Registry No. $RhCl_3$, 10049-07-7; η^3-$C_3H_5Co[P(OCH_3)_3]_3$, 42603-27-0; C_6H_4, 71-43-2; $CH_3C_6H_5$, 108-88-3; $CH_3CH_2C_6H_5$, 100-41-4; $CH_3CH_2CH_2C_6H_5$, 103-65-1; $(CH_3)_2CHC_6H_5$, 98-82-8; $(CH_3)_3CC_6H_5$, 98-06-6; $F_3CC_6H_5$, 98-08-8; $CH_3OC_6H_5$, 100-66-3; H_2O, 7732-18-5; H_2, 1333-74-0; Aliquat 336, 63393-96-4; naphthalene, 91-20-3; methylcyclohexane, 108-87-2; ethylcyclohexane, 1678-91-7; *tert*-butylcyclohexane, 3178-22-1; benzene-d_6, 1076-43-3; toluene-d_6, 1076-43-3; ethylbenzene-d_{10}, 25837-05-2.

The Reactions of 1-Adamantyl Radicals with Acetonitrile and Their Bearing on the Oxidative Decomposition of 1,1'-Azoadamantane

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1-Adamantyl radicals (Ad•) have been generated photochemically from azo-1,1'-adamantane (AA) in acetonitrile (MeCN). Product analysis by GC accounted for 98% of the Ad groups as a mixture of adamantane (AdH), 1,1'-biadamantane (AdAd), and the coupling product (**5**) of Ad(Me)C=N• with solvent-derived •CH_2CN. The remaining 57% of the •CH_2CN groups that could be found appeared as succinonitrile. Kinetic modeling of the product distribution shows that Ad• abstracts hydrogen from MeCN roughly four times as fast as it adds to the nitrile carbon. In our previous work[7] on the oxidative decomposition of AA in MeCN, induced by the thianthrene cation radical ($Th^{•+}$), very little AdH but significantly larger amounts of AdAd and AdCOMe were obtained. We propose, therefore, that virtually no free Ad• is formed or survives oxidation in the oxidative decomposition of AA. Further, the AdAd found in the oxidative reaction cannot have come from the dimerization of free Ad• but may have arisen, instead, from the biadamantane cation radical ($AdAd^{•+}$), formed within a solvent cage.

Introduction

Acetonitrile (MeCN) is a solvent frequently used in electrochemistry[1] and in cation radical reactions.[2-5] While its reactions with carbocations are well documented,[6,7] many free-radical reactions have been carried out in MeCN solution without clear evidence of solvent participation. For example, in some now classical studies of the decomposition of di-*tert*-butyl peroxide[8] and of hydrogen atom abstraction by *tert*-butoxy radical,[9] MeCN functioned as one of a number of inert solvents. Again, in the superoxide-induced decomposition of *tert*-butyl hydroperoxide in MeCN, in which *t*-$BuOO^-$, *t*-BuOO•, and *t*-BuO• all participate, *t*-$BuOO^-$ added to MeCN, but apparently, reactions of the radicals with the solvent did not occur.[10] Hydroxyl radical abstracted hydrogen atom from MeCN in aqueous solution, leading to an 18% yield of succinonitrile.[11] It is surprising that so little is known about the reaction of radicals with liquid MeCN, especially in view of the substantial radical-stabilizing ability of the cyano group.[12-17]

The present investigation arose from questions about radical reactions with MeCN that remained unanswered in the oxidative decomposition of azo-1,1'-adamantane (AA) by the thianthrene cation radical ($Th^{•+}$) in MeCN.[7] Whereas 91% of the adamantyl (Ad) groups from AA appeared in cation-derived products, adamantane (AdH) and 1,1'-biadamantane (AdAd) were obtained only in 0.2% and 2.5% yield, respectively. Also, the Ad group was found in an unexpected product, adamantyl methyl ketone (AdCOMe, **1**), formed in 5.5% yield. We were puzzled as to why so little AdH but much more AdCOMe and AdAd were obtained. It seemed to us that if free Ad• radicals were generated singly, for example, by single-electron transfer (SET) from AA to $Th^{•+}$, and escaped oxidation to Ad^+, they should react preferentially with the solvent, so the yield of AdAd should be insignificant. Any AdAd observed, in that case, would suggest its formation in some sort of a cage reaction. Furthermore, we attributed the formation of AdCOMe to addition of Ad• to the cyano group of MeCN and the subsequent hydrolysis by water adventitiously in the solvent or added during workup, of Ad(Me)C=NH (**2**) or $Ad(Me)C=NH_2^+$. If this hypothesis were correct, the ratio of addition of Ad• at cyano group carbon to abstraction of a hydrogen atom from the methyl group of MeCN would be 5.5/0.2, that is, 27.5. These surprising results led us to investigate the reactions of Ad•, generated in a more conventional way, with MeCN. Ad• is conveniently produced by irradiation of *trans*-AA.[18] The cis isomer, formed initially, undergoes thermolysis

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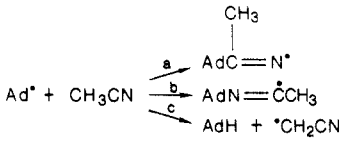
Table I. Products from Photolysis of AA in MeCN

compd	t_r, min	FID[a] factor	mmol found		% Ad[d]		% CH_2CN[e]	
			run 1[b]	run 2[c]	run 1	run 2	run 1	run 2
AdH	8.4	1.046	0.602	0.665	54.9	57.5		
$(NCCH_2)_2$ (3)	9.9	0.234	0.088	*f*			29.2	
AdCN	13.5		*h*	*h*				
AdNHCOMe (4)	18.1	0.993	0.008	0.005	0.73	0.43	1.3	0.75
5	21.0	0.677	0.158	0.181	14.4	15.7	26.2	27.2
AdAd	25.1	1.945	0.158	0.140	28.8	24.2		
6	42.0		*h*	*h*				
Total[g]					98.8	98.3	56.7	28.0

[a] GC peak area per unit weight of compound relative to decane (FID factor = 1.0). [b] 0.548 mmol of AA in 100 mL of MeCN irradiated for 70 h at 350 nm at ambient temp. GC analysis employed a 5 ft × $^1/_8$ in. OV-17 packed column programmed from 50 to 260 °C at 10 deg/min. Solution after irradiation was concentrated, by controlled evaporation of solvent, for analysis. [c] 0.578 mmol of AA in 100 mL of MeCN. Solution was analyzed by GC without being concentrated. [d] 100 × (mmol of product) × (number of Ad groups in product)/(2 × initial mmol of AA). [e] 100 × (mmol of product) × (number of CH_2CN groups in product)/mmol of AdH. [f] The unconcentrated solution was too dilute for this measurement. [g] Total of Ad or CH_2CN groups accounted for. [h] Trace.

even at ambient temperature to give two Ad· in a solvent cage.

Earlier studies of the decomposition of AA in other solvents showed the dominant reactions of Ad· to be cage recombination and attack on solvent.[19] In MeCN solution, free Ad· could conceivably attack the solvent in the ways shown: (a) at carbon, (b) at nitrogen, and (c) with hydrogen abstraction. We wanted to know the relative importance of these reactions. We have now found that, indeed, all three reactions occur, with path c being dominant, path a being of considerable importance, and path b being very minor. We found evidence, also, for the coupling of $\cdot CH_2CN$ with iminyl radical of path a, and we can apply our findings to the earlier questions that remained unanswered.[7]



Results

A degassed solution of AA in MeCN was irradiated at 25 °C with 350-nm light. Because the half-life of *cis*-AA is approximately 20 min at this temperature and the extinction coefficient of cis-AA is six times larger than that of *trans*-AA,[16] photoreversion of cis to trans is expected to be important. This phenomenon is held responsible for the long irradiation time (70 h) needed for complete destruction of AA. The reaction mixture was analyzed by GC/MS, which allowed structural assignments to be made of the eight products shown below. Four minor products

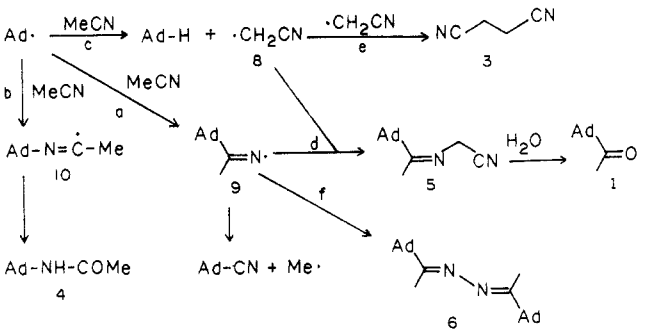
AdH AdAd AdCN

AdCOMe (1) $NCCH_2CH_2CN$ (3) AdNHCOMe (4)

$AdC(Me)=NCH_2CN$ (5) $AdC(Me)=NN=C(Me)Ad$ (6)

could not be identified despite numerous attempts to isolate them by preparative GC. Compounds 4–6 and AdAd were synthesized independently, while commercial samples of AdH, succinonitrile (3), 1-cyanoadamantane (AdCN), and AdCOMe (1) were used for identification of these compounds. Several of the products were isolated by preparative GC, and their NMR spectra were compared with those of the authentic materials.

Scheme I. Mechanism of Product Formation from Adamantyl Radicals and Acetonitrile



The imine 5 was synthesized by treating 1 with aminoacetonitrile hydrochloride and pyridine in the presence of molecular sieves. Preparative GC allowed for isolation of 5 in moderate yield. This compound proved to be very sensitive to moisture, undergoing hydrolysis to 1. In fact 1 was absent in freshly opened tubes of irradiated AA but appeared as the solutions aged. Any 1 detected was therefore included (Table I) in the yield of 5. The imine Ad(Me)C=NH (2), which was considered earlier as being a source of 1,[7] was shown by comparison of GC traces with those of known imine to be absent in freshly opened irradiation samples. Authentic 2 was prepared, contaminated with 1, by reaction of AdCN with MeMgBr followed by workup with MeOH. Azine 6 is not readily hydrolyzed[7] and therefore cannot be the source of 1 in aged solutions of irradiated AA. Although *N*-adamantyl adamantyl methyl ketimine [Ad(Me)C=NAd, 7] is a possible solvent-derived product in the photolysis of AA, we were unable to find evidence (GC/MS) for its presence.

Quantitative GC analysis of the product mixture gave the results shown in Table I. While AdH was the major product, substantial amounts of 3, 5, and AdAd were also found. An attempt was made to detect ketene imines by their characteristic 2020-cm^{-1} IR band. No such band was seen in freshly opened irradiated samples but this result is clouded because of the low extinction coefficient ($\simeq$600) of ketene imines,[20] the short path length of IR cells, and interference by MeCN bands.

Discussion

The products we found in the reaction of Ad· with MeCN can be rationalized by Scheme I. Addition of radicals to the nitrile carbon gives the ketiminyl radical 9, a process that has been reported for other nitriles.[21-26]

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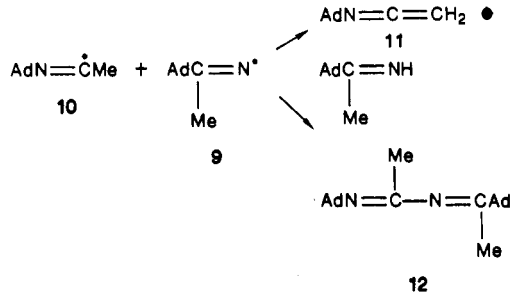
Ketiminyl radicals are known to dimerize[27,28] and to undergo β-scission with liberation of an alkyl radical and formation of a nitrile.[29] These reactions occurred only to a small extent with our ketiminyl radical **9**, leading to low yields of the dimer **6** and β-scisson product AdCN. The small extent of these reactions is understandable in that hindered iminyl radicals are known to dimerize only slowly,[28] and β-scission becomes important only when a favorable alkyl radical can be released,[28] a characteristic not possessed by **9**. The major fate of **9** is the scavenging of cyanomethyl radical, affording the imine **5**. To our knowledge, this is the first reported case of the apparent coupling of a ketiminyl with an unlike radical.

Although **5** accounts for a portion of the Ad• radicals that were formed, the major fate of the Ad• was to become AdH. This observation requires that hydrogen atom abstraction from solvent CH_3CN occurred, generating cyanomethyl radicals (**8**). In our computation of yields (Table I) we have equated the amount of **8** that was formed with the amount of AdH that was assayed. The anticipated dimer, succinonitrile (**3**), was found and assayed by GC.

Small amounts of *N*-adamantylacetamide (**4**) were obtained. We suggest that formation of **4** begins with the addition of Ad• to the nitrogen atom of MeCN, giving the imidoyl radical **10**.[30] Disproportionation or combination of **10** with **9** gives respectively products **11** and **12**, each of which could be hydrolyzed to **4** by stray water.



Viewing the products more quantitatively, we note in Table I that 98–99% of the Ad• have been accounted for. This figure is surprisingly high in view of the fact that it represents only four Ad-containing products. The product balance for CH_2CN groups, obtained only in run 1, was not as good, namely, 57%. We are unable to account for the loss of CH_2CN groups, although four other products, not included in Table I, were observed by GC but could not be identified. By analogy with the well-studied 2-cyanopropyl radical,[20,31] $•CH_2CN$ radicals can dimerize to produce the ketene imine **13** as well as succinonitrile (**3**). In fact, both modes of dimerization have been reported by Eberson as arising from $•CH_2CN$ radicals formed by anodic oxidation of cyanoacetic acid. *N*-acetylglycinonitrile (**14**), the product of hydration of **13**, and **3** were obtained in the rather surprising estimated ratio of 3:2.[32] We searched in vain by GC/MS for the presence of **14** among our products. Calculations and ESR spin density data show that the $•CH_2CN$ radical has some, but not marked, ketiminyl character, leading to an estimate that the radicals should dimerize by C–N and C–C coupling in the ratio of about 1:6.[33] Since **13** could either hydrolyze or polymerize,[31] it is probable that **13** was formed in our reactions, but we were unable to find evidence for its presence. Nevertheless, **13** would account for only 5% of the missing $•CH_2CN$ groups if the 1:6 ratio were correct.

$$2\ •CH_2CN \rightarrow \underset{\textbf{13}}{NCCH_2N{=}C{=}CH_2} \xrightarrow{H_2O} \underset{\textbf{14}}{NCCH_2NHCOCH_3}$$

Table II. Product Distribution for Ad• + MeCN

product	rel mmol[a]	rel mmol[b]
$NC(CH_2)_2CN$ (**3**)	12.6	13.9
$Ad(Me)C{=}NCH_2CN$ (**5**)	24.9	26.8
$[Ad(Me)C{=}N]_2$ (**6**)	0.049	*c*
AdH	(100)	(100)
AdAd	0	23.5
$Ad(Me)C{=}NAd$ (**7**)	0.013	*d*
$AdCH_2CN$	0.0068	*d*

[a] Calculated. [b] Experimental, from Table I. [c] Trace. [d] None.

In order to understand why expected products like $Ad(Me)C{=}NAd$ and $AdCH_2CN$ were absent, the product distribution was simulated, by using the computer program EPFIT[34] to handle the differential equations. We considered reactions a and c–f in Scheme I plus the reactions 1–5.

$$AA \xrightarrow{g} 2Ad• \quad (1)$$

$$2Ad• \xrightarrow{h} AdAd \quad (2)$$

$$Ad• + •CH_2CN \xrightarrow{i} AdCH_2CN \quad (3)$$

$$Ad• + 9 \xrightarrow{j} Ad(Me)C{=}NAd \quad (4)$$

$$•CH_2CN + MeCN \xrightarrow{k} MeC(=N•)CH_2CN \rightarrow \text{unknowns} \quad (5)$$

This system of 11 differential equations and 10 rate constants yielded predicted steady-state product ratios, with the assumption that all radical–radical reactions were diffusion controlled ($k_d = k_e = k_h = k_i = k_j = 5 \times 10^9\ M^{-1}\ s^{-1}$) except for dimerization of **9**. Since sterically bulky iminyl radicals recombine slowly,[28] we estimated $k_f = 5 \times 10^6\ M^{-1}\ s^{-1}$. The rate of generation of Ad• was set equal to the effective light intensity of 5×10^{-6} mol/s. Unfortunately, no absolute rate constants are known for reaction of radicals with nitriles; however, the data could be fit only when attack of Ad• on MeCN was assumed to be more rapid at hydrogen than carbon with $k_a = 10^4\ M^{-1}\ s^{-1}$ and $k_c = 4 \times 10^4\ M^{-1}\ s^{-1}$. It will be noted that this ratio,[35] k_a/k_c, is 0.25, differing sharply from the ratio 27.5 suggested by the results of the reaction of AA with $Th^{•+}$; an explanation for the difference will be offered below.

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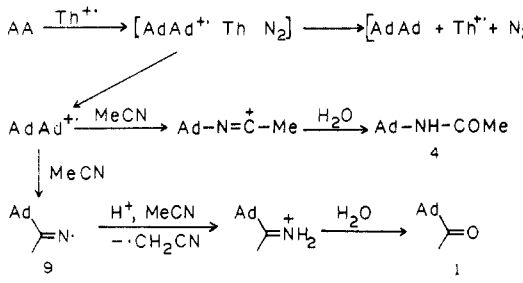
(34) We are grateful to Professor David Stanbury for providing this program.
(35) If the yield of AdH represents hydrogen abstraction (k_c) and the yield of **5** represents addition to MeCN (k_a), the ratio of these products is k_a/k_c, which equals 0.27, according to Table II. We thank a referee for pointing out this general approach.

Scheme II. Possible Minor Reaction Pathways in the Oxidation of AA by Thianthrene Cation Radical



The results of this calculation (cf. Table II) are in accord with experiment. Thus the most important products are indeed AdH and **5**, while neither **7** nor $AdCH_2CN$ were present. Without reaction k, the calculated fit was poor because there was no way to allow for the deficiency of CH_2CN groups in the measured products. However, attack of $^{\bullet}CH_2CN$ on MeCN must be slow since values of k_k above 13 M^{-1} s^{-1} gave too little succinonitrile. The much slower reaction of MeCN with $^{\bullet}CH_2CN$ than with Ad$^{\bullet}$ ($k_a = 10^4$ M^{-1} s^{-1}) is attributed to the unfavorable attack of the electron-deficient $^{\bullet}CH_2CN$ on the electrophilic cyano carbon.[36] The experimental yield of AdAd was much higher than the calculated value; however, the cage effect was not included in the calculation. In accord with our earlier conclusion,[19] AdAd must be a cage product.

What bearing do our findings have on our earlier work on the oxidative decomposition of AA by $Th^{\bullet+}$?[7] In the absence of a competing reaction, Ad$^{\bullet}$ is destined to abstract hydrogen atom from MeCN rather than to dimerize to AdAd. Therefore, in the reaction of AA with $Th^{\bullet+}$, free Ad$^{\bullet}$ was either not formed, or, if it was formed, it did not survive oxidation by $Th^{\bullet+}$. Moreover, the relatively large amount of AdAd (2.5%) obtained in that reaction[7] must have come only from a cage recombination. Cage recombination in the oxidative decomposition of AA could not be between two Ad$^{\bullet}$ but rather between Ad^+ and Ad$^{\bullet}$, to give the biaadamantane cation radical, $AdAd^{\bullet+}$. Conversion of $AdAd^{\bullet+}$ into AdAd would have to occur by an electron-trnasfer reaction, possibly from thianthrene (Th) within the solvent cage. In that case $Th^{\bullet+}$ would have served to form AdAd from AA catalytically. Whether or not $AdAd^{\bullet+}$ would survive long enough to be reduced to AdAd outside of the solvent cage is unknown to us. In the earlier work,[7] $BrCCl_3$ was used as a radical trap, and we feel that, in the presence of added $BrCCl_3$, any $AdAd^{\bullet+}$ which escaped the solvent cage would have ended as AdBr and Ad^+. Anodic oxidation of AdAd and fragmentation of $AdAd^{\bullet+}$ have been reported.[37]

The origin of the ketone **1** in the oxidative decomposition of AA cannot have been the imine **5**. Our reasoning here is that insufficient hydrogen atom abstraction (0.2% of AdH) occurred to provide the necessary $^{\bullet}CH_2CN$ radicals for forming **5** as shown in Scheme I. Similarly, **1** could not have come from conversion of **9** into **2**, as originally thought,[7] because free Ad$^{\bullet}$ attacks MeCN more at hydrogen than at carbon, yet very little AdH was found in the oxidative decomposition. Moreover, **2** was absent in the photochemical reaction of Ad$^{\bullet}$ with MeCN. We are attracted to the idea that $AdAd^{\bullet+}$ outside of the solvent cage may transfer both Ad^+ and Ad$^{\bullet}$ to MeCN, the former to the nitrogen and the latter to the carbon atom of the CN group (cf. Scheme II) In this way, we can arrive at ketiminyl radicals **9** without the requirement of free Ad$^{\bullet}$. We visualize the **9** as now being stabilized against β-scission by protonation, since acid-forming, adventitious hydrolysis of $Th^{\bullet+}$ is never absent in $Th^{\bullet+}$ reactions. The protonated **9** would now be more capable than **9** itself of hydrogen atom abstraction from solvent[7] and provide protonated ketimine for hydrolysis into **1**.

In conclusion, the results of photolysis of AA in MeCN show that the main reaction of free adamantyl radicals is abstraction of hydrogen atom from the solvent, though addition to the nitrile carbon is also important. In contrast, the formation and reactions of free Ad$^{\bullet}$ are not significant in the oxidative decomposition of AA by $Th^{\bullet+}$.

Experimental Section

General. NMR spectra were obtained on a JEOL FX-90Q spectrometer. Melting points were determined on a Mel-temp apparatus and are uncorrected. A Cary-17 spectrometer was employed for obtaining UV–vis absorption spectra while a Finnigan 3300 GC/MS system was used for mass spectra.

Azo-1,1′-adamantane (AA) was prepared as reported previously:[18,19,38] mp 280–281 °C; UV (hexane) λ_{max} 366.6 nm (ϵ 14.9).

1,1′-Biadamantane (AdAd)[39] was recrystallized three times from methanol, mp 292–293 °C.

***N*-Adamantylacetamide (4)** was made from the amine according to the literature,[40] mp 147–148 °C. The synthesis of **adamantyl methyl ketazine (6)** was carried out by using adamantyl methyl ketone and hydrazine in the usual manner;[41,42] mp 199–201 °C; ^1H NMR (C_6D_6) δ 1.70 (br s), 1.81 (s), 1.92 (br s); MS, *m/e* (relative intensity) 352 (M^+, 1), 311 (13), 217 (14), 176 (97), 150 (10), 135 (100), 93 (31), 91 (25), 79 (44).

Adamantyl methyl ketimine (2) was prepared, by the general method of Pickard and Tolbert,[43] from reaction of AdCN with MeMgCl.[42] Workup gave a white solid: mp 142–143 °C; MS, *m/e* (relative intensity) 177 (M^+, 83), 162 (16), 135 (81), 42 (100).

***N*-Cyanomethyl Adamantyl Methyl Ketimine (5).** A suspension of 1 g (5.6 mmol) of **1** and 0.78 g (8.4 mmol) of aminoacetonitrile hydrochloride in 2 mL of dry pyridine was stirred over molecular sieves for 4 h. The resulting yellow reaction mixture was separated by GC to afford 242 mg (20%) of imine **5** as a white solid, mp 106.5–107.5 °C. The imine hydrolyzed slowly on standing in air to the starting ketone **1**: ^1H NMR (C_6D_6) δ 1.10 (s, 3 H), 1.5–1.7 (br d, 12 H), 1.85–2.0 (br s, 3 H), 3.28 (s, 2 H); ^{13}C NMR ($CDCl_3$) δ 13.21 (CH_3), 28.17 (CH), 36.68 (CH_2), 38.57 (CH_2CN), 39.22 (CH_2), 42.96 ($C(C)_4$), 117.70 (C≡N), 183.07 (C=N); IR (CCl_4) $\nu_{C=N}$ 1640 cm^{-1}, $\nu_{C\equiv N}$ not visible;[44] MS, *m/e* (relative intensity) 216 (M^+, 39), 201 (10), 189 (34), 135 (93), 107 (34), 93 (76), 81 (87), 79 (100), 67 (50), 55 (46), 41 (84); high-resolution MS calcd for $C_{14}H_{20}N_2$ *m/e* 216.16264 (M^+), found *m/e* 216.16262.

Product Analysis. After completion of the photolysis, the Pyrex tube was opened, and the reaction mixture was analyzed by GC once with and once without concentrating the solution. A Varian Model 3700 GC and a computer-integrator were used. Good separations were obtained with a 5 ft × $^1/_8$ in. stainless-steel column, packed with 10% OV-17 on 80/100 gas-Chrom Q II (Alltech), programmed from 50 to 260 °C, at 10 deg/min, and with injector temperature 250 °C. The retention times under these conditions are given in Table I.

Preparative Gas Chromatography. An Antek 300 gas chromatograph with TC detector was set as follows to enable separation and isolation of AdH, **3**, and ketone **1**: injector at 200

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°C; 8 ft × 1/4 in. 5% OV-17 packed stainless steel column with the oven temperature programmed from 50 to 250 °C at 10 deg/min. Imine **5** was isolated at a constant oven temperature of 250 °C and detector at 200 °C.

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Registry No. **1**, 1660-04-4; **2**, 87429-27-4; **3**, 110-61-2; **4**, 880-52-4; **5**, 108418-81-1; **6**, 87429-30-9; AdAd, 3732-31-8; AdCN, 23074-42-2; AA, 21245-62-5; Ad•, 2819-03-6; AdH, 281-23-2; aminoacetonitrile hydrochloride, 6011-14-9; acetonitrile, 75-05-8.

Oxidation Chemistry of 5-Hydroxytryptamine. 1. Mechanism and Products Formed at Micromolar Concentrations

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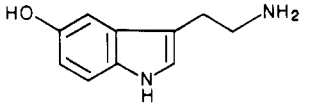
The oxidation of very low concentrations (<30 μM) of 5-hydroxytryptamine (**1**) in 0.01 M HCl has been studied by using electrochemical and other analytical techniques. The initial oxidation is a 1e,1H$^+$ reaction, giving a phenoxyl radical which exists in equilibrium with aryl, C(4)•, and N(1)• radicals. At low potentials the latter radicals can react to give dimeric products. At higher potentials, however, the primary phenoxyl radical is further oxidized (1e,1H$^+$) to a reactive quinone imine. The quinone imine is rapidly attacked by water to give 4,5-dihydroxytryptamine (**7**), which is further oxidized to tryptamine-4,5-dione (**B**). In aqueous solution at pH 2 **B** is slowly attacked by water to give 4,5,7-trihydroxytryptamine, which is further oxidized (2e,2H$^+$) to 5-hydroxytryptamine-4,7-dione (**11**). Compounds **B** and **11** then react together to give a hydroxylated tryptamine dimer. The facile oxidation of **1** to give at least two neurotoxins, **7** and **9**, might provide insight into the previously proposed anomolous oxidative metabolism of **1** as an underlying cause of various mental disorders.

5-Hydroxytryptamine (**1**) occurs naturally in the central and peripheral nervous system where it functions as a chemical neurotransmitter. Among the presumed roles of **1** in the central nervous system (CNS) are the regulation



1

of body temperature, sleep, and certain emotional states.[1] Udenfriend et al.[2] demonstrated that **1** is converted into 5-hydroxyindole-3-acetaldehyde by monoamine oxidase (MAO) and then to 5-hydroxyindole-3-acetic acid by aldehyde dehydrogenase. The major known metabolites of **1** found in urine result from the initial action of MAO.[3,4]

In the early 1950s it was suggested[5,6] that a faulty mechanism in the metabolism of **1** might be related to the onset of certain types of psychotic behavior. More recent reports suggest that depression and schizophrenia might result from such faulty metabolic pathways.[7-10] A recurring suggestion is that a defect in the metabolism of **1** leads to formation of more highly hydroxylated and therefore more reactive compounds that in some way lead to mental disorders.[2,3,11,12] Indeed, minor oxidation products of **1** in rats and rabbits have been speculated to be 4,5- or 5,6-dihydroxytryptamine.[3,12-14] Such speculations have merit in view of the subsequent discovery that dihydroxytryptamines such as 5,6-dihydroxytryptamine (5,6-DHT) and 5,7-DHT are powerful neurotoxins.[15-21] In addition, there is now considerable evidence that **1** is oxidized in biological media by routes other than the oxidative deamination pathways mentioned earlier. For example, human serum and ceruloplasmin concentrates oxidize **1** to give colored solutions although products have not been identified.[13,22-26] Hemolysates of rat erythrocytes

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