

(Heat Systems; Microson; 80% power) for 5 min at ambient temperature. The vesicular solution thus obtained was equilibrated at 30 °C, and reactions were initiated by addition of 1.0 μmol iodosylbenzene<sup>7</sup> (50 μL of a 20 mM solution in 1/1 methanol/water). After 2 h the reactions were quenched by addition of ether and vigorous shaking to destroy the vesicles. The substrate and product were purified by passing the organic phase over a dry alumina column, and the resulting mixture was analyzed by GLPC and GC-MS. Fatty acids were methylated with diazomethane prior to purification.

The results of the steroid epoxidations (Table I) show that the steroidal porphyrin Fe(ChP)Cl-bilayer assembly is indeed a site selective catalytic system. All the sterols were epoxidized *exclusively on the side chain*, while epoxidations with iodosylbenzene in a homogeneous methylene chloride solution with chloro-*meso*-tetra-*p*-tolylporphyrinatoiron(III) [Fe(TpTP)Cl] showed that the Δ<sup>5</sup> double bond in the steroid nucleus was considerably more reactive.<sup>8</sup> Desmosterol was found to be slightly more reactive than fucosterol, possibly because the approach to the double bond in the latter is more hindered. Significantly, stigmasterol with a Δ<sup>22</sup>-double bond only two bond lengths closer to the hydrophilic end (approximately 11 carbon-carbon bonds vs. 13 for desmosterol and fucosterol) was found to be unreactive under these conditions as was cholesterol. This evidence indicates that the catalytic-bilayer assembly is very rigid, and a "perfect fit" is necessary for successful epoxidation.

The epoxidations of polyunsaturated fatty acids (Table II) showed considerably less regioselectivity. Epoxidations under conditions identical with those used for sterols showed that the epoxidation of the double bond closer to the hydrophobic terminus in the bilayer was favored but by a ratio of less than 2:1. C<sub>20</sub> fatty acids showed only slightly less site selectivity than C<sub>18</sub> fatty acids. Esterification of the carboxylic acid had little effect on the results, and, as expected, trans isomers gave lower yields.<sup>7</sup> The reduced site selectivity may be due to the fact that phospholipid bilayers become less rigid upon addition of polyunsaturated fatty acids, as is born out by the significant decrease in the phase transition temperature, T<sub>p</sub>.<sup>9</sup> For example, the T<sub>p</sub> of a DMPC vesicle is 24 °C, but the T<sub>p</sub> of an egg yolk lecithin bilayer (partially unsaturated) is -15 °C. Loss of rigidity would enable free motion in the bilayer and lead to the decreased regioselectivity of the epoxidation reaction. Addition of cholesterol to the bilayer (Table II, last entry) resulted in a significantly more selective fatty acid epoxidation as expected for a more rigid system.<sup>10</sup> The results of the fatty epoxidation also show that yields are higher for the vesicular reactions than in homogeneous organic phases of comparable concentration. We attribute this to a favorable orientation effect in the bilayer. One must note that this comparison cannot be made for the sterol epoxidations since the double bonds are not of equal reactivity.

To summarize, a cholesterylmetalloporphyrin has been synthesized which upon intercalation into a synthetic biomembrane catalyzes the regioselective epoxidations of polyunsaturated sterols and fatty acids at the double bond closest to the hydrophobic terminus of the molecule. The characterization of this membrane-spanning porphyrin and generality of this lipid-induced specificity are now being explored.

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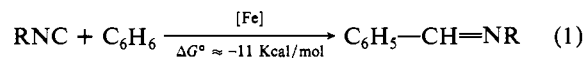
## The Catalytic Activation and Functionalization of C-H Bonds. Aldimine Formation by the Insertion of Isonitriles into Aromatic C-H Bonds

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Many examples of the activation of aromatic and aliphatic carbon-hydrogen bonds by homogeneous transition-metal complexes have appeared over the past few years, offering attractive new routes to organometallic species.<sup>1</sup> While several of these reports involve oxidative addition of low valent metal complexes to alkanes or arenes, these new adducts have not proven to be useful for the generation of functionalized hydrocarbon products.<sup>2</sup> Reports of successful metal-based alkane functionalization include free radical oxidations,<sup>3</sup> intramolecular cyclizations of alkyl carbenoid species to give cyclopentanones,<sup>4</sup> aromatic isonitrile insertion to give indoles,<sup>2b</sup> and alkane dehydrogenation to produce olefins.<sup>5</sup> Arene functionalization reactions commonly depend upon the presence of teathering groups,<sup>6</sup> although the production of benzaldehyde,<sup>7</sup> benzoic acid,<sup>8</sup> styrene,<sup>9</sup> and phenylsiloxane<sup>10</sup> insertion products have been recently reported.<sup>11</sup> We report here a new type of iron catalyzed insertion of isonitrile into the C-H bond of arenes to produce aldimines (eq 1).



In 1975, Muetterties<sup>12a</sup> and Karsch and Klein<sup>12b</sup> reported the preparation of Fe(PMe<sub>3</sub>)<sub>4</sub> by the reduction of FeCl<sub>2</sub> with magnesium in the presence of PMe<sub>3</sub>.<sup>13</sup> We have found that reaction of a THF solution of this complex with ~3 equiv of isocyanide results in the formation of orange, air-sensitive crystals of Fe-

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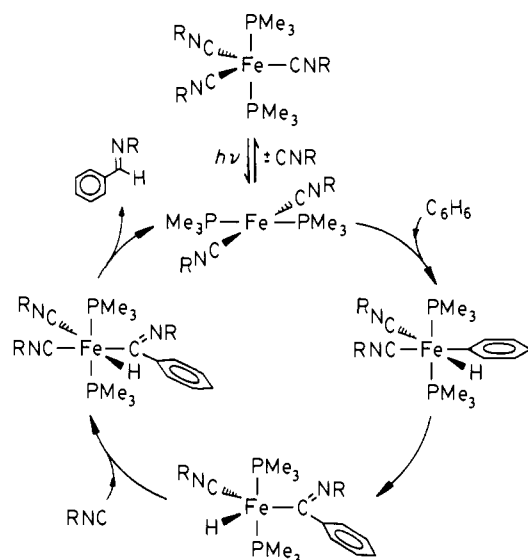
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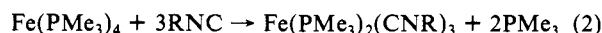
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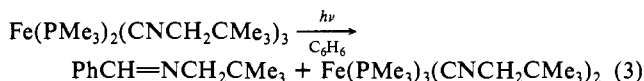
Scheme I



$(\text{PMe}_3)_2(\text{CNR})_3$  for a variety of R groups (R = Me, *t*-Bu,  $\text{CH}_2\text{CMe}_3$ , Ph, 2,6-xylyl; eq 2).<sup>14</sup> Most of these complexes are thermally stable below 60 °C, at which temperature phosphine is readily and reversibly lost as evidenced by exchange with  $\text{P}(\text{CD}_3)_3$ .



Pyrex-filtered irradiation (Hg or W) of a ~0.023 M benzene solution of the complex  $\text{Fe}(\text{PMe}_3)_2(\text{CNCH}_2\text{CMe}_3)_3$ , **1**, ( $\lambda_{\text{max}} = 327 \text{ nm}$ ) results in the formation of aldimine  $\text{PhCH}=\text{NCH}_2\text{CMe}_3$  in 88% yield (based on iron). A new organometallic product is also formed in 35% yield and is identified as  $\text{Fe}(\text{PMe}_3)_3(\text{CNCH}_2\text{CMe}_3)_2$ , **2**, on the basis of its  $^1\text{H}$  and  $^{31}\text{P}$  NMR spectrum (eq 3). A similar experiment in toluene solution gives a 2.8:1



mixture of the analogous *m*- and *p*-tolylaldimines in 55% combined yield. Irradiation of the xylyl isocyanide complex  $\text{Fe}(\text{PMe}_3)_2(\text{CN-2,6-C}_6\text{H}_3\text{Me}_2)_3$  in benzene (~0.008 M) also gives the corresponding aldimine in 89% yield (based on iron) after 40 min of irradiation.<sup>15</sup>

Preliminary mechanistic studies have allowed the formulation of a probable sequence of events. Irradiation of a benzene solution of  $\text{Fe}(\text{PMe}_3)_2(\text{CN-2,6-C}_6\text{H}_3\text{Me}_2)_3$  and  $\text{Me}_3\text{CCH}_2\text{NC}$  at -55 °C shows in the formation of free CN-2,6-xylyl and  $\text{PMe}_3$  in a 1:2 ratio.<sup>16</sup> Irradiation of **1** in the presence of  $\text{PMe}_3$  produces **2**, as indicated by changes in the  $^1\text{H}$  NMR spectrum of the sample. These observations are consistent with the photochemical labilization of the  $\pi$ -acceptor isocyanide ligand in addition to the  $\sigma$ -donor  $\text{PMe}_3$  group. Irradiation of **1** in  $\text{C}_6\text{D}_6$  solvent gives  $\text{C}_6\text{D}_5\text{CD}=\text{NCH}_2\text{CMe}_3$  as determined by  $^1\text{H}$  NMR spectroscopy and mass spectral data, indicating that the solvent (and not the  $\text{PMe}_3$  ligand) is the source of the aldimine hydrogen.

The mechanism proposed in Scheme I indicates the sequence of events anticipated upon production of the low valent electron rich intermediate  $[\text{Fe}(\text{PMe}_3)_2(\text{CNR})_2]$ . It is interesting to note that the thermally accessible intermediate  $[\text{Fe}(\text{PMe}_3)(\text{CNR})_3]$  does not produce aldimine; apparently the species with three

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(16) The low temperature was used in order to ensure the absence of thermal scrambling of the isocyanide ligands prior to photolysis.

Table I. Yield of  $\text{PhCH}=\text{NCH}_2\text{CMe}_3$  upon Irradiation of **1** and  $\text{CNCH}_2\text{CMe}_3$  in Benzene Solution

[1]	$[\text{CNCH}_2\text{CMe}_3]$	no. of turnovers <sup>a</sup>	% conversn <sup>b</sup>
0.004	0.004	2.1	53
0.002	0.004	3.5	69
0.001	0.004	5.1	72
0.0005	0.004	6.6	60
0.00025	0.004	8.4	44
0.0005	0.0005	2.7	67
0.0005	0.001	4.9	97
0.0005	0.002	5.7	82
0.0005	0.004	7.5	68
0.0005	0.008	7.1	37
0.0005	0.016	0.6	2

<sup>a</sup>Based on iron. <sup>b</sup>Based on total isocyanide, both in **1** and free in solution.

$\pi$ -acceptor ligands is not sufficiently "electron rich" to induce benzene oxidative addition.

The proposed mechanism indicates that in the presence of added RNC, the aldimine-producing reaction should be catalytic with respect to iron. However, since the role of light is to induce isocyanide dissociation, the back-reaction of RNC with  $[\text{Fe}(\text{PMe}_3)_2(\text{CNR})_2]$  to give **1** must be suppressed by keeping the absolute concentration of isocyanide very low. As shown in Table I, catalytic behavior with respect to iron and efficient conversion of both the free and coordinated isocyanide can be obtained by working in the mM concentration range. The catalysis stops if irradiation is discontinued.

Irradiation of **1** in cyclohexane or pentane solution at 25 °C or at -55 °C does not lead to alkane functionalization. Apparently,  $[\text{Fe}(\text{PMe}_3)_2(\text{CNCH}_2\text{CMe}_3)_2]$  does not oxidatively add to alkanes.<sup>17</sup>

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### Direct Observation of a Dienolate Intermediate in the Base-Catalyzed Isomerization of 5-Androstene-3,17-dione to 4-Androstene-3,17-dione

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We describe here the first direct observation of an intermediate dienolate ion during the base-catalyzed isomerization of a  $\beta,\gamma$ -unsaturated ketone to its conjugated isomer. In addition, we report the ionization constant for this  $\beta,\gamma$ -unsaturated ketone (5-androstene-3,17-dione) in aqueous solution as well as the rate constants for the formation of the dienolate ion intermediate and its protonation at both  $\beta$ - and  $\gamma$ -carbon atoms.

The conversion of  $\beta,\gamma$ -unsaturated carbonyl compounds to their  $\alpha,\beta$ -unsaturated isomers is a simple example of a larger class of prototropic rearrangements.<sup>1</sup> This reaction has been examined by several groups for both acidic<sup>2</sup> and basic<sup>2d,e,g,3</sup> solutions. In

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