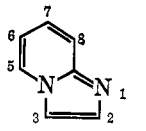
The electron-density calculations of Paudler and Blewitt[3b] successfully predict electrophilic substitution at position 3 for imidazo[1,2-a]pyridine. This has now been verified for chlorination, bromination, and nitration. The introduction of bromine into the 5-position of 3-methylimidazo[1,2-a]pyridine (VII), however, is not predicted by these electron-density calculations.[3b] In fact, the 5-position is assigned the lowest electron density in the parent ring system itself.

More recent frontier-electron-density calculations[13] predict electrophilic substitution to occur most readily at position 3 followed by position 5. Such calculations are in accord with our experimental observations. The frontier-electron-density calculations[13] for 3-methylimidazo[1,2-a]pyridine do indeed predict bromination at position 5.

(13) W. W. Paudler and H. L. Blewitt, *ibid.*, **30**, 4081 (1965).

TABLE I

ULTRAVIOLET ABSORPTION SPECTRAL DATA FOR CERTAIN IMIDAZO[1,2-*a*]PYRIDINES[a]



Compd.	Substituent	pH 1 λ_{max} (ϵ_{max})	pH 1 λ_{min} (ϵ_{min})	pH 11 λ_{max} (ϵ_{max})	pH 11 λ_{min} (ϵ_{min})
IX	3-Nitro	241 (sh) (10,000)	225 (7100)	248 (sh) (10,400)	226 (4200)
		253 (11,200)	287 (3500)	253 (10,800)	281 (3900)
		257 (sh) (10,800)	358 (5700)	261 (sh) (9800)	316 (2900)
		328 (6400)		294 (4800)	
		364 (5900)		366 (15,300)	
XII	2-Chloro-3-nitro	256 (11,700)	230 (2300)	256 (13,100)	229 (3500)
		266 (9500)	282 (2800)	266 (11,000)	285 (4000)
		303 (4000)	318 (3700)	303 (4800)	318 (4300)
		366 (13,000)		366 (13,500)	
XV	2-Dimethylamino-3-nitro	260 (sh) (11,300)	244 (5300)	231 (16,300)	226 (13,800)
		281 (23,900)	306 (1700)	285 (18,700)	249 (7100)
		366 (14,800)		365 (16,400)	309 (1000)
XIV	2,3-Dichloro	282 (7100)		272 (sh) (4900)	245 (700)
				281 (5500)	290 (4100)
				302 (4500)	
II	3-Chloro	280 (7500)	232 (2400)	269 (sh) (4600)	247 (2600)
				273 (4700)	271 (4500)
				280 (5200)	288 (3500)
				302 (3800)	
III	3-Bromo	281 (7500)	235 (3000)	270 (sh) (4700)	254 (3200)
				274 (4800)	272 (4800)
				280 (5300)	
				300 (4100)	
V	2-Methyl-3-bromo	223 (23,800)	238 (2800)	231 (23,600)	255 (2900)
		283 (8200)		274 (4600)	292 (4000)
				283 (5300)	
				306 (4600)	
VI	2-Dibromomethyl-3-bromo	235 (sh) (7500)	254 (4800)	230 (28,800)	234 (28,000)
		283 (9200)		239 (29,500)	273 (6000)
				280 (6300)	287 (5100)
				317 (6600)	
XVI	3-Dimethylaminomethyl	265 (sh) (7200)	228 (1900)	269 (sh) (4600)	240 (2600)
		273 (8100)		279 (5200)	
				297 (4100)	
VIII	3-Methyl-5-bromo	294 (8400)	255 (3000)	278 (sh) (5200)	256 (2900)
				287 (6200)	
				300 (sh) (5000)	

[a] Values of λ given in millimicrons.

It is noteworthy that in the study of electrophilic substitution reactions of imidazo[1,2-*a*]pyridine in each instance a single monosubstituted product was obtained with apparently no significant amount of contaminating isomer. It is evident from the present study that imidazo[1,2-*a*]pyridine is indeed an aromatic nucleus with considerable delocalization of π electrons. The electron density evident at position 5 by present studies and the difficulty with which nucleophilic substitution occurs at this position[7] strongly suggest that the bridgehead nitrogen is *not* comparable to a quaternized pyridine-type nitrogen atom. The lack of ability to protonate such a typical bridgehead nitrogen atom[7,14] is strong evidence that this nitrogen is part of a planar system, with sp^2 bonding and contributes two π electrons to the aromatic system. Such a nitrogen atom is similar to the nitrogen in pyrrole. It thus appears quite likely that the chemistry of a bridgehead-type nitrogen atom which is thus a part of an aromatic system can best be explained on this basis.

(14) W. L. F. Armarego, *J. Chem. Soc.*, 4226 (1964).

Experimental Section

The ultraviolet spectra of certain imidazo[1,2-*a*]pyridines are described in Table I.

3-Nitroimidazo[1,2-*a*]pyridine (IX).—To 40 ml. of concentrated sulfuric acid was added, with stirring, imidazo[1,2-*a*]pyridine (I, 12 g.). The mixture was cooled to 10° in an ice bath and to the cold stirred mixture was added gradually, over a period of 5 min., 12 ml. of concentrated nitric acid. The mixture was then stirred at room temperature for 20 min. and the reaction mixture was poured onto 400 g. of ice. To this cold mixture was added 20% potassium hydroxide solution with stirring, until pH 4–5 was attained. The mixture was then filtered and the filter cake was washed with cold water. The yellow solid was dried in air and weighed, 14.3 g. (86.3%). The material crystallized from 1,2-dimethoxyethane to give yellow platelets, m.p. 203–204°.

Anal. Calcd. for $C_7H_5N_3O_2$: C, 51.5; H, 3.07; N, 25.8. Found: C, 51.6; H, 3.18; N, 25.7.

3-Chlorimidazo[1,2-a]pyridine (II).—To 30 ml. of chloroform was added imidazo[1,2-*a*]pyridine (6 g.) and N-chlorosuccinimide[15] (8 g.) dissolved in chloroform (50 ml.). The mixture became warm and was stirred at room temperature for 1 hr. and then stored in a refrigerator for 16 hr. The chloroform solution

(15) Purchased from Matheson Coleman and Bell, Inc., Norwood, Ohio.

was extracted with 100 ml. of 15% potassium hydroxide solution and percolated through a column of alumina (Merck, basic, 120 g.). The column was then washed with an additional 100 ml. of chloroform, and all of the colored material, which was moving, was eluted. This solution was evaporated to an oil which weighed 6.2 g. This residue was triturated with warm cyclohexane (three 100-ml. portions). The cyclohexane extracts were combined and percolated through a column of Florisil (100 g.). The column was washed with an additional 100 ml. of cyclohexane. The effluent liquid was evaporated to an oil weighing 3.3 g. (42.6%), which solidified on standing. This material crystallized from pentane, giving a solid which melted at 42–44°.

Anal. Calcd. for $C_7H_5ClN_2 \cdot H_2O$: C, 49.3; H, 4.11; Cl, 20.1; N, 16.4. Found: C, 49.1; H, 4.32; Cl, 19.4; N, 16.4.

2-Methyl-3-bromoimidazo[1,2-*a*]pyridine (V).—To 50 ml. of water was added 2.5 g. of 2-methylimidazo[1,2-*a*]pyridine hydrochloride,[16] (IV). Then 50 ml. of 20% potassium carbonate solution was added and the mixture was extracted with chloroform (three 50-ml. portions). The chloroform extracts were combined and percolated through a column of Florisil (2 × 10 cm.). The column was then eluted with 50 ml. of chloroform. To the chloroform solution was added 2.6 g. of N-bromosuccinimide.[17] The reaction mixture was stirred at room temperature for 20 min. Then 50 ml. of 20% potassium carbonate solution was added, and the mixture was stirred for 10 min. The chloroform layer was separated and percolated through a column of Florisil (2 × 20 cm.). The column was washed with 25 ml. of chloroform which was evaporated to yield 2.4 g. (76.7%) of brown oil. Methanolic hydrogen chloride was added and the solution was evaporated to a solid which crystallized as a hydrochloride hydrate, m.p. 187–188° dec.

Anal. Calcd. for $C_8H_8BrClN_2 \cdot H_2O$: C, 36.1; H, 3.76; Br, 30.1; Cl, 13.8; N, 10.6. Found: C, 36.0; H, 3.71; Br, 30.3; Cl, 14.3; N, 10.5.

3-Bromo-2-dibromomethyl[1,2-*a*]pyridine (VI).—To 100 ml. of 20% potassium carbonate solution was added 2-methylimidazo[1,2-*a*]pyridine hydrochloride[16] (10 g.). The mixture was extracted with chloroform and percolated through a column of Florisil (2 × 10 cm.). This chloroform solution was added to 200 ml. of chloroform containing 25 g. of N-bromosuccinimide. The mixture was heated on a steam bath for 2 min. and then allowed to stand at room temperature for 30 min. Sodium hydroxide solution was (20%, 200 ml.) added and the chloroform phase was separated and percolated through a column of Florisil (2.5 × 30 cm.). The column was then washed with 150 ml. of chloroform and the effluent liquid was evaporated to dryness. The residue was triturated with warm benzene and filtered. The filtrate was evaporated to dryness giving 4.1 g. (18.8%) of tan solid melting at 126–130°. Repeated crystallization from Skellysolve B gave needles melting at 141–142° dec.

Anal. Calcd. for $C_8H_5Br_3N_2$: C, 26.0; H, 1.35; Br, 65.1; N, 7.6. Found: C, 26.2; H, 1.36; Br, 64.9; N, 7.5.

2-Chloro-3-nitroimidazo[1,2-*a*]pyridine (XII).—To 30 ml. of concentrated sulfuric acid was added gradually 3 g. of 2-chloroimidazo[1,2-*a*]pyridine[7] (XI). When solution was attained, 3 ml. of concentrated nitric acid was added and the mixture was heated on a steam bath for 2 min. and then let stand at room temperature for 30 min. The reaction mixture was then poured over ice and diluted with water to 400 ml. A solid formed, which was filtered, washed, and dried to yield 2.53 g. (65.1%). This compound crystallized from Skellysolve C as yellow needles melting at 170–171°.

Anal. Calcd. for $C_7H_4ClN_3O_2$: C, 42.6; H, 2.03; Cl, 18.0; N, 21.3. Found: C, 42.6; H, 2.17; Cl, 18.2; N, 21.5.

2,3-Dichloroimidazo[1,2-*a*]pyridine (XIV).—To 35 ml. of chloroform was added 1 g. of 2-chlorimidazo[1,2-*a*]pyridine[7] (XI) and N-chlorosuccinimide (1.4 g.). The mixture was heated on a steam bath for 2 min. and then stirred at room temperature for 30 min. To the reaction mixture was added 30 ml. of 20% potassium carbonate solution. This was stirred for 20 min. and the chloroform layer was separated and dried over potassium carbonate. The dry chloroform solution was evaporated to give 1.3 g. of a brown solid. This crude product was dissolved in benzene and percolated through a column of Florisil (1.5 × 6 cm.), and the column was washed with 50 ml. of benzene. The effluent liquid was evaporated to dryness giving a yellow solid (0.9 g) which crystallized from petroleum ether (b.p. 60–110°) to give white platelets, m.p. 111–112°.

Anal. Calcd. for $C_7H_4Cl_2N_2$: C, 44.9; H, 2.14; N, 15.0. Found: C, 44.9; H, 2.56; N, 15.0.

3-Bromoimidazo[1,2-*a*]pyridine (III). Method A.—To 20 ml. of chloroform was added imidazo[1,2-*a*]pyridine (2 g.) and N-bromoacetamide[17] (2.2 g.). The mixture was heated on a steam bath for 10 min. and then poured into 50 ml. of iced potassium hydroxide solution (10%), and the solution was extracted with chloroform (three 50-ml. portions). The chloroform extracts were combined and dried over sodium sulfate and percolated through a column of basic alumina (Merck, 30 g.). The effluent liquid was evaporated to dryness and a white crystalline solid (0.1 g., 63%) was obtained. This material crystallized from Skellysolve B as needles, m.p. 90–93°. Recrystallization from Skellysolve B raised the melting point to 92–94°.

Anal. Calcd. for $C_7H_5BrN_2$: C, 42.6; H, 2.54; Br, 40.6; N, 14.2. Found: C, 42.8; H, 2.52; Br, 40.1; N, 14.3.

Method B.—To 150 ml. of water was added bromine (4 ml.). The mixture was cooled and 50 ml. of 20% sodium hydroxide solution was added. This basic solution was added to a solution of imidazo[1,2-*a*]pyridine (4 g.) in 50 ml. of ice–water. This mixture was stirred for 5 min. and kept cold by the addition of ice. A white solid formed. This solid was filtered and washed with cold water. The dry solid weighed 5.3 g. (79.5%). This material crystallized from Skellysolve B giving needles melting at 92–94°. A comparison of III prepared by method A showed the infrared spectra to be identical and the mixture melting point to be undepressed.

2-Dimethylamino-3-nitroimidazo[1,2-*a*]pyridine (XV).—To 25 ml. of 1,2-dimethoxyethane was added 2-chloro-3-nitroimidazo[1,2-*a*]pyridine (XII) (250 mg.) and dimethylamine (50 ml. of 25% aqueous solution). This mixture was heated to dryness on a steam bath and the resulting product, a pad of yellow needles, was crystallized from Skellysolve C, giving 190 mg. of yellow needles melting at 151–153°.

Anal. Calcd. for $C_9H_{10}N_4O_2$: C, 52.4; H, 4.86; N, 27.2. Found: C, 52.1; H, 4.84; N, 26.9.

3-Dimethylaminomethylimidazo[1,2-*a*]pyridine[12] (XVI).—To 22 ml. of 25% aqueous dimethylamine was added, with cooling, 15 ml. of cold acetic acid. Then 8.6 g. of cold 37% aqueous formaldehyde solution was added. This was poured onto 11.8 g. of imidazo[1,2-a]pyridine and the solution was allowed to stand at 30° for 20 hr. Then the mixture was poured, with cooling, into 150 ml. of 2.5 *N* potassium hydroxide solution. This solution was cooled and extracted with chloroform. The solvent was evaporated and the oil which was obtained solidified on standing. This material weighed 17.1 g. (100%) and was crystallized from cyclohexane. White crystals were obtained which were further purified by sublimation *in vacuo* to give a product, m.p. 80–82°. Additional material was obtained by percolating the cyclohexane mother liquor through a column of Florisil and evaporation of the effluent liquid to an oily residue which subsequently solidified, m.p. 78–80°.

Anal. Calcd. for $C_{10}H_{13}N_3$: C, 68.6; H, 7.43; N, 24.0. Found: C, 68.8; H, 7.58; N, 23.7.

5-Bromo-3-methylimidazo[1,2-*a*]pyridine (VIII).—To 30 ml. of 10% potassium carbonate solution was added 2.8 g. of 3-methylimidazo[1,2-*a*]pyridine hydrobromide.[7] This mixture was extracted with chloroform (three 35-ml. portions). The chloroform extracts were combined and percolated through a column of Florisil (2 × 10 cm.). The column was washed with 25 ml. of chloroform. To the effluent liquid was added 2.3 g. of N-bromosuccinimide. This mixture was stirred at room temperature for 20 min.; then 50 ml. of 20% potassium carbonate solution was added and the mixture was stirred for an additional 10 min. The chloroform layer was percolated through a column of Florisil (2 × 30 cm.) and the column was washed with 25 ml. of chloroform. The chloroform solution was evaporated to yield an oil weighing 1.83 g. (79.5%). This oil solidified on standing and was crystallized from Skellysolve B. The melting point was 84–85°.

Anal. Calcd. for $C_8H_7BrN_2$: C, 45.5; H, 3.32; Br, 37.9; N, 13.3. Found: C, 45.7; H, 3.36; Br, 38.1; N, 13.6.

3-Oximinoimidazo[1,2-*a*]pyridone-2 (XVII).—To 2-chloroimidazo[1,2-*a*]pyridine[7] (1 g.), in 25 ml. of 2.5 *N* hydrochloric acid, was added sodium nitrite solution (0.55 g. in 5 ml. of water). The temperature was maintained at 5° during addition. After addition was complete, the mixture was stirred at room temperature for 1 hr. Then 10 ml. of concentrated ammonium

(16) A. E. Tschitschibabin, *Ber.*, **59**, 2048 (1926).

(17) Purchased from Arapahoe Chemical, Inc., Boulder, Colo.

hydroxide was added and the mixture was evaporated to one-half volume, *in vacuo*, on a steam bath. A yellow solid formed. The mixture was cooled and filtered, giving 0.5 g. (46.7%). The infrared spectrum of this compound was superimposable upon that of a sample of 3-oximinoimidazo[1,2-*a*]pyridin-2-one, prepared according to the method of Tschitschibabin.[11]

Anal. Calcd. for $C_7H_5N_3O_2$: C, 51.5; H, 3.08; N, 25.7. Found: C, 51.7; H, 3.38; N, 25.41.

3-N-Acetylaminoimidazo[1,2-*a*]pyridine[10] (X).—To 100 ml. of absolute ethanol was added 0.75 g. of 3-nitroimidazo[1,2-*a*]-pyridine (IX) and a small amount of Raney nickel catalyst. This mixture was hydrogenated on a low-pressure Parr shaker at 42 p.s.i. of hydrogen for 16 hr. The solution was then filtered through a Celite pad and ethereal hydrogen chloride was added to the filtrate. The filtrate was then evaporated to dryness, the resulting solid was dissolved in water, and the solution made basic with aqueous ammonia and extracted with chloroform. The chloroform extract was dried over anhydrous sodium sulfate and evaporated to give 0.43 g. of an oil. This oil was dissolved in 10 ml. of acetic anhydride and the solution was refluxed for 45 min. The excess acetic anhydride was removed and the residue was triturated with iced aqueous ammonia and extracted with chloroform. Evaporation of the chloroform gave a residue which was triturated with benzene, leaving a brown solid (0.45 g.). This crude solid was recrystallized from water (charcoal added) to yield 0.22 g. of white solid, m.p. 197°. An authentic sample of 3-N-acetylaminoimidazo[1,2-*a*]pyridine prepared by the method of Bristow, *et al.*,[10] melted at 197–198° (lit.[10] m.p. 196–199°). A mixture melting point showed no depression. Infrared spectra of the two samples were identical in every respect.

Reduction of Pyrrolyl-2,3,4,5-tetramercuric Acetate with Ferrocene

GRACE N. O'CONNOR,[1a] JEAN V. CRAWFORD, AND CHI-HUA WANG[1b]

Department of Chemistry, Wellesley College, Wellesley, Massachusetts 02181

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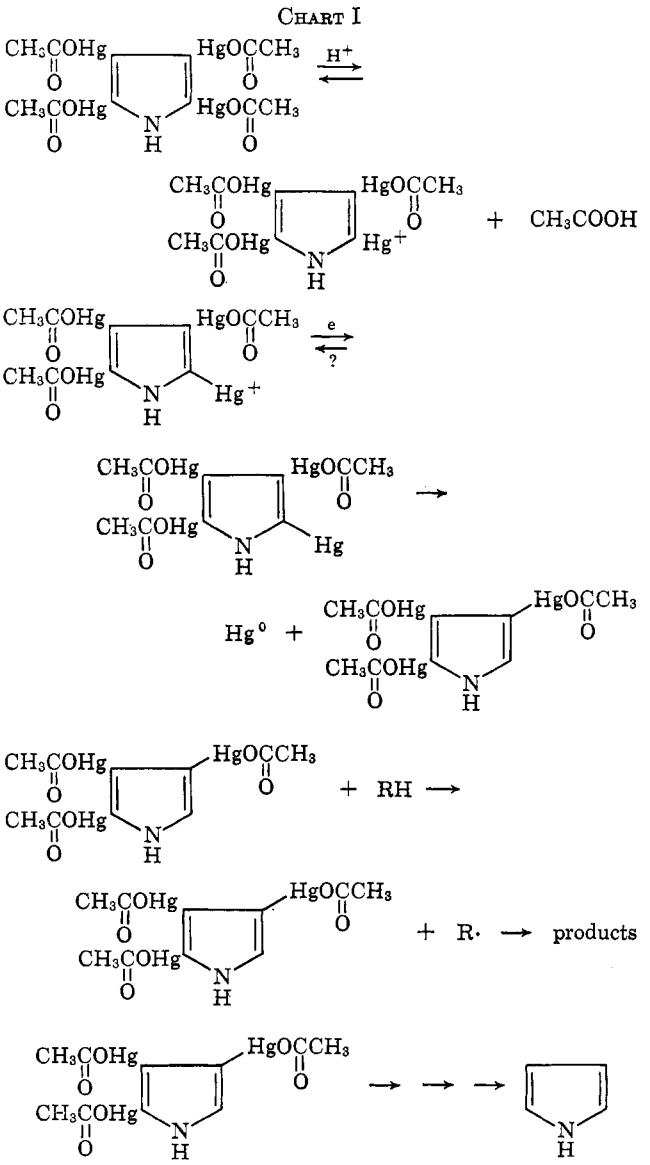
Pyrrolyltetramercuric acetate was prepared and characterized by elementary and infrared spectral analysis. The pyrrolylmercuric cation from solvolysis of the parent compound in acetic acid–toluene was reduced by ferrocene and the major product of the reaction was identified as pyrrole. The free-radical mechanism of the reaction was presented.

To continue our study of the reduction of organometallic cations as a means of generation of free radicals in solution, we have examined the solvolysis and reduction of pyrrolyl-2,3,4,5-tetramercuric acetate, an example of heteroaromatic mercuric compound, for comparison with that of phenylmercuric acetate.[2]

Under rather mild conditions, pyrrole and mercuric acetate furnished pyrrolyltetramercuric acetate and no monomercuric acetate or other identifiable products. Nevertheless, pyrrolyltetramercuric acetate underwent acid-catalyzed hydrolysis in acetic acid–toluene, and subsequent reduction with ferrocene to give pyrrole in good yield. We believe that the observed reaction follows a parallel route with that of phenylmercuric acetate, *e.g.*, Chart I.

Pyrrolyl-2,3,4,5-tetramercuric Acetate.—Mercuric compounds of pyrrole have been investigated by Kottnitz,[3] Willestatter and Asahina,[4] Fischer and Muller,[5] and Cuisa and Grillo.[6] Treating mercuric chloride with pyrrole, Kottnitz obtained a compound with the composition $C_4H_5N \cdot 2HgCl_2$. Willestatter showed that mercuration occurred on the carbon atoms rather than on the nitrogen atom. However, under different conditions, using mercuric chloride, Fischer isolated a double compound, $(C_4H_4N)_2Hg(HgCl_2)_4$, the empirical formula of which is based on elementary analysis. Cuisa and Grillo, treating mercuric acetate, reported the preparation of pyrrolyltetramercuric acetate based on mercury and nitrogen analysis. Because the lack of definitive information about the chemistry of this type of compound, we decided to follow up the more recent work of Cuisa and Grillo. Pyrrolyltetramercuric acetate was prepared and

CHART I



(1) (a) Participant of the Wellesley College Institute of Chemistry supported by the National Science Foundation. (b) To whom inquiries should be addressed.

(2) C.-H. Wang, *J. Am. Chem. Soc.*, **85**, 2339 (1963).

(3) M. Kottnitz, *J. Prakt. Chem.*, **6**, 136 (1872).

(4) R. Willestatter and Y. Asahina, *Ann.*, **385**, 188 (1911).

(5) H. Fischer and R. Muller, *Z. physiol. Chem.*, **148**, 156 (1925).

(6) R. Cuisa and G. Grillo, *Gazz. chim. ital.*, **57**, 323 (1926).