

## Electronic Supplementary Information

for

### **Isotope Effect Profiles in the *N*-demethylation of *N,N*-dimethylanilines. A Key to Determine the *pK*<sub>a</sub> of Nonheme Fe(III)-OH Complexes**

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**Instrumentation.** NMR spectra were recorded on a 300 MHz spectrometer. The spectra were internally referenced to the residual proton solvent signal. UV-Vis spectra were registered by a double-ray spectrophotometer. GC analyses were carried out on a gas chromatograph equipped with a capillary methylsilicone column (30 m x 0.25 mm x 25  $\mu$ m) Chrompack CP-Sil 5 CB. GC-MS analyses were performed with a mass detector (EI at 70eV) coupled with a gas chromatograph equipped with a melted silica capillary column (30 m x 0.2 mm x 25  $\mu$ m) covered with a methylsilicone film (5% phenylsilicone, OV5).

**Starting Materials.** All chemicals obtained from Sigma-Aldrich were the best available purity and used without further purification. Iodosylbenzene was prepared by a literature method and stored at 0°C under inert atmosphere.<sup>S1</sup> (N4Py)Fe(OTf)<sub>2</sub> was prepared by metallation of the ligand N4Py<sup>S2</sup> with Fe(OTf)<sub>2</sub> according to a literature method.<sup>S3</sup> [(N4Py)Fe<sup>IV</sup>=O]<sup>2+</sup> was prepared by reacting Fe(N4Py)(OTf)<sub>2</sub> with excess solid PhIO.<sup>S4</sup> *N*-methyl-*N*-(trideuteriomethyl)anilines and *N,N*-di(trideuteriomethyl)anilines were prepared by reaction of the corresponding *N*-methylanilines or anilines with CD<sub>3</sub>I according to literature method.<sup>S5</sup>

**Oxidation Procedures.** Iodosylbenzene (12.5  $\mu$ mol) was added to a stirred solution of the catalyst (2.5  $\mu$ mol) and 4-*X-N*-methyl-*N*-trideuteriomethylanilines (X= OCH<sub>3</sub>, CH<sub>3</sub>, Br, CF<sub>3</sub>, CN, NO<sub>2</sub>) (50  $\mu$ mol) in acetonitrile (500  $\mu$ L). In the case of the intermolecular isotope effects, iodosylbenzene (12.5  $\mu$ mol) was added to a stirred solution of the catalyst (2.5  $\mu$ mol), 25  $\mu$ mol of 4-*X-N,N*-di(trideuteriomethyl)anilines and 25  $\mu$ mol of 4-*X-N,N*-dimethylanilines (X= OCH<sub>3</sub>, CH<sub>3</sub>, Br, CF<sub>3</sub>, CN, NO<sub>2</sub>) in acetonitrile (500  $\mu$ L). The mixture was vigorously stirred at room temperature for 50 min. An

internal standard were added and an aliquot of the reaction mixture (0.2 mL) was directly analysed by GC, GC-MS and  $^1\text{H}$  NMR. Product analysis revealed that 4-X-*N*-methylanilines were produced as major reaction products (comparison with authentic specimens) with yields, referred to the amount of substrate, ranging from 5.5 % to 9.5 % (22 - 38 % referred to the amount of oxidant). Substrate conversion was kept low (< 12.5 %) in order to avoid the further oxidation of *N*-methylanilines<sup>S6</sup> which may alter the results of the kinetic isotope effects studies. From the GC-MS and  $^1\text{H}$  NMR analysis *N*-methylformanilides (yields, referred to the amount of substrate, ranging from 1.0 % to 2.8 %) were also identified by comparison with the spectral data reported in the literature.<sup>S7</sup> No formation of *N*-methylformanilides occurred when the oxidation of 4-NO<sub>2</sub>-*N,N*-dimethylaniline and 4-CH<sub>3</sub>-*N,N*-dimethylaniline was carried out in a degassed (freeze-thaw) reaction mixture. *N*-methylanilines were the exclusive reaction products. The remaining reaction mixture (0.3 mL) was treated with 2 mL of a 0.2 M dimedone solution in 0.2 M NaOH and stirred at room temperature for 30 min. Then hydrochloric acid (4 M) was added dropwise until the mixture became acidic (pH=4). The dimedone adducts (Figure S1) were extracted with diethyl ether (3 × 1 mL), dried over anhydrous sodium sulfate, and analyzed by GC-MS (SIM mode). The  $(k_{\text{H}}/k_{\text{D}})_{\text{intra}}$  and  $(k_{\text{H}}/k_{\text{D}})_{\text{inter}}$  values was determined as the ratio of the signal intensities at *m/z* 294 and 292. The KDIE values determined in this way have been confirmed in the *N*-demethylation of 4-X-*N,N*-dimethylanilines (X = CH<sub>3</sub>, Br, CF<sub>3</sub>, NO<sub>2</sub>), by measuring the *N*-methylaniline/*N*-trideuteriomethylaniline ratio in the reaction mixture. The same method could not be applied in the *N*-demethylation of 4-CH<sub>3</sub>O-*N,N*-dimethylaniline and 4-CN-*N,N*-dimethylaniline because of the overlap of the *N*-methylaniline and *N,N*-dimethylaniline peaks in the GC-MS analysis. The absence of oxygen had no effect on the intramolecular,  $(k_{\text{H}}/k_{\text{D}})_{\text{intra}}$ , and intermolecular,  $(k_{\text{H}}/k_{\text{D}})_{\text{inter}}$ , kinetic isotope effect values.

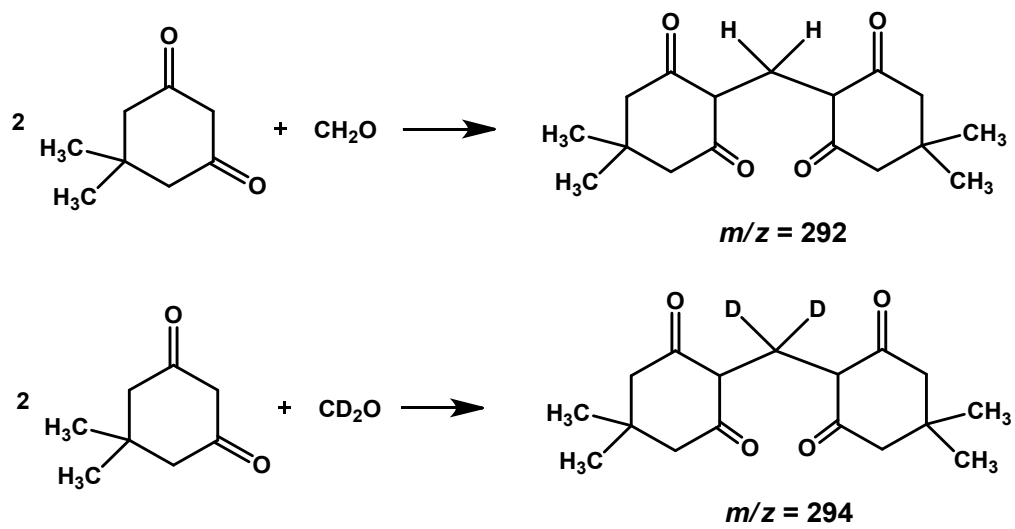


Figure S1

### Calculation of the pKa of *N,N*-dimethylaniline radical cations in CH<sub>3</sub>CN

The pK<sub>a</sub> of the *N,N*-dimethylaniline radical cations in CH<sub>3</sub>CN were estimated by the following equation:<sup>S8</sup>

$$\text{pKa} = 1/2.3RT[\Delta G^\circ_{\text{hom}} - 23.06 E^\circ_{\text{ArNMe}_2+\bullet/\text{ArNMe}_2} + 23.06 E^\circ_{\text{H}^+/\text{H}\bullet}]$$

where  $\Delta G^\circ_{\text{hom}}$  is the standard free energy associated with the homolytic cleavage of the NCH<sub>2</sub>-H bond, taken as 82.7 kcal mol<sup>-1</sup> (at 25°C), resulting from the difference between  $\Delta H^\circ_{\text{hom}}$  (91 kcal mol<sup>-1</sup>), an average value for the NCH<sub>2</sub>-H homolytic bond dissociation enthalpy for a number of *N,N*-dimethylanilines,<sup>S9</sup> and  $T\Delta S^\circ_{\text{hom}}$ , where  $\Delta S^\circ = 27.5$  cal K<sup>-1</sup> is the standard entropy of the hydrogen atom.<sup>S10</sup>  $E^\circ_{\text{ArNMe}_2+\bullet/\text{ArNMe}_2}$  are the standard redox potential (V vs NHE in H<sub>2</sub>O) of the couple ArN<sup>+</sup>•Me<sub>2</sub>/ArNMe<sub>2</sub> obtained from the values reported in Table 1 by adding 0.24 V.  $E^\circ_{\text{H}^+/\text{H}\bullet}$ , the standard redox potential of the couple H<sup>+</sup>/H•, is taken as -1.77 V vs NHE in CH<sub>3</sub>CN.<sup>S11</sup>

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