(3) **1a:** NMR ($CDCl_3$, 270 MHz) δ 6.28 (1 H, dd, J = 14 and 7 Hz), 5.56–5.41 (1 H, m), 5.09–4.98 (2 H, m), 4.72–4.65 (2 H, m), 4.24 (1 H, dd, J = 14 and 1.5 Hz), 3.93 (1 H, dd, J = 7 and 1.5 Hz), 3.51 (1 H, td, J = 10 and 4 Hz, H_{C_1}–H_{C_2} trans), 2.20–1.22 (8 H, m), 1.63 (3 H, s). **1b:** NMR ($CDCl_3$, 270 MHz) δ 6.27 (1 H, dd, J = 14 and 7 Hz), 5.84–5.66 (1 H, m), 5.03–4.92 (2 H, m), 4.72 (1 H, br s), 4.69 (1 H, br s), 4.29 (1 H, dd, J = 14 and 1.5 Hz), 4.01 (1 H, q, J = 3 Hz, H_{C_1}–H_{C_2} cis), 3.96 (1 H, dd, J = 7 and 1.5 Hz), 2.46 (1 H, td, J = 12 and 3 Hz), 2.14–1.21 (7 H, m), 1.60 (3 H, s). **2b:** NMR ($CDCl_3$, 270 MHz) δ 6.35 (1 H, dd, J = 14 and 7 Hz), 5.84–5.68 (1 H, m), 5.19–5.03 (2 H, m), 4.79 (1 H, br s), 4.63 (1 H, br s), 4.30 (1 H, dd, J = 14 Hz and 1.5 Hz), 4.03 (1 H, dd, J = 7 and 1.5 Hz), 3.87 (1 H, dt, J = 12 and 4 Hz, H_{C_1}–H_{C_2} cis), 2.97–2.88 (1 H, m), 2.12–2.03 (1 H, m), 1.96–1.21 (6 H, m), 1.71 (3 H, s).

(4) **2b:** MS (70 eV) m/e (rel intensity) 192 (M^+, 1.2), 149 (56), 148 (31), 93 (91), 81 (100).

(5) For related Cope isomerizations, see K. Morikawa and Y. Hirose, *Tetrahedron Lett.*, 869 (1969); G. L. Lange, M. A. Huggins, and E. Neidert, *ibid.*, 4409 (1976); P. A. Wender and J. C. Lechleiter, *J. Am. Chem. Soc.*, **99**, 267 (1977); J. R. Williams and J. F. Callahan, *J. Chem. Soc., Chem. Commun.*, 404 (1979).

(6) In similarly substituted Claisen and Cope rearrangements, the former reaction usually has a smaller $\Delta G^{\ddagger}$ at a specific temperature. See S. J. Rhoads and N. R. Raulins, *Org React.*, **22**, 1 (1975).

(7) A referee has suggested that the strain energy associated with the (*E,E*)-1,5-cyclodecadiene 7 and its *E,E* Claisen product could also account for a high $\Delta G^{\ddagger}_{\text{Claisen}}$.

(8) F. E. Ziegler, *Acc. Chem. Res.*, **10**, 227 (1977), and references cited therein.

(9) Strictly speaking, these data do not rule out the possibility of the formation of the *E,E* isomer of **10** from the trans isomers **1** in an undetectable amount, since the associated strain (cf. note 7) could allow a retro-Claisen rearrangement.[10]

(10) (a) M. Rey and A. Dreiding, *Helv. Chim. Acta*, **48**, 1985 (1965); (b) S. J. Rhoads and R. D. Cockroft, *J. Am. Chem. Soc.*, **91**, 2815 (1969); (c) M. T. Hughes and R. O. Williams, *Chem. Commun.*, 587 (1968).

Frederick E. Ziegler,* John J. Piwinski
Sterling Chemistry Laboratory, Yale University
New Haven, Connecticut 06520
Received August 13, 1979

Nitrogen 1s Photoelectron Spectra of Octaethylporphyrin and Tetraphenylporphine Complexes of Lanthanides

Sir:

X-ray photoelectron spectroscopy (ESCA) has been proved to be a powerful method for the elucidation of structure and bonding in complex molecules of f transition elements.[1] In our previous work on ESCA spectra for a series of lanthanide (Ln) and actinide (An) compounds, $Ln(OH)_3$,[2] $H(LnPc_2)$, and $AnPc_2$,[3] we gave our attention to the satellite phenomena in Ln $3d_{5/2}$ and An $4d_{5/2}$ spectra. The observations suggested that f orbitals [either half-occupied or vacant orbital(s)] played an important role in the core ionization process which gave sharp variations in the satellite intensity of the spectra. As an extension of our ESCA study of f transition metal complexes, we now focus on lanthanide complexes of octaethylporphyrin (OEP), Ln(OEP)(OH) (Ln = Eu, Gd, Yb, and Lu), and of tetraphenylporphine (TPP), Ln(TPP)(acac) (Ln = Sm, Gd, Er, and Yb; acac = acetylacetonate).

We report here new findings derived from our observations of nitrogen 1s photoelectron spectra of Ln(OEP)(OH) and Ln(TPP)(acac). For a comparison, we measured also N 1s spectra of H_2TPP and H_2OEP. N 1s spectra have been shown to be a source of valuable information on the geometry of both porphyrins and metalloporphyrins.[4-8] Besides the geometrical viewpoint, we found a noticeable correlation between the line width (fwhm) of the N 1s signal and the number of unpaired electrons in the lanthanide-porphyrin complexes. This indicates that unpaired valence electrons are not localized in the lanthanide 4f orbitals but are bound in MO's delocalized over N and lanthanide orbitals, and that the induced spin density on the N atoms provides an exchange interaction with the ionized N 1s core.

Octaethylporphyrin complexes Ln(OEP)(OH) have been prepared by T. Saran Srivastava. We synthesized and purified tetraphenylporphine complexes Ln(TPP)(acac) by the method described by Wong et al.[9] though the Sm compound seems to decompose gradually to metal-free TPP in chloroform. X-ray photoelectron spectra were obtained with a Hewlett-Packard 5950-Å ESCA spectrometer employing Al Kα X-ray excitation. The charging effects were neutralized by using an electron flood gun. The samples were prepared by carefully brushing each compound on double-stick scotch tape. We observed neither any visible evidence of decomposition nor change in the photoelectron spectra of the lanthanide porphyrins during the course of experiments performed, except for the case of Sm(TPP)(acac).[10] The spectra were calibrated using a C 1s binding energy at 284.8 eV which arises from the carbon atoms having hydrocarbon character in the porphyrin rings.

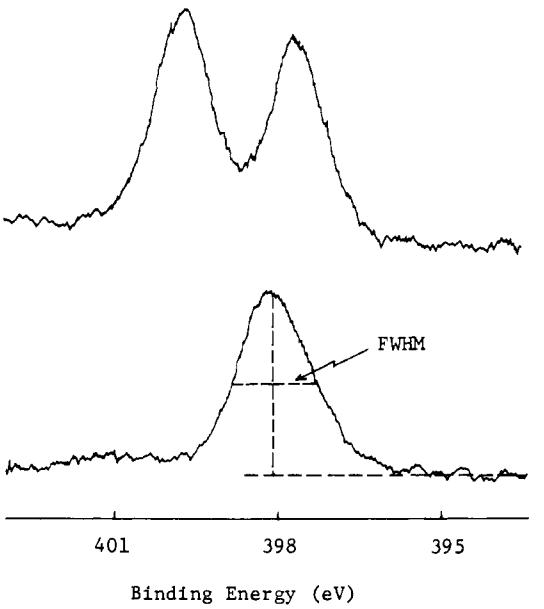


Figure 1. Typical N 1s signals of free-base prophyrin (top) and lanthanide porphyrin (bottom). The fwhm of a N 1s peak for each lanthanide porphyrin was estimated with a procedure shown by broken lines.

The N 1s spectrum measured for either H_2OEP or H_2TPP exhibits a doublet due to the selective protonation of two of the central nitrogens. Observed binding energies of each doublet are 399.7 and 397.7 eV for H_2OEP and 400.0 and 398.0 eV for H_2TPP, and individual peaks have fwhm values of $\sim 1.2_5$ eV. These binding energies are in agreement with those obtained previously by other groups[5,6,8] and differ only slightly from others which could be because of the use of different reference lines. We note here that our fwhm values (1.2_5 eV) are close to the value of 1.1 eV given by Niwa et al.[5] which is the narrowest N 1s signal obtained for porphyrins in the solid state. This seems to warrant the subsequent discussion concerning the N 1s line width of lanthanide porphyrins.

In complexing a lanthanide ion with OEP or TPP, the N 1s spectrum collapses to a single peak with a binding energy value directly in between the corresponding porphyrin doublet. This is schematically drawn in Figure 1, where the N 1s spectra of free-base and metal-incorporated porphyrins are typified by those of H_2OEP and of Yb(OEP)(OH), respectively. The single N 1s peak indicates the existence of four equivalent nitrogens in the lanthanide porphyrins and thus the equalized four Ln-N interactions. The situation is achieved only when a lanthanide is located equidistant between the four nitrogen atoms.

The binding energies and the fwhm values determined for a series of lanthanide porphyrins are summarized in Table I. No significant difference in the binding energies can be seen between the lanthanide porphyrins studied, indicating that the

0002-7863/80/1502-0882$01.00/0

Table I. N 1s Binding Energies[a] and fwhm[b] of Ln(OEP)(OH) and Ln(TPP) (acac)[c]

	binding energy	fwhm
Eu(OEP)(OH)	398.1	1.7_7
Gd(OEP)(OH)	398.2	1.9_1
Yb(OEP)(OH)	398.2	1.6_0
Lu(OEP)(OH)	398.1	1.3_8
Gd(TPP)(acac)	398.0	1.7_7
Er(TPP)(acac)	398.4	1.4_3
Yb(TPP)(acac)	398.3	1.3_5

[a] Referred to C 1s = 284.8 eV. [b] The full widths at half-maximum of photopeak. [c] In electronvolts.

electronegativities of lanthanides are very similar to each other. The observed binding energies are somewhat higher than a value anticipated from the general-belief that a Ln-ligand bond has strong ionic character, and are even close to values obtained for metalloporphyrins of d-transition elements.[5] The result seems to imply the presence of some covalent character in Ln-N bond [11] similar to a M-N bond in d transition metal complexes.

As shown in Table I, the fwhm changes noticeably from 1.3_8 to 1.9_1 eV in the Ln(OEP)(OH) series and from 1.3_5 to 1.7_7 in the Ln(TPP)(acac) series, respectively. The most striking broadening of the N 1s peak in either of the series was observed for the Gd complex (f^7). We now see a correlation between the fwhm of the N 1s peak and *the number of unpaired electrons in the complex*. This is shown in Figure 2.

The most plausible interpretation of the broadening is multiplet splitting of the N 1s core level arising from an exchange interaction between the ionized core and unpaired valence electrons induced on the nitrogen atoms. Multiplet splitting of core-level peaks has been reported for inner 3s and 3p levels of d transition metals[13,14] for 4s and 5s levels of lanthanides[15] and for 1s levels of NO and O_2.[16,17] In every case the magnitude of the multiplet splitting (ΔE) of core s orbitals was found to be in good agreement with approximate theoretical estimates based on the equation[17,18]

$$\Delta E \simeq f_i H^i (2S + 1) \qquad (1)$$

where f_i is the fraction of an unpaired electron on the ith atom, H^i denotes the core s electron-valence electron exchange integral, and S is a total spin. Among compounds of a type similar to the Ln(OEP)(OH) or Ln(TPP)(acac) series, f_i may be considered to be constant throughout the series. Thus, the magnitude of the multiplet splitting ΔE simply correlates with total spin, i.e., the number of unpaired electrons of the compound in question. Unfortunately, we could observe a level broadening instead of a level splitting which is expected from the exchange mechanism. Nevertheless, eq 1 seems to provide a theoretical verification of our interpretation for the correlation obtained between the N 1s fwhm and the number of unpaired electrons.

The unpaired electrons on N atoms must be induced from half-occupied Ln 4f levels through a direct or an indirect interaction between N valence and Ln 4f orbitals. Possible mechanisms which cause spin polarization at the ligand site in f transition metal complexes are (1) direct delocalization of f electrons into vacant ligand MO's,[20,21] (2) charge transfer from filled ligand MO's to vacant metal f orbitals[21] or to metal outer 6s, 6p, or 5d orbitals,[22] (3) similar charge transfer from ligand to half-occupied metal f orbitals, and (4) interaction of ligand orbitals with filled metal orbitals which is exchange polarized by the f shell.[23] Mechanism 1 induces unpaired spin on the ligand which is polarized parallel to that of the f shell, while mechanisms 2, 3, and 4 give antiparallel spin. From only the ESCA results, we cannot conclude which mechanism is responsible for the spin polarization of the N atoms in

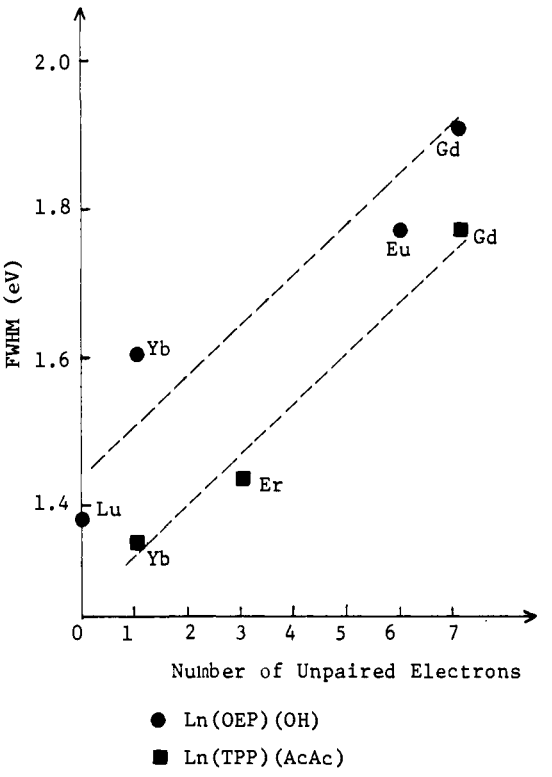


Figure 2. The line widths (fwhm) of N 1s peaks plotted against the number of unpaired electrons in the complexes.

Ln(OEP)(OH) and Ln(TPP)(acac). However, our ESCA study implies strongly the presence of overlap-covalent interaction of lanthanide 4f and/or outer (6s, 6p, 5d) orbitals with N valence orbitals.

Acknowledgment. This work was supported by the Robert A. Welch Foundation (Grant No. A420).

References and Notes

(1) Examples: (a) C. K. Jørgensen, *Struct. Bonding (Berlin)*, **13**, 199 (1973); (b) A. J. Signorelli and R. G. Hayes, *Phys. Rev. B*, **8**, 81 (1973); (c) J. J. Pireaux, N. Mårtensson, R. Didriksson, K. Siegbahn, J. Riga, and J. Verbist, *Chem. Phys. Lett.*, **46**, 215 (1977); (d) A. F. Orchard and G. Thornton, *J. Electron Spectrosc.*, **10**, 1 (1977); (e) R. Dubois, J. C. Carver, and M. Tsutsui, *J. Coord. Chem.*, **6**, 123 (1976).
(2) K. Tatsumi, M. Tsutsui, G. W. Beall, D. F. Mullica, and W. O. Milligan, *J. Electron Spectrosc.*, **16**, 113 (1979).
(3) K. Tatsumi, K. Kasuga, and M. Tsutsui, *J. Am. Chem. Soc.*, **101**, 484 (1979).
(4) M. V. Zeller and R. G. Hayes, *J. Am. Chem. Soc.*, **95**, 3855 (1973).
(5) Y. Niwa, H. Kobayashi, and T. Tsuchiya, *J. Chem. Phys.*, **60**, 799 (1974); *Inorg. Chem.*, **13**, 2891 (1974).
(6) D. Karweik, N. Winograd, D. G. Davis, and K. M. Kadish, *J. Am. Chem. Soc.*, **96**, 591 (1974).
(7) M. Seno, S. Tsuchiya, and S. Ogawa, *J. Am. Chem. Soc.*, **99**, 3014 (1977).
(8) J. P. Macquet, M. M. Millard, and T. Theophanides, *J. Am. Chem. Soc.*, **100**, 4741 (1978).
(9) (a) C.-P. Wong, R. F. Venteicher, and W. DeW. Horrocks, Jr., *J. Am. Chem. Soc.*, **96**, 7149 (1974); (b) W. DeW. Horrocks, Jr., and C.-P. Wong, *ibid.*, **98**, 7157 (1976).
(10) For Sm(TPP)(acac), an additional peak appeared at ~1.8 eV above the main N 1s signal at 398.0 eV and the intensity of the peak relative to the main N 1s line was increased with a passage of time under X-ray irradiation. The additional peak seems to arise from pyrrole-type nitrogens in H_2TPP indicating that Sm(TPP)(acac) is decomposed by X-ray irradiation.
(11) The "covalency" does not necessarily mean f-orbital participation in bonding. Lanthanide atoms have also outer 5d, 6s, and 6p orbitals which can effectively interact with ligand orbitals.[12]
(12) D. W. Clack and K. D. Warren, *J. Organomet. Chem.*, **122**, C28 (1976).
(13) (a) C. S. Fadley, D. A. Shirely, A. J. Freeman, P. S. Bagus, and J. V. Mallow, *Phys. Rev. Lett.*, **23**, 1397 (1969); (b) C. S. Fadley and D. A. Shirley, *Phys. Rev. A*, **2**, 1109 (1970).
(14) J. C. Carver, G. K. Schweitzer, and T. A. Carlson, *J. Chem. Phys.*, **57**, 973 (1972).
(15) R. L. Cohen, G. K. Wertheim, A. Rosencwaig, and H. J. Guggenheim, *Phys. Rev. B*, **5**, 1037 (1972).
(16) J. Hedman, P.-F. Hedén, C. Nordling, and K. Siegbahn, *Phys. Lett. A*, **29**, 178 (1969).

(17) D. W. Davis and D. A. Shirley, *J. Chem. Phys.*, **56**, 669 (1972).
(18) H. Basch, *Chem. Phys. Lett.*, **20**, 233 (1973).
(19) The multiplet splitting of N 1s peak measured for NO and di-*tert*-butyl-NO radicals are 1.412 and 0.539 eV, respectively.[17] The magnitude of broadenings of N 1s peaks for Gd(OEP)(OH) [$+0.5_3$ eV relative to Lu(OEP)(OH)] and for Gd(TPP)(acac) [$+0.4_2$ eV relative to Yb(TPP)(acac)] seems to be in the range of values which can be anticipated from multiplet splitting.
(20) R. E. Watson and A. J. Freemann, *Phys. Rev. Lett.*, **156**, 251 (1967).
(21) A. Streitwieser, Jr., D. Dempf, G. N. LaMar, D. G. Karraker, and N. Edelstein, *J. Am. Chem. Soc.*, **93**, 7343 (1971).
(22) W. B. Lewis, J. A. Jackson, J. F. Lemons, and H. Taube, *J. Chem. Phys.*, **36**, 694 (1962).
(23) R. E. Watson and A. J. Freeman, *Phys. Rev. Lett.*, **6**, 277 (1961).
(24) Robert A. Welch Postdoctoral Fellow, Texas A & M University, 1977–1979.

Kazuyuki Tatsumi,[21] Minoru Tsutsui*
Department of Chemistry, Texas A & M University
College Station, Texas 77843
Received August 17, 1979

Mechanism of Inactivation of Mitochondrial Monoamine Oxidase by *N*-Cyclopropyl-*N*-arylalkyl Amines

Sir:

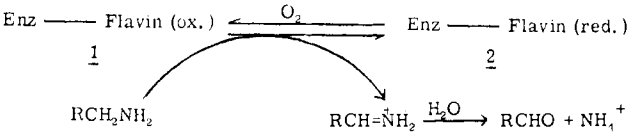
Mitochondrial monoamine oxidase (MAO, E C 1.4.3.4), a flavin-dependent enzyme which catalyzes the oxidative deamination of physiologically active monoamines, has been the target of inhibition for hundreds of potential antihypertensive and antidepressant agents.[1] The reaction catalyzed by mitochondrial MAO is shown in Scheme I.

One class of irreversible MAO inhibitors, the propargyl amines, has been studied extensively[2] and a possible mechanism of action has been proposed.[3] The mechanism of another class of potent and specific MAO inhibitors, the *N*-cyclopropyl-*N*-arylalkyl amines,[4] however, has not been determined. We report here our initial findings on the mechanism of action of this important class of compounds.

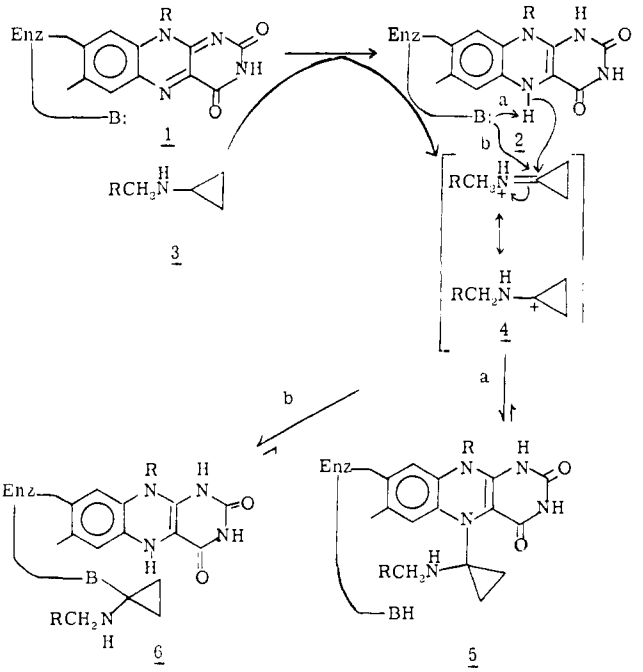
The *N*-cyclopropyl-*N*-arylalkyl amines that we have studied are mechanism-based inactivators of purified mitochondrial MAO from pig liver. A mechanism-based or suicide[5] inactivator is an unreactive compound which is catalytically transformed by the target enzyme into a highly reactive species. While sequestered in the active site, this then reacts with an enzymatic functional group and results in covalent bond formation with the enzyme. Scheme II depicts the proposed mechanism for the inactivation of MAO by *N*-cyclopropyl-*N*-arylalkyl amines. It is postulated that the cyclopropyl carbon attached to the nitrogen is oxidized, yielding the highly reactive cyclopropanone[6] imine (**4**) which reacts either with N-5 of reduced flavin (**2**) (pathway a) to give the mixed diamino ketal of cyclopropanone (**5**)[7] or with an active site nucleophile (pathway b) to give **6**. There is ample precedent for the generation of cyclopropanone imines in the inactivation of amine oxidases by cyclopropylamines.[8] Cyclopropanone (hydrate) generated from coprine recently has been implicated as the reactive species in the inactivation of aldehyde dehydrogenase.[10]

Mechanism-based inactivation of MAO by *N*-cyclopropyltryptamine (**3a**, R = indolylmethyl) and *N*-cyclopropylbenzylamine (**3b**, R = phenyl) was concluded from the following experiments: (1) a first-order time-dependent loss of enzyme activity was observed ($t_{1/2}$ = 1.5 min for 50 μM *N*-cyclopropyltryptamine and $t_{1/2}$ = 2.8 min for 50 μM *N*-cyclopropylbenzylamine at 25 °C, pH 9.0); (2) the rate of inactivation was considerably slower at pH 7.0 than at pH 9.0, the pH optimum of the enzyme; (3) the rate of inactivation was considerably slower in the presence of the substrate, benzylamine; (4) extensive dialysis of inactivated enzyme against pH 7.0 buffer led to recovery of <5% of the enzyme activity; (5) incubation of MAO with [*phenyl*-^{14}C]-*N*-cyclopropylbenzylamine,[11] followed by dialysis, led to association of the radioactivity with the protein to the extent of 1.2–1.4 mol[12] of inactivator/mol of enzyme; and (6) incubation of MAO with *N*-[1-^{3}H]cyclopropylbenzylamine[13] resulted in a time-dependent release of 0.73 mol of ^{3}H/mol of [*phenyl*-^{14}C]-*N*-cyclopropylbenzylamine bound to the active site. Kinetics of inactivation of MAO by *N*-cyclopropylbenzylamine (**3b**) are depicted in Figure 1.

Scheme I. Oxidation of Monoamines by Monoamine Oxidase



Scheme II. Proposed Mechanism for the Inactivation of MAO by *N*-Cyclopropyl-*N*-arylalkyl Amines



The mechanism of the inactivation was deduced from the following results. Using *N*-[1-^{2}H]cyclopropylbenzylamine,[13] a deuterium isotope effect of 1.5 was observed at a concentration of 17 μM (pH 9.0, 0 °C), but, as the concentration of the inactivator was increased, the isotope effect approached 1.0. This is reminiscent of the findings of Belleau and Moran[14] for the isotope effect of deuterated substrates with MAO. In conjunction with the tritiated inactivator experiment, this suggests that the proton is lost in a partially rate-determining step at low concentrations of inactivator. The cyclopropyl group is essential for irreversible inactivation since *N*-isopropylbenzylamine is a competitive (K_i = 320 μM) *reversible* inhibitor of the enzyme. The cyclopropyl group must be attached directly to the nitrogen as evidenced by the observation that *N*-cyclopropylmethyltryptamine is also a competitive (K_i = 100 μM) *reversible* inhibitor. Oxidation of the benzylic methylene of **3b**, as in benzylamine (Scheme I, R = Ph), would lead to *N*-benzylidenecyclopropylamine. To determine whether this compound was responsible for inactivation, MAO was anaerobically reduced (by benzylamine) and then was treated with *N*-benzylidenecyclopropylamine at pH 9.0.[16] No irreversible inhibition of the enzyme occurred. Aerobically, this compound was observed to be a potent noncompetitive (K_i = 56 μM) reversible inhibitor of MAO. During the inactivation of MAO, the optical spectrum of the flavin coenzyme changes

0002-7863/80/1502-0884$01.00/0