it is rather difficult to determine the structure of the portion in parenthesis for $CH_3CH{=}CH{-}(C_3H_5Cl)_4{-}CH{=}CHCH_3$. Four structures could be derived; however, the mass spectral data indicate one of the structures as 4,6,9,11-tetrachloromethyl-2,12-tetradecadiene.

An excess amount of allyl bromide (60 mL) reacted with 6 g of fresh uranium powder at 25 °C. The liquid chromatogram showed four products with comparable peak heights in a reaction time of 8 h which subsequently merge into a single product after 60 h. unreacted allyl bromide (15 mL) was recovered, and the final product was collected and characterized as $C_{21}H_{36}Br_6$. Although mass spectral data did not give a parent peak, characteristic fragmentation did occur at *m/e* (assignment in parentheses) 360 ($C_9H_{15}Br_3^+$), 320 ($C_{12}H_{18}Br_2^+$), 280 ($C_9H_{14}Br_2^+$), 240 ($C_6H_{10}Br_2^+$), 200 ($C_9H_{13}Br^+$), 160 ($C_6H_9Br^+$), 119 ($C_3H_4Br^+$), 93 (CH_2Br^+), 80 (HBr^+), 79 ($C_6H_9^+$ or Br^+), 67 ($C_5H_7^+$), 57 ($C_4H_9^+$), 55 ($C_4H_7^+$), 43 ($C_3H_7^+$), 41 ($C_3H_5^+$), neglecting the isotopic ions. Elemental analyses are as follows: Anal. Calcd for $C_{21}H_{36}Br_6$: C, 32.81; H, 4.69; Br, 62.50. Found: C, 31.45; H, 4.42; Br, 64.52.

The infrared spectra give characteristic absorptions of *trans*-RHC=CHR′ at 1640 (w) and 1250 (s), CH_2Br at 1250 (s), 650 (m), and 572 (s), and CH_3C at 1440 (s) and 1380 (m). The ^1H NMR spectrum exhibits three regional broad band peaks at 5.21, 3.57, and 1.55, corresponding to HC=CH:CH_2Br:CH, respectively, with the integrated area in the ratio 2:10:22 in comparison with the theoretical ratio of 2:10:22. ^{13}C NMR shows 21 different environments of the carbon atoms. The presence of double bonds at terminal positions might be improbable because of the chemical shifts at 129.48 and 128.75 ppm. Although a fragment corresponding to $C_5H_7Br^+$ was not observed, its presence seems reasonable since the C–Br bond is as easily broken as the C–H bond to give a 40 mass unit difference; however the cleavage of the C–Cl bond is more difficult. Therefore the structure is assumed to be similar to the allyl chloride system—4,6,8,10,12-pentakisbromomethyl)-2-octadecene.

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Reaction of Primary Amines with the Dichlorocarbene Complex of Iron(II) Tetraphenylporphyrin [$Fe^{II}TPP(CCl_2)$]

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The hepatotoxicity of $CHCl_3$ has been related to the irreversible binding of its metabolites to cellular macromolecules.[1] Recent evidence supports the view the $CHCl_3$ hepatic metabolism is at least partly cytochrome P-450 dependent[2] and involves the formation of a dichlorocarbene intermediate.[3-6] Mansuy and collaborators[7,8] have shown that various polyhalogenated compounds form stable iron(II) porphyrin halocarbenes under reducing conditions and the carbene moiety of $Fe^{II}TPP(CCl_2)$ to be susceptible to aminolysis.[9] Herein we report the results of a kinetic investigation which establishes two alternate mechanisms for the reaction of primary amines with $Fe^{II}TPP(CCl_2)$.[10]

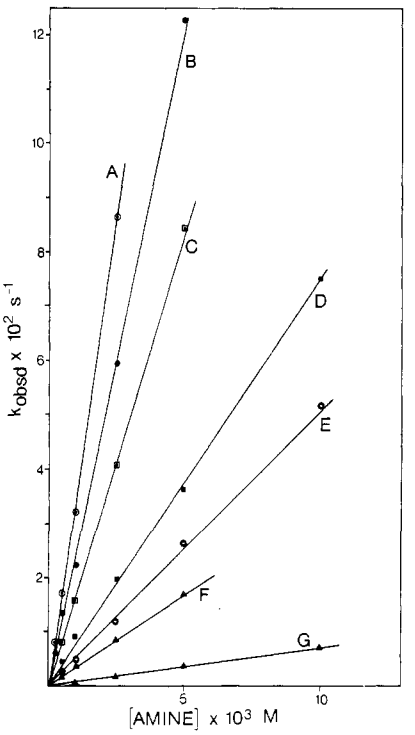

Figure 1. Plot of the pseudo-first-order rate constants (k_{obsd}, s^{-1}) at 30 °C vs. amine concentration for the reaction of representative amines with the corresponding amine complex of $Fe^{II}TPP(CCl_2)$. (A) *n*-Butylamine in toluene; (B) benzylamine in toluene; (C) *n*-butylamine in dioxane; (D) cyclohexylamine in toluene; (E) *n*-butylamine in *tert*-butyl alcohol; (F) isopropylamine in toluene; (g) *o*-phenylenediamine in toluene.

We have found that primary amines react with $Fe^{II}TPP(CCl_2)$ to provide the axial coordinated complex $RNH_2Fe^{II}TPP(CCl_2)$ which then reacts with additional primary amine. Sterically hindered or weakly basic primary amines provide as products both the amine–isonitrile complex [RNH_2Fe(II)TPP(C=NR)][9,11] and the diamino complex [$(RNH_2)_2Fe^{II}TPP$], while the remaining primary amines yield the amine–isonitrile complex as the overwhelming product. Thus, the reaction of $Fe^{II}TPP(CCl_2)$ [λ_{max} 408 nm (ϵ 2×10^5 M^{-1} cm^{-1}) and 524 (1.5×10^4)] with 1 equiv of *n*-$BuNH_2$ in toluene (30 °C) provides (*n*-$BuNH_2$)$Fe^{II}TPP$

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(10) Solvents and amines were dried by refluxinng over CaH_2, distilled under N_2, and further degassed by purging with N_2 or by several cycles of freeze–vacuum–thaw. Inert atmosphere techniques were employed *throughout* the study. Tetraphenylporphyrin (Aldrich) was converted to $Fe^{III}TPPCl$ and separated from $O[Fe^{III}TPP]_2$ by chromatography over dry alumina (activity grade I) with anhydrous chloroform. $Fe^{II}TPP(CCl_2)$ was prepared by addition of 1 mL CCl_4 and 500 mg of iron powder (see ref 7) to 50 mg $Fe^{III}TPPCl$ in 50 mL of CH_2Cl_2/CH_3OH (9:1) and shaking it by hand for ~30 min. It is important to activate the iron powder by washing with glacial acetic acid, dry CH_3OH, and CH_2Cl_2 under a dry inert atmosphere. After filtration, the pink solution was reduced in volume by purging with N_2 and the residue recrystallized three times from CH_2Cl_2 and CH_3OH.
The product $Fe^{II}TPP(CCl_2)$ was identified by comparison of IR, visible, and H NMR spectra to the literature values.[7] That the dichlorocarbene complex was truly in hand was further established by showing that 1,1-dichloronorcarane was formed when oxygen was passed through a toluene solution 1 M in cyclohexene containing ~20 mg of $Fe^{II}TPP(CCl_2)$. 1,1-Dichlorononorcarane product was detected via GC (Apiezone Carbowax) and shown by this means to be identical with an authentic sample (Doering, W. von E.; Hoffmann, A. K. *J. Am. Chem. Soc.* **1954**, *76*, 6162).
(11) With *n*-$BuNH_2$ the isonitrile complex was shown to be identical with the product of Mansuy et al. by comparison of IR (ν_{CN} 2135 cm^{-1}) as well as visible spectra (lit.[9]).

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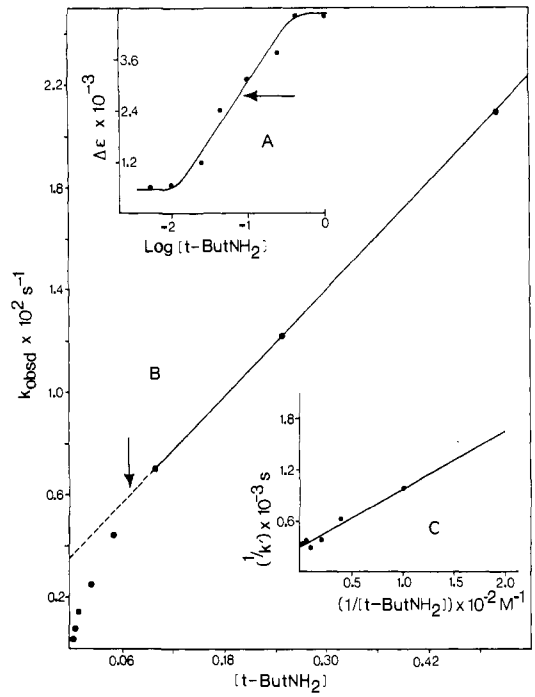


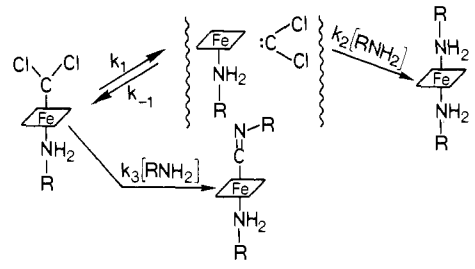
Figure 2. (A) A plot of the total optical density change at 534 nm (in units of $\Delta\epsilon_{534} = (\epsilon_\infty - \epsilon_0)_{534} \times 10^{-3}$ M^{-1} cm^{-1}) with [t-$BuNH_2$]. Arrow indicates [t-$BuNH_2$] = 7.5×10^{-2} M. (B) A plot of k_{obsd} for the reaction of t-$BuNH_2Fe^{II}TPP(CCl_2)$ with t-$BuNH_2$ in toluene (30 °C) vs. [t-$BuNH_2$]. Arrow indicates [t-$BuNH_2$] = 7.5×10^{-2} M. (C) A plot of $1/(k_{obsd} - k_3[t\text{-}BuNH_2])$ vs. $1/[t\text{-}BuNH_2]$ according to eq 3. $k' = (k_{obsd} - k_3[t\text{-}BuNH_2])$.

(CCl_2) [λ_{max} 428 nm (2.35×10^5 M^{-1} cm^{-1}) and 545 (1.3×10^4)] with k_2 for the reaction $>10^6$ M^{-1} s^{-1}. On addition of excess n-$BuNH_2$, there is seen a slower reaction, isobestic points at 428, 517, 544, and 627 nm, which yields the amine–isonitrile complex [λ_{max} 432 nm (ϵ 2.6×10^5 M^{-1} cm^{-1}), 534 (2×10^4), and 568 (7.0×10^3)] in quantitative yield (determined spectrally and based on initial [$Fe^{II}TPP(CCl_2)$]). With [RNH_2] $\gg$ [$RNH_2Fe^{II}TPP(CCl_2)$], the conversion of $RNH_2Fe^{II}TPP(CCl_2)$ to $RNH_2Fe^{II}TPP(C{=}NR)$ follows pseudo-first-order (k_{obsd}, s^{-1}) kinetics to at least ~95% completion. In figure 1 there is plotted the values of k_{obsd} vs. [RNH_2] for a number of primary amines. The slopes of the plots of Figure 1 equal the second-order rate constants k_2 of eq 1.[12]

$$RNH_2Fe^{II}TPP(CCl_2) + RNH_2 \xrightarrow{k_2} RNH_2Fe^{II}TPP(C{=}NR) + 2HCl \quad (1)$$

In the reactions of sterically hindered or weakly basic primary amines (e.g., t-$BuNH_2$, 2-aminopyridine, aniline) with $Fe^{II}TPP(CCl_2)$ in toluene (30 °C), the absorbance at 534 nm, at completion of reaction [A_∞(534 nm)] increases with increase in initial [amine] and then becomes independent of [amine] (see Figure 2, inset A). At the higher values of [amine], the product spectrum at t_∞ is that of $RNH_2Fe^{II}TPP(C{=}NR)$ [for t-$BuNH_2$, 90% yield based on the ϵ for (n-$BuNH_2$)$Fe^{II}TPP(C{=}N$-n-Bu)], while at the lower concentrations of amine, λ_{max} values at t_∞ are shifted toward that of $(RNH_2)_2Fe^{II}TPP$ [λ_{max} 426 nm (ϵ 2.7×10^5 M^{-1} cm^{-1}), 530 (1.7×10^4), 562 (6.5×10^3)].[13,14] Under the conditions of [RNH_2] $\gg$ [$RNH_2Fe^{II}TPP(CCl_2)$] the change in A_{534} is pseudo

Scheme I



first order to at least 4 half-lives of reaction, and addition of more RNH_2 at t_∞ does not alter A_∞. These observations establish that the products arise via competing parallel pseudo-first-order reactions and the reaction providing $[RNH_2]_2Fe^{II}TPP$ exhibits saturation in [RNH_2] (Scheme I). Kinetic analysis of the reaction was carried out in more detail with t-$BuNH_2$ and aniline. For the reaction of t-$BuNH_2Fe^{II}TPP(CCl_2)$ with t-$BuNH_2$, a plot of k_{obsd} vs. [t-$BuNH_2$] shows (arrow in Figure 2B) a change in slope in the region of [t-$BuNH_2$] $\simeq$ $2\text{–}7 \times 10^{-2}$ M. Below [t-$BuNH_2$] $\simeq 2 \times 10^{-2}$ M, $k_2[t\text{-}BuNH_2] \leq k_{-1}$ and the reaction of amine with t-$BuNH_2Fe^{II}TPP(CCl_2)$ is predominantly by way of the dissociative path. At [t-$BuNH_2$] $\simeq$ 0.1 M, k_1 becomes rate limiting so that the slope of the plot represents k_3 (3.6×10^{-2} M^{-1} s^{-1}) of the direct displacement reaction. An alternate kinetic analysis is based upon the fact that $^1/_2$ k_{obsd} = k_3 [t-$BuNH_2$] when A_∞ is that anticipated for equal formation of $[t\text{-}BuNH_2]_2Fe^{II}TPP$ and $[t\text{-}BuNH_2]Fe^{II}TPP(C{=}N\text{-}t\text{-}Bu)$. This occurs when [$t$-$BuNH_2$] = 7.5×10^{-2} M (arrow in Figure 2A), and k_3 calculated by this method was found to be 3.8×10^{-2} M^{-1} s^{-1}, in agreement with the value of 3.6×10^{-2} M^{-1} s^{-1} obtained from the slope of the plot of k_{obsd} vs. [t-$BuNH_2$]. Subtraction of $k_3[t\text{-}BuNH_2]$ from k_{obsd} at each amine concentration provides eq 2. From the plot of

$$k_{obsd} - k_3[t\text{-}BuNH_2] = \frac{k_1k_2[t\text{-}BuNH_2]}{k_{-1} + k_2[t\text{-}BuNH_2]} \quad (2a)$$

$$\frac{1}{k_{obsd} - k_3[t\text{-}BuNH_2]} = \frac{k_{-1}}{k_1k_2\,[t\text{-}BuNH_2]} + \frac{1}{k_1} \quad (2b)$$

$1/(k_{obsd} - k_3[t\text{-}BuNH_2])$ vs. $1/[t\text{-}BuNH_2]$ there is obtained as intercept $1/k_1$ ($k_1 = 3.6 \times 10^{-3}$ s^{-1}) and as intercept/slope the partition coefficient $k_2/k_{-1} \sim 50$ M^{-1} (see inset C to Figure 2). The value of $k_1 = 3.6 \times 10^{-3}$ s^{-1} is also seen as the intercept of the plot of k_{obsd} vs. [t-$BuNH_2$] extrapolated to [t-$BuNH_2$] = 0 from the linear phase of the plot where the slope equals k_3 (3.6×10^{-2} M^{-1} s^{-1}). For aniline, k_1 also equals 3.6×10^{-3} M and $k_2/k_{-1} = 16$ M^{-1}. Thus, in accord with Scheme I, the dissociation of the carbene complex (k_1) is independent of the nature of the primary amine, while the partitioning of the intermediates (k_{-1}/k_2) has some dependence upon the nature of the primary amine. The reaction of pyridine with $Fe^{II}TPP(CCl_2)$ to form $(C_5H_5N)Fe^{II}TPP(CCl_2)$ is, as in the case of primary amines, very rapid (complexation does not occur with the sterically hindered triethylamine). With pyridine, Mansuy determined the equilibrium constant for formation of $(C_5H_5N)Fe^{II}TPP(CCl_2)$ [λ_{max} 432 nm (ϵ 2.4×10^5 M^{-1} cm^{-1}), 504 (9.6×10^3), 544 (12×10^3), benzene solvent, 20 °C] to be 3.5×10^3 M^{-1}.[7] We find that $(C_5H_5N)Fe^{II}TPP(CCl_2)$ is converted to $(C_5H_5N)_2Fe^{II}TPP$[15] with a rate constant of 2×10^{-4} M^{-1} s^{-1} (toluene, 30 °C) and that saturation of rate by pyridine is not approached at [C_5H_5N] = 1.0 M. The inability of pyridine to donate a proton to displaced chloride ion eliminates the S_N2 pathway of nucleophilic displacement on $(C_5H_5N)Fe^{II}TPP(CCl_2)$. With the assumption that $(C_5H_5N)_2Fe^{II}TPP$ is formed through the dissociative mechanism of Scheme I and a knowledge of k_1, the value of k_2/k_{-1} may be calculated to be 2.4 M^{-1}. From the values of the partition constants (k_2/k_{-1}) the ratio of k_2 values are determined to be t-$BuNH_2$:$C_6H_5NH_2$:C_5H_5N $\simeq$ 20:7:1. The trapping of the

(12) Values of k_2 (M^{-1} s^{-1}) for the various primary amines (toluene, 30 °C) are n-$BuNH_2$, 30.3; benzylamine, 23.4; cyclohexylamine, 7.6; isopropylamine, 3.6; o-phenylenediamine, 0.73.

(13) $Fe^{II}TPP(RNH_2)_2$ compounds are obtained by reduction of (7×10^{-3} mol) $Fe^{III}TPP(Cl)$ with $Na_2S_2O_4$ (7.0 g; 5.7×10^{-3} mol) in toluene–water (9:1). A small excess of RNH_2 over porphyrin was then added to the dried toluene solution.

(14) Both $(RNH_2)_2Fe^{II}TPP$ (first Fraction) and $(RNH_2)Fe^{II}TPP(C{=}NR)$ (second fraction) complexes were isolated from toluene reaction solutions by precipitation with methanol.

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$(RNH_2)Fe^{II}TPP$ and $:CCl_2$ moieties by t-$BuNH_2$, aniline, and pyridine in the dissociative mechanism are thermodynamically favored reactions with small activation energies. Therefore, it is not surprising that there is little sensitivity of k_2 to amine pK_a.

Cytochrome P-450 destruction by haloalkanes may occur through formation of Fe(II)-bonded carbenes which, through a dissociative pathway, generates $:CCl_2$ (a reactive species) that migrates to porphyrin or protein functionalities. Callot and Schaeffer[16] have established electrophilic alkyl group migration from porphyrincobalt(III) alkyl to yield (alkylporphyrinato)cobalt(III).

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A Novel P-450 Model System for the *N*-Dealkylation Reaction

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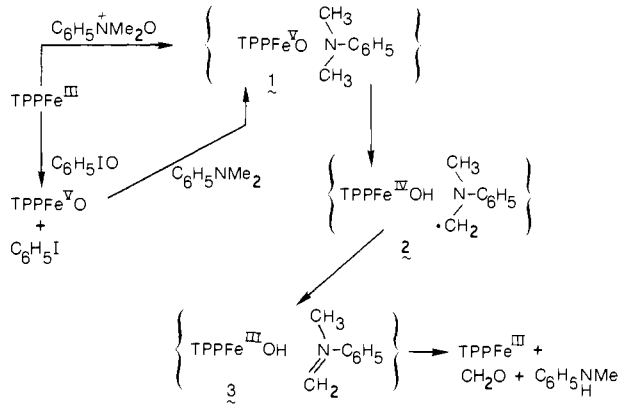
The enzymatic oxidations of secondary and tertiary xenobiotic and naturally occurring amines are initiated by flavin and cytochrome P-450 monooxygenases.[1] Whereas flavin-dependent monooxygenases are capable of N-oxidation, the heme-protein dependent monooxygenases carry out both N-oxidation and N-dealkylation of amines and, along with other oxygen insertion reactions of P-450 monooxygenases, constitute an area of wide concern and growing scientific interest. Both the flavoenzyme reaction mechanism[2] and, that of its biomimetic counterpart, the noncatalytic 4a-hydroperoxyflavin N-oxidation reaction[3] have been investigated; the essential features of both processes appear to be comparable. In concert with our investigation of the flavin dependent reaction, we have pursued the modeling of the P-450 N-dealkylation of amines.

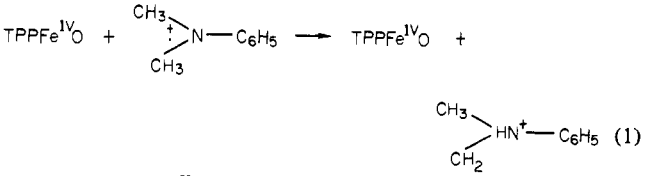
The P-450 enzyme juxtaposes the penultimate oxidizing species and substrate by catalyzing, in a sequence of steps, two one-electron reductions of enzyme–substrate–$^3O_2$ complex. The formation of product occurs following the rate-determining addition of the second electron; the oxidative event is too rapid to allow any characterization of the iron–oxygen species. Therefore, the actual oxidative event is rendered kinetically invisible, and the oxidizing reagent has eluded absolute identification. In a number of studies porphyrin bound Fe^VO^{+3} has been suggested to be responsible for substrate oxidation. Generation of cytochrome P-450 oxidizing species has been accomplished by the use of a wide variety of "oxene" transfer reagents such as iodosobenzene, peroxy acids, and numerous other peroxy compounds including hydrogen peroxide.[4] We report here the use of *N*,*N*-dimethylaniline *N*-oxide (DMANO) as a novel means of entrance into the catalytic cycle in a biomimetic system. In reactions of chlorotetraphenylporphyrinatoiron(III) [$TPPFe^{III}$] with DMANO, the arylamine *N*-oxide acts as both the oxene donor and, thereafter, the juxtaposed substrate (**1** in Scheme I) as in the enzymatic reaction.

Scheme I



Reaction of excess DMANO with $TPPFe^{III}$ (10^{-5} M) in anhydrous (Mg dried), nitrogen outgassed ethanol (30 °C) results in an initial shift in the porphyrin absorption bands (from λ_{max} 415, 575 nm to λ_{max} 403, 567, 607 nm) with a concomitant and continuing increase in absorbance at 290–295 nm accompanying product formation. Analysis by HPLC and GC/MS revealed that *N*,*N*-dimethylaniline (DMA) and the N-demethylated product, *N*-methylaniline (NMA), as well as formaldehyde and varying, lesser amounts of aniline are produced catalytically in the reaction. Under the condition [DMANO] ≫ [$TPPFe^{III}$], product formation is linear with time, and the zero-order velocities are proportional to [$TPPFe^{III}$] and initial [DMANO] (Figure 1A). The yields of the products depend only on the total amount of initial DMANO present. No other products were detected even after greater than 500 turnovers of the catalyst. Product formation was terminated in certain reactions by the crystallization of an ethanol insoluble TPPFe complex. Upon dissolution of this complex in $CHCl_3$, CH_2Cl_2, etc. under anaerobic conditions, the absorbance spectrum smoothly and rapidly (30 °C) converts to that of authentic $TPPFe^{III}$. Further characterization of this crystalline precipitate is in progress.

The mechanism of the reaction may be envisioned as in Scheme I. The entity **1** (the $TPPFe^VO$ moiety is written as such for electron bookkeeping purposes; the exact structure, as in the case of P-450, is unknown) must possess a lifetime of sufficient duration to allow escape of DMA, since the formation of aniline can only be accounted for by the exchange of NMA product for DMA in complex **1**. Formation of **2** is consistent with either (i) transfer of an electron from the amine nitrogen to Fe^VO to yield an anilinium cation radical and subsequent H-atom transfer from C to N (eq 1) or (ii) transfer of an H atom directly from an *N*-methyl



substituent to Fe^VO. Though, in both chemical and electrochemical oxidations of amines, the transfer of an electron from N to yield an aminium cation radical is often the rate-determining step,[5] this may not be so as a result of $TPPFe^VO$ involvement in

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