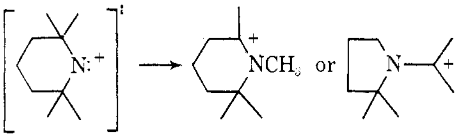
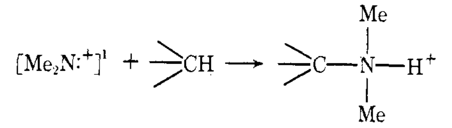
its greater reluctance to accommodate a positive charge. Nitrenium ions are firmly established as intermediates in many chemical reactions.[27] The thermochemistry of the proposed reaction is uncertain as is the subsequent fate of the nitrenium ion. If aminiums react predominantly as singlet pairs the nitrenium ion will be formed in its singlet state. This is of higher energy than the ground state which is a triplet.[27,28] In principle, the singlet nitrenium ion may (i) rearrange, *e.g.*



(ii) insert into a convenient bond, *e.g.*



$$[\mathrm{Me_2N{:}^+}]^1 + \;\gt\mathrm{CH} \longrightarrow \;\gt\mathrm{C}{-}\overset{\mathrm{Me}}{\underset{\mathrm{Me}}{\mathrm{N}}}{-}\mathrm{H}^+$$

or (iii) interconvert to the triplet ground state. If the aminiums react as triplet pairs the nitrenium ion will be formed directly in this state and the reaction would probably not be chain terminating. That is, triplet nitrenes behave as biradicals[27,28] like triplet carbenes and so they would probably react with a suitable hydrogen donor to regenerate an aminium radical, *e.g.*

$$[\mathrm{Me_2N{:}^+}]^3 + \mathrm{R'H} \longrightarrow \mathrm{Me_2NH}\cdot^+ + \mathrm{R'}\cdot$$

Gassman[27,29] and others[30] have undertaken extensive studies of the rearrrangement products formed from singlet bi- and tricyclic nitrenium ions and of the change in products that occurs when the singlet ion is converted to the triplet state before it can rearrange. Studies of the same kind on the products formed in the bimolecular self-reaction of structurally similar aminium radicals should reveal whether or not nitrenium ions are actually produced in this reaction.

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(27) For a detailed review of nitrenium ion chemistry, see P. G. Gassman, *Accounts Chem. Res.*, 3, 26 (1970).

(28) S. T. Lee and K. Morokuma, *J. Amer. Chem. Soc.*, 93, 6863 (1971).

(29) P. G. Gassman and G. D. Hartman, *J. Chem. Soc., Chem. Commun.*, 853 (1972); *J. Amer. Chem. Soc.*, **95**, 449 (1973).

(30) V. Rautenstrauch, *Chem. Commun.*, 1122 (1969); D. C. Horwell and C. W. Rees, *ibid.*, 1428 (1969); P. Kovacic, J.-H. Liu, P. D. Roskos, and E. M. Levi, *ibid.*, 1034 (1970); *J. Amer. Chem. Soc.*, **93**, 5801 (1971); J.-M. Biehler and J.-P. Fleury, *Tetrahedron*, 27, 3171 (1971).

Protonated Nitroxide Radicals[1]

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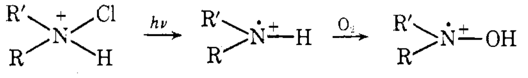
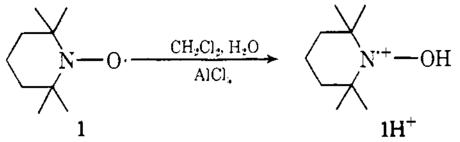
Contribution from the Division of Chemistry, National Research Council of Canada, Ottawa, Canada. *Received March 13, 1973*

Abstract: In contrast to earlier reports, it is shown that dialkyl nitroxides are stable in strong acid solutions at room temperature. The nitroxides yield epr spectra indicating that they are protonated in solutions such as 100% H_2SO_4 which have Hammett acidity function values, H_0, more negative than *ca.* −7.5. In solutions having H_0 more positive than *ca.* −3.5 the unprotonated nitroxide epr spectrum is obtained. Between these two acidities no epr signal is observed because of line broadening resulting from rapid proton exchange. The pK_a for dialkyl nitroxides is -5.5 ± 1. It is concluded from the ^{14}N hyperfine coupling constants that the geometry of the nitrogen atom in a particular protonated nitroxide is very similar to that in the same unprotonated radical despite the fact that the absolute geometry for different dialkyl nitroxides varies substantially. The value of the proton hyperfine coupling constant decreases as the angle that the NO bond makes with the CNC plane increases.

While engaged in a kinetic study of aminium radicals by epr spectroscopy,[3] we observed that in the presence of oxygen spectra attributable to protonated nitroxide radicals were obtained as well as the desired aminium radicals. The only protonated dialkyl nitroxide that has been reported previously was that derived from 2,2,6,6-tetramethylpiperidine *N*-oxyl (**1**) by treating wet methylene chloride solutions of the radical with Lewis acids such as aluminum chloride.[4]





1 1H$^+$

In contrast to the earlier report,[4] we find that the paramagnetic center of **1** is not completely destroyed by concentrated sulfuric acid at room temperature, nor is **1** destroyed by trifluoroacetic acid. In this paper we report some interesting observations on **1H**$^+$ and on two new radicals of this type, one derived from di-*tert*-butyl nitroxide (**2**)[5] and the other from 9-azabicyclo[3.3.1]nonane *N*-oxyl (**3**).

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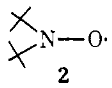
(1) Issued as National Research Council of Canada No. 13423.

(2) National Research Council of Canada Postdoctorate Fellow, 1972–1973.

(3) V. Malatesta and K. U. Ingold, *J. Amer. Chem. Soc.*, **95**, 6400 (1973).

(4) B. M. Hoffman and T. B. Eames, *ibid.*, **91**, 2169 (1969).

(5) This radical has also been reported to be unstable in acid: W. Brackman and C. J. Gaasbeek, *Recl. Trav. Chim. Pays-Bas*, **85**, 221 (1966).



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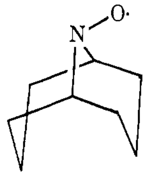

3

Experimental Section

Radicals **1** and **2** were commericial materials that were carefully purified before use. The preparation and purification of radical **3** have been described previously.[6] The radicals were dissolved in the appropriate acid and the epr spectra were recorded on either an E-3 or an E-12 Varian epr spectrometer.

Results

Radicals **1**, **2**, and **3** are protonated only in very strong acids. The usual method for reporting the acidity of such media is by way of the Hammett acidity function,[7,8] H_0. This quantity is derived from the ionization equilibrium of uncharged bases

$$\mathrm{B} + \mathrm{H}^+ \rightleftharpoons \mathrm{BH}^+$$

and is defined by

$$H_0 = -\log K_{\mathrm{BH}^+} - \log ([\mathrm{B}]/[\mathrm{BH}^+])$$

where K_{BH^+} is the thermodynamic ionization constant in molar concentration units (referred to ideal dilute solution in water). In dilute aqueous solution the acidity function becomes equal to the pH.

In acetic acid the three radicals exhibit their normal nitroxide spectra (Table I). At room temperature in aqueous sulfuric acid the spectra of the nitroxides are obtained at H_0 values of -0.35 (10% H_2SO_4 by weight[9]) and -1.73 (30% H_2SO_4).[9] Increasing the acid to 40 wt % ($H_0 = -2.42$) causes the epr lines to broaden and they disappear entirely at $H_0 = -3.68$ (54% H_2SO_4). However, the paramagnetic center is not destroyed completely because on increasing the sulfuric acid to 80 wt % ($H_0 = -7.46$) a weak, broad line epr signal due to the protonated nitroxide appears. In concentrated sulfuric acid ($H_0 = -11$) the lines sharpen and become much stronger. The epr spectra of the protonated nitroxides **1H**$^+$ and **2H**$^+$ have six lines each while that of **3H**$^+$ has only three lines. The epr spectral parameters in concentrated sulfuric acid at room temperature are recorded in Table I. Under these experimental conditions the protonated radicals are stable for many days. However, rather surprisingly the yield of protonated nitroxide is only about 0.3% when solid **1** or **2** is added to concentrated sulfuric acid. This yield is not improved by first dissolving the nitroxide in CF_3COOH and then adding the sulfuric acid.

Table I. Epr Spectral Parameters for Nitroxides and Protonated Nitroxides at 25°

Radical	Solvent	a^N, G[a]	a^H_{NOH}, G	g	Ref
1	CH_2Cl_2	15.87		2.0059	4
1	Benzene	15.54		2.0063	This work
2	Benzene	15.23		2.0060	This work
3	Benzene	17.99		2.0067	This work
1	CH_3COOH	16.42		2.0063	This work
2	CH_3COOH	16.26		2.0059	This work
3	CH_3COOH	19.14		2.0058	This work
1H$^+$	H_2SO_4	21.57	3.12	2.0046	This work
1H$^+$	CH_2Cl_2	21.8	3.3	2.0042	4
1D$^+$	D_2SO_4	21.74	0.51[b]	2.0046	This work
1D$^+$	CH_2Cl_2	21.9	(0.507)[c]		4
2H$^+$	H_2SO_4	20.66	6.84	2.0047	This work
2D$^+$	D_2SO_4	20.19	1.01[b]	2.0047	This work
3H$^+$	H_2SO_4	24.50	*c*	2.0041	This work

[a] The high field ($m_N = +1$) lines are somewhat broader than the low field lines (*cf.* G. B. Fraenkel, *J. Phys. Chem.*, **71**, 139 (1967)). [b] a^D_{NOD}. [c] Not resolved.

For radicals **1** and **2** the epr spectra were also recorded in 98% D_2SO_4 (Table I). Within the limits of experimental accuracy the value of a^H_{NOH}/a^D_{NOD} is equal to the ratio of the proton to deuteron gyromagnetic ratios (6.5).[10] The spectral parameters for **1H**$^+$ and **1D**$^+$ in sulfuric acid are in satisfactory agreement with the values reported by Hoffman and Eames[4] for these radicals in methylene chloride (see Table I).

None of the three nitroxides gave an epr spectrum in trifluoroacetic acid ($H_0 = -3.03$).[11] Once again this is not due to destruction of the paramagnetic center since upon the addition of sulfuric acid broad, weak signals due to the protonated nitroxide develop at 0.94 *M* acid ($H_0 = -7.33$)[11] and become strong and sharp at sulfuric acid concentrations of 1.87 *M* ($H_0 = -8.07$).[11]

The proton hyperfine coupling constant, a^H_{NOH}, for **1H**$^+$ was dependent on the temperature. In concentrated sulfuric acid it decreases linearly with increasing temperature from a value of 3.3 G at 12° to 2.4 G at 85°.[12] Up to this temperature the change is reversible, but on warming to 100° the nitroxide is irreversibly destroyed. In 1:1 v/v CF_3COOH-H_2SO_4, a^H_{NOH} decreased approximately linearly from 3.4 G at $-10°$ to 2.9 G at 50°. However, at 60° a^H_{NOH} was $\sim$1.6 G and at 80° the proton splitting could not be resolved, the spectrum having collapsed to a triplet with lines just as sharp as in the sextet observed at lower temperatures. This change was reversible.

The spectrum of **2H**$^+$ in concentrated sulfuric acid also depends on the temperature. The decrease in a^H_{NOH} between 25 and 80° is only just detectable. However, splitting by the *tert*-butyl protons which is indetectable at 25° becomes noticeable, though by no means fully resolved, at 80° with $a^H_{CH_3} \sim 0.5$ G.[14] This increase in resolution may be due to the decrease in the viscosity of the acid at the higher temperatures.

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(6) G. D. Mendenhall and K. U. Ingold, *J. Amer. Chem. Soc.*, **95**, 6395 (1973).

(7) L. P. Hammett and A. J. Deyrup, *ibid.*, **54**, 2721 (1932).

(8) For reviews on this function and its application, see L. P. Hammett, *Chem. Rev.*, **16**, 67 (1935); M. A. Paul and F. A. Long, *ibid.*, **57**, 1 (1957); R. J. Gillespie and T. E. Peel, *Advan. Phys. Org. Chem.*, **9**, 1 (1971).

(9) C. D. Johnson, A. R. Katritzky, and S. A. Shapiro, *J. Amer. Chem. Soc.*, **91**, 6654 (1969).

(10) T. F. Wimett, *Phys. Rev.*, **91**, 499 (1953).

(11) H. Hyman and R. A. Garber, *J. Amer. Chem. Soc.*, **81**, 1847 (1959).

(12) Eames and Hoffman[13] have reported similar behavior for **1** and **2** complexed with boron halides and aluminum chloride. In these complexes both a^N and a^M (M = metal) decrease linearly with increasing temperature, the temperature variation for the metal nuclei being generally greater than for the nitrogen nuclei.

(13) T. B. Eames and B. M. Hoffman, *J. Amer. Chem. Soc.*, **93**, 3141 (1971); see also **91**, 5168 (1969).

(14) For **2** $a^H_{CH_3}$ has been estimated[15] to be -0.11 G. The larger splitting for **2H**$^+$ is consistent with a higher spin density on the nitrogen atom in the protonated radical (*vide infra*).

(15) K. H. Hausser, H. Brunner, and J. C. Jochims, *Mol. Phys.*, **10**, 253 (1966).

A sample of **2** in 1:1 (v/v) $CF_3COOH-H_2SO_4$ was stable at 40° and the *tert*-butyl protons were partly resolved (0.5 G) at this temperature, though not at 25°. The radical was destroyed when this sample was warmed to 100°.

The behavior of the free radical 2,2,6,6-tetramethylpiperid-4-one *N*-oxyl contrasts with that of radicals **1**, **2**, and **3**. In trifluoroacetic acid this radical is stable for hours and exhibits an ordinary three-line nitroxide spectrum. The value of a^N is increased somewhat by the addition of concentrated sulfuric acid up to an $H_0 = -5.8$ (70% H_2SO_4). Further addition of sulfuric acid (80%, $H_0 = -7.4$) destroys the nitroxide irreversibly without any signal attributable to the protonated nitroxide appearing. The anomalous behavior of this radical can presumably be attributed to the presence of the carbonyl group.[16]

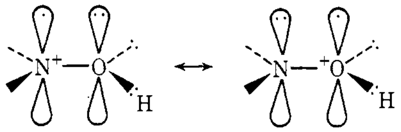
Two stable iminoxy radicals, R(R′)C=NO·, di-*tert*-butyliminoxy[18] and 1-adamantyl-*tert*-butyliminoxy,[18] were rapidly decomposed in trifluoroacetic acid and in concentrated sulfuric acid.

Discussion

As Hoffman and Eames[4] have pointed out, the increase in a^N and decrease in the g factor upon protonation of a nitroxide indicates that the site of protonation is the nitroxide oxygen atom. The proton draws the two bonding π electrons toward the oxygen and shifts the antibonding unpaired π^* electron toward the nitrogen as a consequence of which the spin density on nitrogen (ρ^N) increases and hence a^N increases. The decrease in g factor results from the decreased spin density on oxygen and a blue shift in the n–π^* transition.[19] In the complexes Hoffman and Eames[13] prepared of **1** and **2** with boron trihalides and aluminum trichloride, it was found that the g factors for **1M** and **2M** were similar and that a^M for **2M** was greater than for **1M**. The protonated nitroxides show similar behavior. However, in the metal complexes a^N for **2M** was greater than for **1M** whereas the reverse is true for **2H⁺** and **1H⁺**.

Changes in a^N for nitroxides and in a^N and $a^H{}_{NOH}$ for protonated nitroxides must reflect changes in the electronic structure of these radicals. In general, an increase in a^N appears to reflect an increase in the angle, θ, that the NO bond makes with the CNC plane.[20,21] On the basis of an electron diffraction study it has been reported[22] that $\theta = 0°$ for **2**.[23] While **1** and **3** have not themselves been examined by X-ray methods, studies on analogous compounds indicate that θ should be *ca.* 17 ± 1° for **1**[21a,21c,21e] and *ca.* 30° for **3**.[21d] It can be seen from the data in Table I that a^N increases as θ increases both in benzene and in acetic acid. The a^N values for the protonated nitroxides also increase in the same order, *i.e.*, **2** < **1** < **3**. Of greater interest is the fact that the a^N values increase on protonation by a very similar factor for all three nitroxides. Thus, the ratios $a^N{}_{NOH}/(a^N{}_{NO})_{benzene}$ are 1.39, 1.36, and 1.36 for **1**, **2**, and **3**, respectively, and for $a^N{}_{NOH}/(a^N{}_{NO})_{acetic\ acid}$ they are 1.31, 1.27, and 1.28, respectively. These ratios are sufficiently similar that it seems rather unlikely that the geometry of any of the protonated radicals differs very much from that of their unprotonated parents.[24] However, we cannot exclude the possibility[25] that all three nitroxides become less planar upon protonation but the same factor(s) that cause **3** to be nonplanar at nitrogen cause **3H⁺** to be more nonplanar than **1H⁺**.

The most interesting features of the epr parameters of the protonated nitroxides are the large differences in $a^H{}_{NOH}$. As Danen and Rickard[26] suggested with reference to protonated amino radicals, $R_2NH\cdot^+$, it seems likely that the ratio $a^N{}_{NOH}/a^H{}_{NOH}$ should be fairly sensitive to the configuration of the radicals and should increase with increasing deviation from planarity at the nitrogen atom. The increase in this ratio along the series **2** < **1** < **3** is in accord with the deviation of the NO bond from the CNC plane in the nitroxides and, for the reasons outlined above, also with the deviation in the protonated nitroxides. In these species the oxygen is presumably protonated on one of its lone pairs of electrons. This means that in the most stable conformation (with resonance structures **4** ↔ **5**) the proton would not be expected to interact with the unpaired electron except by a spin polarization mechanism since the proton will lie in the nodal plane of the orbital containing the unpaired electron. The structure with a high spin density on oxygen (*i.e.*, **5**) is expected to be favored by an sp² (planar) nitrogen and disfavored with increasing deviation of the NO bond from the CNC plane. That is, spin polarization would be expected to produce an increase in a_H along the series **2** < **1** < **3** as is observed.



4 **5**

The presence of nitroxide epr signals in solutions with H_0 values more positive than *ca.* −3.5 and of protonated nitroxide signals at H_0 values more negative than −7.5 implies that the pK_a for dialkyl nitroxides is in this range, say −5.5 ± 1.[27] Dialkyl nitroxides

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[16] The structurally analogous radicals, 2,2,6,6-tetramethylpiperid-4-hydroxy *N*-oxyl and 4-benzoyloxy *N*-oxyl, have been reported to be unstable in hydrochloric acid.[17]

[17] V. A. Golubev, E. G. Rozantsev, and M. B. Neiman, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1927 (1965).

[18] G. D. Mendenhall and K. U. Ingold, *J. Amer. Chem. Soc.*, **95**, 2963 (1973).

[19] T. Kawamura, S. Matsunami, and T. Yonezawa, *Bull. Chem. Soc. Jap.*, 40, 1111 (1967).

[20] For leading references, see J. Douady, Y. Ellinger, A. Rassat, and R. Subra, *Mol. Phys.*, 17, 217 (1969); G. R. Underwood and V. L. Vogel, *ibid.*, **19**, 621 (1970); A. W. Salotto and L. Burnelle, *J. Chem. Phys.*, 53, 333 (1970); H. Hayat and B. L. Silver, *J. Phys. Chem.*, 77, 72 (1973).

[21] For X-ray evidence that the NO bond in a variety of nitroxides does not lie in the CNC plane, see, *e.g.* (a) J. Lajzbrowicz-Bonneteau, *Acta Crystallogr., Sect. B*, 24, 196 (1968); (b) D. M. Hawley, G. Ferguson, and J. M. Robertson, *J. Chem. Soc. B*, 1255 (1968); (c) L. J. Berliner, *Acta Crystallogr., Sect. B*, 26, 1198 (1970); (d) A. Capiomont, B. Chion, and J. Lajzerowicz, *ibid.*, 27, 322 (1971); (e) A. Capiomont, *ibid.*, 28, 2298 (1972).

[22] B. Andersen and P. Andersen, *Acta Chem. Scand.*, **20**, 2728 (1966).

[23] An angle of 3° or so could not, probably, be distinguished from an angle of 0° by this technique.

[24] See also ref 13.

[25] Suggested by a referee.

[26] W. C. Danen and R. C. Rickard, *J. Amer. Chem. Soc.*, **94**, 3254 (1972).

[27] The pK_a of diaryl nitroxides must be lower since di(4-methoxyphenyl) nitroxide has been observed to protonate in trifluoroacetic acid.[28] The pK_a of 2,2,6,6-tetramethylpiperid-4-one *N*-oxyl and of the 4-hydroxy *N*-oxyl have been reported on the basis of potentiometric titration to be 7.4 and 9.6, respectively.[29] It is difficult to believe that

are therefore much weaker bases than dialkylhydroxylamines ($pK_a = 5.2$[32]) or dialkylamino radicals ($pK_a = 7.0 \pm 0.5$[33]), both of which must be protonated on nitrogen.[34] The absence of any epr signal at H_0 values between −3.5 and −7.5 is a line-broadening effect which results from a very rapid protonation and deprotonation of the radicals.

$$R_2NO\cdot + H^+ \underset{\text{fast}}{\overset{\text{fast}}{\rightleftharpoons}} R_2NOH\cdot^+$$

The absence of an epr signal from $-3.5 < H_0 < -7.5$ implies that the decrease in $a^{H}{}_{NOH}$ for **1H**$^+$ with increasing temperature (particularly in 1:1 (v/v) $CF_3COOH–H_2SO_4$ in which the proton hfc was not resolvable at 80°) cannot be due merely to the conversion of **1H**$^+$ to **1**. That is, conversion to the unprotonated form, because of a decrease in H_0[9] or shift in the equilibrium constant, would require that the epr signal of **1H**$^+$ first broaden and then disappear entirely before that due to **1** developed. However, the epr signal was present at all temperatures and the lines remained sharp as they coalesced. We therefore suggest that the geometry of **1H**$^+$ at low temperatures differs from that at high temperatures.[24] The decreased interaction between the unpaired electron and the proton at the higher temperatures might, in principle, be due to (i) a more tetrahedral geometry at nitrogen, (ii) a shift of the proton into the nodal plane of the unpaired electron orbital, or (iii) a rapid inversion of the nitrogen atom ($k \sim 2 \times 10^7$ sec^{-1}). The first possibility seems unlikely since a^N remains unchanged or decreases slightly as the temperature is raised implying that the geometry of the nitrogen remains unchanged or that it becomes slightly more planar. Even if (ii) or (iii) provide the correct explanation for this phenomenon it is not obvious why **1H**$^+$ behaves differently in concentrated sulfuric acid, nor is it clear why **2H**$^+$ should behave differently from **1H**$^+$ in both media. It is to be hoped that future studies of these radicals will answer some of the questions raised by the present work.

Acknowledgment. We are grateful to Professor Hoffman for a number of helpful comments and suggestions.

the ketone or alcohol group could have such a profound effect on p*K*. We therefore attempted to repeat the potentiometric titration on a very pure sample of 2,2,6,6-tetramethylpiperid-4-one *N*-oxyl.[30] There was no break in the titration curve from pH 8 to 2 and the nitroxide still gave a strong epr signal. It must be concluded that Rozantsev and Gintsberg titrated an impurity.

(28) H. Hogeveen, H. R. Gersmann, and A. P. Praat, *Recl. Trav. Chim. Pays-Bas*, **86**, 1063 (1967).

(29) E. G. Rozantsev and E. G. Gintsberg, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 571 (1965).

(30) Purified by slow sublimation at room temperature, mp 40° (lit.[31] mp 38°), 100% pure by glc on a 12-ft 10% silicone rubber column at 120°.

(31) R. Briere, H. Lemaire, and A. Rassat, *Bull. Soc. Chim. Fr.*, 3273 (1965).

(32) T. C. Bissot, R. W. Parry, and D. H. Campbell, *J. Amer. Chem. Soc.*, **79**, 796 (1957).

(33) R. W. Fessenden and P. Neta, *J. Phys. Chem.*, **76**, 2857 (1972).

(34) The pK_a for phenylhydroxylamine protonated on nitrogen is 2.0.[35] The estimated pK_a for protonation on oxygen is < -1.74.[35]

(35) A. Darchen and P. Boudeville, *Bull. Soc. Chim. Fr.*, 3809 (1971).

Pteridines. XXVIII. A New, General, and Unequivocal Pterin Synthesis[1]

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Margareta Séquin-Frey,[2] and Peter A. Jacobi

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Princeton, New Jersey 08540. Received February 17, 1973

Abstract: A versatile new synthetic route to pterins is described. Reaction of an α-ketoaldoxime or α-ketoketoxime with esters of α-aminocyanoacetic acid gives 2-amino-3-alkoxycarbonylpyrazine 1-oxides which are cyclized with guanidine to pterin 8-oxides. Deoxygenation of the pyrazine and pterin *N*-oxides, and the conversion of the latter to 7,8-dihydropterins, are described.

The classical synthetic route to pteridines involves condensation of a 4,5-diaminopyrimidine with an α,β-dicarbonyl compound, and it is a fair estimate that more than 90% of all known synthetic pteridines have been prepared by some modification of this condensation reaction.[3] Its usefulness and flexibility result from the wide diversity of substitution patterns possible with both components and the generally high yield with which the condensation proceeds. The use of α-ketoaldehydes in this so-called Isay pteridine synthesis[4] leads, however, to the preferential formation of 7- rather than 6-substituted isomers, while the use of other unsymmetrical α,β-dicarbonyl compounds necessarily gives products of ambiguous structure.[3,5] Thus,

(1) (a) Part XXVII: E. C. Taylor, S. F. Martin, Y. Maki, and G. P. Beardsley, *J. Org. Chem.*, **38**, 2238 (1973). (b) This work was supported in its initial stages by grants to Princeton University from the National Institutes of Health, Public Health Service (Grants No. CA-02551 and CA-12876), and from the U. S. Army Medical Research and Development Command (Contract No. DA-49-193-MD-2777). This is Contribution No. 1195 in the Army research program on malaria.

(2) Postdoctoral Fellow of the Swiss National Science Foundation.

(3) For general references on pteridine chemistry, see (a) "Pteridine Chemistry," W. Pfleiderer and E. C. Taylor, Ed., Pergamon Press, London, 1964; (b) R. C. Elderfield and A. C. Mehta, "Heterocyclic Compounds," Vol. 9, R. C. Elderfield, Ed., Wiley, New York, N. Y., 1967, pp 1–117; (c) W. Pfleiderer, *Angew. Chem., Int. Ed. Engl.*, **3**, 114 (1964).

(4) O. Isay, *Ber.*, **39**, 250 (1906).

(5) See, for example, (a) R. F. W. Spickett and G. M. Timmis, *J. Chem Soc.*, 2887 (1954); (b) R. Tschesche and G. Sturm, *Chem. Ber.*, **98**, 851 (1965).

Taylor, et al. / Pterin Synthesis