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### First iron-catalyzed synthesis of oximes from styrenes<sup>†‡</sup>

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Aryl-substituted olefins react with *t*-butyl nitrite and sodium borohydride in the presence of  $iron(\pi)$ phthalocyanine to give oximes in moderate to high yields.

The development of general methods for the formation of carbon–nitrogen bonds from olefins is an important challenge in organic synthesis.<sup>1</sup> For some years we have been interested in this area and reported advancements in catalytic hydroamination,<sup>2</sup> and hydroaminomethylations.<sup>3</sup> Recently, we also showed that NO can be used as a practical amination reagent for the non-catalytic synthesis of nitro olefins.<sup>4</sup> Based on this work, we got attracted in catalytic conversions of olefins and NO or NO-releasing reagents. Herein, we wish to report the first iron-catalyzed synthesis of oximes from olefins by employing a biomimetic iron phthalocyanine complex catalyst and easily available reagents (NaBH<sub>4</sub> and *t*-BuONO).<sup>5,6</sup>

Until now, few studies have been performed on the catalytic nitrosation of olefins applying nitric oxide or alkyl nitrites in the presence of various reductants.<sup>7</sup> In general, cobalt complexes were used as catalysts in these reactions. However, Sugamoto and co-workers reported the utilization of iron(III) meso-tetraphenylporphine chloride [Fe(TPP)Cl] for nitrosation.<sup>7/</sup> Unfortunately, this complex showed no catalytic activity using *t*-BuONO.

For our initial experiments, the reaction of styrene with *tert*. butyl nitrite in the presence of iron phthalocyanine complex (Fe(Pc)) was chosen as a model. Selected results of the optimization of reaction conditions are summarized in Table 1. First tests showed only low conversion of the olefin. However, a survey of solvents indicated that high activity is observed in EtOH using NaBH<sub>4</sub> as reductant. Notably, higher catalyst concentration as well as prolonged reaction time led to decomposition of the product (Table 1, entries 5–9). In addition, some complexation between the initially formed nitrosoalkane and the iron centre of catalyst might occur,<sup>8</sup> and side-products such as 2,3-diphenylbutane and ethylbenzene, which resulted from reduction of styrene,<sup>9</sup> are detected by GC

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 Table 1
 Iron-catalyzed synthesis of oximes<sup>a</sup>

| Fe(Pc), NaBH <sub>4</sub> , <i>t</i> -BuONO<br>solvent, rt, time |                  |                               |                                  |     |                           |                |  |  |
|--|------------------|-------------------------------|----------------------------------|-----|---------------------------|----------------|--|--|
| Entry  | Fe(Pc)<br>(mol%) | NaBH <sub>4</sub><br>(equiv.) | Solvent                          | t/h | Conv.<br>(%) <sup>b</sup> | Yield $(\%)^c$ |  |  |
| 1  | 20               | 1.5                           | DME- <i>i</i> -PrOH <sup>e</sup> | 24  | 19                        | 12             |  |  |
| 2  | 20               | 1.5                           | <i>i</i> -PrOH                   | 24  | 14                        | 10             |  |  |
| 3  | 20               | 1.5                           | DME                              | 24  | 32                        | 30             |  |  |
| 4  | 20               | 1.5                           | Toluene-i-PrOH <sup>e</sup>      | 24  | 12                        | 6              |  |  |
| 5  | 20               | 2                             | EtOH                             | 24  | 98                        | $24^{f}$       |  |  |
| 6  | 10               | 2                             | EtOH                             | 24  | 99                        | 32             |  |  |
| 7  | 5                | 2                             | EtOH                             | 24  | 97                        | 33             |  |  |
| 8  | 1                | 2                             | EtOH                             | 24  | 98                        | 58             |  |  |
| 9  | 1                | 2                             | EtOH                             | 3   | 98                        | 66             |  |  |
| $10^d$   | 1                | 2                             | EtOH                             | 3   | 99                        | 83             |  |  |
|  |                  |                               |                                  |     |                           | (79)           |  |  |
| 11   | 1                | 1.2                           | EtOH                             | 3   | 53                        | 27             |  |  |
| 12   | 0.5              | 2                             | EtOH                             | 24  | 75                        | 39             |  |  |

<sup>*a*</sup> Reaction conditions: 1 mmol of styrene and 2.5 mmol of *t*-BuONO in 4 mL of solvent at room temperature under Ar. <sup>*b*</sup> Determined by GC after the reaction. <sup>*c*</sup> Determined by GC after workup; isolated yield is given in parenthesis. <sup>*d*</sup> The reaction was performed in autoclave with additional 10 bar of H<sub>2</sub>. <sup>*e*</sup> The ratio for mixed solvents is 1:1 v/v. <sup>*f*</sup> Trace of 1-phenylethylamine is observed by GC after the reaction.

in up to 20%. This is in agreement with the work of Eckert *et al.* who demonstrated that oxime **2** can be reduced to 1-phenylethylamine in the presence of a large amount of catalyst and NaBH<sub>4</sub>.<sup>10</sup> However, under our conditions only traces of 1-phenylethylamine are observed (Table 1, entry 5). The best yield of **2** is obtained when the reaction was performed in the presence of 10 bar H<sub>2</sub> (Table 1, entry 10).

A survey of different metal phthalocyanines (Table 2, entries 1–3) showed that the iron complex is by the far the most active and selective catalyst for the model reaction. Noteworthy, also vitamin  $B_{12}$  and the cobalt complex Co(DH<sub>2</sub>)(py)Cl showed significant activity (Table 2, entries 4–5). Moreover, using different nitrogen ligands in the presence of 10 mol% FeCl<sub>3</sub> or FeCl<sub>2</sub> gave the corresponding product in 5–61% yield (Table 2, entries 7–14). The best result was achieved when the reaction was performed in the presence of terpyridine L1 (Table 2, entry 8). In general, monodentate (L6) and bidentate ligands (L5) exhibited much lower activity compared to tridentate ligands (L1–L4).

With respect to the mechanism, we propose that oxime formation proceeds similarly compared to the reaction in the presence of cobalt complexes (Scheme 1).<sup>7</sup> Remarkably, at the initial stage of the reaction hydrogen evolution is observed. Moreover,  $B(OEt)_3$  is detected by GC. Key step in the

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<sup>&</sup>lt;sup> $\dagger$ </sup> Electronic supplementary information (ESI) available: General procedure, characterization data for compounds **2**, **4a–4k** and **5** and <sup>1</sup>H and <sup>13</sup>C NMR spectra of compounds **2**, **4a–4k** and **5**. See DOI: 10.1039/b900326f

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| Entry | Catalyst (mol%)               | Ligand<br>(equiv./catalyst) | Conv. $(\%)^d$ | Yield (%) <sup>e</sup> |
|-------|-------------------------------|-----------------------------|----------------|------------------------|
| 1     | $Co(Pc)^{b}$ (10)             | _                           | 12             | 2                      |
| 2     | $Mn(Pc)^{b}(10)$              | _                           | 39             | 9                      |
| 3     | $Ni(Pc)^{6}$ (10)             | _                           | 2              | <1                     |
| 4     | Vit $B_{12}(1)$               | _                           | 73             | 44                     |
| 5     | $Co(DH_2)(py)Cl^c$ (10)       | _                           | 55             | 22                     |
| 6     | $\operatorname{FeCl}_{3}(1)$  | L1 (2)                      | 43             | 16                     |
| 7     | $\operatorname{FeCl}_{2}(10)$ | L1(2)                       | 97             | 55                     |
| 8     | $\operatorname{FeCl}_{3}(10)$ | L1(2)                       | 94             | 61                     |
| 9     | $\operatorname{FeCl}_{3}(10)$ | _                           | 29             | 5                      |
| 10    | $\operatorname{FeCl}_{3}(10)$ | L2(2)                       | 99             | 46                     |
| 11    | $FeCl_3(10)$                  | L3(2)                       | 99             | 32                     |
| 12    | $FeCl_3$ (10)                 | L4(2)                       | 76             | 34                     |
| 13    | $FeCl_3$ (10)                 | L5(3)                       | 44             | 7                      |
| 14    | $\operatorname{FeCl}_{2}(10)$ | L6 (4)                      | 55             | 8                      |

<sup>*a*</sup> Reaction conditions: 1 mmol of styrene, 2 mmol of NaBH<sub>4</sub> and 2.5 mmol of *t*-BuONO in 4 mL of EtOH, 3 h at room temperature under Ar. <sup>*b*</sup> Pc = phthalocyanine. <sup>*c*</sup> DH<sub>2</sub> = dimethylglyoxime, py = pyridine. <sup>*d*</sup> Determined by GC after the reaction. <sup>*e*</sup> Determined by GC after work-up.



Scheme 1 Proposed reaction mechanism.

mechanism is the formation of the  $\sigma$ -alkyliron(III) complex **A**, which reacts with *t*-BuONO to afford the corresponding oxime.

Finally, the scope and limitations of the reaction were investigated by employing various olefins (Table 3). For convenience the reactions were performed without additional hydrogen pressure. Different *para-* and *meta-*substituted styrene derivatives gave the desired products in good yields (Table 3, entries 1–2 and 4–6), while *ortho-*substituted substrates afforded the corresponding oximes in somewhat lower yields (Table 3, entries 3 and 7). In addition, 2-vinylpyridine showed high activity and selectivity, leading to **4h** in 88% yield (Table 3, entry 8). 1,2-Disubstituted aryl olefins (**3i–3k**)

Table 3 Scope and limitations<sup>a</sup>

|       | R1 - R2   | Fe(Pc), NaBH <sub>4</sub> , t-BuONO                                | R <sup>2</sup> |                |  |  |
|-------|---|--|----------------|----------------|--|--|
|       | 3a-3k   | 4a-  | 4a-4k          |                |  |  |
| Entry | Olefin  | Product  | Conv. $(\%)^b$ | Yield $(\%)^c$ |  |  |
| 1     | MeO 3a  | Meo 4a   | 97             | 65             |  |  |
| 2     | Me 3b   | Me 4b  | 95             | 69             |  |  |
| 3     | Me<br>3c  | NOH<br>4c Me   | 92             | 56             |  |  |
| 4     | Br 3d   | Br 4d  | 99             | 83             |  |  |
| 5     | CI 3e   | CI 4e  | 98             | 73             |  |  |
| 6     | Cl 3f   | CI 4f  | 99             | 86             |  |  |
| 7     | GI 3g CI  | NOH<br>4g Cl   | 97             | 59             |  |  |
| 8     | N<br>3h   | NOH<br>4h  | 100            | 88             |  |  |
| 9     | 3i  | NOH<br>Et<br>4i  | 85             | 40             |  |  |
| 10    | J 3j  | NOH<br>4j  | 60             | 44             |  |  |
| 11    |   |  | 100            | 32             |  |  |
| 12    | $R^1 \xrightarrow{O} OEt$<br>$R^1 = C_3H_7$ , Ph, CH <sub>3</sub> , H | $R^{1} \xrightarrow{O} OEt$<br>$R^{1} = C_{3}H_{7}, Ph, CH_{3}, H$ | 61–100         | 61–100         |  |  |

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<sup>*a*</sup> Reaction conditions: 3 mmol of olefin, 1 mol% of Fe(Pc), 6 mmol of NaBH<sub>4</sub> and 7.5 mmol of *t*-BuONO in 18 mL of EtOH, 3 h at room temperature under additional 10 bar of  $H_2$ . <sup>*b*</sup> Determined by GC after the reaction. <sup>*c*</sup> Isolated yield.

were converted to the corresponding oximes (4i-4k) in moderate yields (Table 3, entries 9–11). In the case of 3k, 3-phenyl-2-isoxazoline (5) is formed from the cyclization of

oximate anion of  $4k^{11}$  as a minor product (14% yield). It should be noted that all products are conveniently isolated by chromatography.

In summary, we have developed the first iron-catalyzed synthesis of oximes from olefins. Noteworthy, the reaction proceeds in the presence of a convenient iron complex and inexpensive reagents.

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