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# High-valent metalloporphyrin, Fe(tpp)OTf, catalyzed rearrangement of α,β-epoxy ketones into 1,2-diketones

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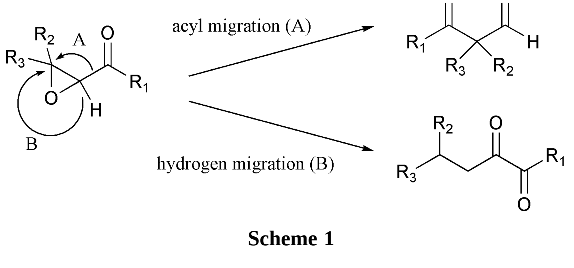
**Iron(III) tetraphenylporphyrin triflate, Fe(tpp)OTf, works as an efficient and characteristic Lewis acid catalyst in the selective rearrangement of α,β-epoxy ketones into 1,2-diketones.**

α,β-Epoxy ketones are an important class of compounds in view of distinct structural features and high synthetic utility. Both the ketone and epoxide moieties can be subjected to a wide variety of further chemical transformations to give potential intermediates and precursors for the synthesis of natural products and biologically active compounds.[1] Since the early work of House *et al.* in the 1950s, epoxy ketones have been known to rearrange into 1,2- and/or 1,3-dicarbonyl compounds with acids.[2] As shown in Scheme 1, the rearrangement involves a cleavage of the C–O bond at the β-position followed by acyl migration (route A) or hydrogen migration (route B), leading to 1,3- or 1,2-diketones. The acyl migration that gives 1,3-diketones can be achieved with various acids such as $BF_3 \cdot OEt_2$, $LiClO_4$ and solid Brønsted acids (zeolites),[2–4] and has been applied to the synthesis of natural products having complex chemical structures.[5] By contrast, fewer examples are documented on the hydrogen migration that allows access to 1,2-diketones. In particular, none of the catalytic versions of such a transformation have hitherto been reported.[6,7] As part of our ongoing studies on the development of a novel function and synthetically useful chemical properties of metalloporphyrins, we have found that high-valent metalloporphyrins promote regioselective hydrogen migration in the rearrangement of epoxides.[8] We, therefore, envisioned that these metalloporphyrins would function as a useful catalyst for the rearrangement of α,β-epoxy ketones. In this communication, we report the first highly efficient catalytic rearrangement of α,β-epoxy ketones into 1,2-diketones, which is applicable to a variety of epoxy ketones.

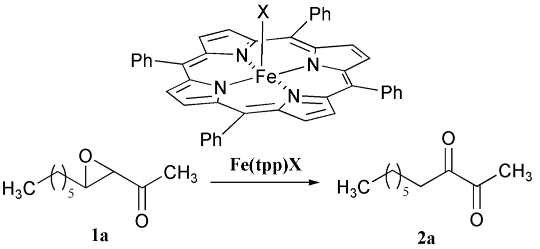
*trans*-3,4-Epoxydecan-2-one (**1a**) was chosen as a model substrate and the rearrangement with several iron(III) tetraphenylporphyrin complexes was investigated (Table 1).† A catalytic amount (2 mol%) of iron(III) tetraphenylporphyrin perchlorate, $Fe(tpp)ClO_4$, was added to a solution of **1a** (5 mmol) in dioxane (3 ml), and the reaction mixture was refluxed for 8 h under a nitrogen atmosphere. After concentration *in vacuo*, florisil column purification provided decane-2,3-dione (**2a**) in 30% yield along with recovered **1a** (45%) (entry 1). Iron(III) tetraphenylporphyrin chloride, Fe(tpp)Cl, instead of $Fe(tpp)ClO_4$, did not effect the reaction, recovering the starting material **1a** (entry 2). On the other hand, the use of iron(III) tetraphenylporphyrin triflate, Fe(tpp)OTf, as a catalyst, remarkably improved the yield of **2a** up to 95% and shortened the reaction time to 1.5 h (entry 3). Although the Fe(tpp)OTf catalyzed reaction proceeded similarly in other solvents such as toluene and 1,2-dichloroethane, the yield of **2a** decreased to 50% and 55%, respectively (entries 4 and 5). The Lewis acidity of the metalloporphyrins in the solvents used seems to affect the reactivity and selectivity of the rearrangement. To evaluate the aptitude of the Fe(tpp)OTf–dioxane catalyst system, we further examined the rearrangement of **1a** with $BF_3 \cdot OEt_2$, $MgBr_2 \cdot OEt_2$ and methylaluminium bis(4-bromo-2,6-di-*tert*-butylphenoxide) (MABR),[9] which are the most representative and commonly used Lewis acid reagents in the rearrangement of various kinds of epoxides. However, all attempts to rearrange **1a** with these Lewis acids under several conditions were unsuccessful, providing only inseparable complex mixtures, halohydrin derivative **3a** or starting material **1a** recovered: neither the desired product **2a** nor the corresponding 1,3-diketone was detected in the $^1H$-NMR spectrum of the crude products (entries 6–10). Consequently, the Fe(tpp)OTf–dioxane system depicted in entry 3 is the most effective metalloporphyrin catalyst system among those examined, and permits the highly selective transformation of **1a** into **2a** at a low catalyst loading without significant loss of catalytic activity.

To explore the generality of the Fe(tpp)OTf–dioxane catalyst system, the ring-opening rearrangement of various α,β-epoxy ketones were examined. As shown in Table 2, the Fe(tpp)OTf



**Scheme 1**

**Table 1** Iron(III) tetraphenylporphyrin, Fe(tpp)X, catalyzed rearrangement of *trans*-3,4-epoxydecan-2-one (**1a**)



| Entry | Conditions<br>Catalyst/Solvent/Time | Yield of **2a** (%)[a] |
|---|---|---|
| 1 | $Fe(tpp)ClO_4$ (2 mol%)/dioxane/8 h[b] | 30[c] |
| 2 | Fe(tpp)Cl (2 mol%)/dioxane/48 h[b] | No reaction[d] |
| 3 | Fe(tpp)OTf (2 mol%)/dioxane/1.5 h[b] | 95 |
| 4 | Fe(tpp)OTf (2 mol%)/$(CH_2)_2Cl_2$/2 h[b] | 50 |
| 5 | Fe(tpp)OTf (2 mol%)/toluene/2 h[b] | 55 |
| 6 | MABR (2 equiv.)/$CH_2Cl_2$/48 h[ef] | Complex mixture |
| 7 | MABR (2 equiv.)/dioxane/48 h[eg] | Complex mixture |
| 8 | $BF_3OEt_2$ (1 equiv.)/$CH_2Cl_2$/2 h[h] | Complex mixture |
| 9 | $BF_3OEt_2$ (1 equiv.)/ether/2 h[h] | No reaction[d] |
| 10 | $MgBr_2OEt_2$ (1 equiv.)/$CH_2Cl_2$/1.5 h[h] | 0[i] |

[a] Isolated yield. [b] Reflux. [c] Recovery of **1a** (45%). [d] Recovery of **1a** (quant). [e] MABR: methylaluminium bis(4-bromo-2,6-di-*tert*-butylphenoxide). [f] −78 °C to rt. [g] −20 °C to rt. [h] 0 °C to rt. [i] 4-Bromo-3-hydroxydecan-2-one **3a** (92%) was obtained.

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catalyzed reaction proved to be general and applicable to a variety of α,β-epoxy ketones.‡ As a whole, a facile and highly selective conversion of epoxy ketones into 1,2-diketones *via* hydrogen migration, *viz.*, route B in Scheme 1, was observed. Acetylepoxides **1b** bearing an alkyl group longer than that of **1a** were easily transformed into the corresponding 1,2-diketone **2b** in 88% yield. In the rearrangement of other acetylepoxides **1c**, **1d** and **1e**, olefinic, cycloalkanoic and aromatic moieties in the substrates were tolerated well, and the corresponding 1,2-diketones **2c**, **2d** and **2e** were obtained in high yields. Both the yield and the reaction time are independent of the carbon-chain length of acyl substituents in the substrates: the reaction of nonanoylepoxide **1f** proceeded smoothly, giving the corresponding 1,2-diketone **2f** as a sole isolable product. Phenyl epoxides **1g** and **1h** were surprisingly susceptible to the catalytic rearrangement. The rearrangements of these epoxides were completed within 15 min under the same conditions, affording 1,2-diketones **2g** and **2h** in high yields. This acceleration in reaction rate should be ascribed to the presence of the β-phenyl group that can stabilize the carbonium ion generated by the C–O bond cleavage at the β-position in the rearrangement.

In summary, we have developed the first catalytic version of the Lewis acid mediated rearrangement of α,β-epoxy ketones into 1,2-diketones. The rearrangement can easily be promoted by high-valent metalloporphyrin complexes, especially Fe(tpp)OTf, at a low catalyst loading (2 mol%) under very mild conditions. 1,2-Diketones have been found to be versatile intermediates in organic synthesis, and their preparation has been widely investigated.[10] As for 1,2-diketone syntheses, the present catalytic process exceeds or competes with other methods reported so far in view of the simplicity, high yields, and availability of starting materials.[11] Elucidation of the precise mechanism and the synthetic applications of the present metalloporphyrin catalyzed rearrangement are in progress.

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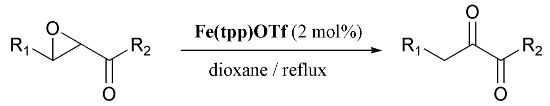
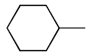
**Table 2** Fe(tpp)OTf catalyzed rearrangement of α,β-epoxy ketones[a]



**1** **2**

| | $R_1$ | $R_2$ | Time | Yield (%)[b] |
|---|---|---|---|---|
| **a** | $CH_3(CH_2)_5$- | $CH_3$- | 1.5 h | 95 |
| **b** | $CH_3(CH_2)_8$- | $CH_3$- | 1.5 h | 88 |
| **c** | $CH_2{=}CH(CH_2)_8$- | $CH_3$- | 2 h | 92 |
| **d** |  | $CH_3$- | 2.5 h | 87 |
| **e** | $Ph(CH_2)_2$- | $CH_3$- | 1.5 h | 87 |
| **f** | $CH_3(CH_2)_2$- | $CH_3(CH_2)_7$- | 1 h | 91 |
| **g** | Ph- | $CH_3$- | 15 m | 85 |
| **h** | Ph- | Ph- | 15 m | 85 |

[a] Conditions: **1** (0.5 mmol), Fe(tpp)OTf (2 mol%), dioxane (3 ml), reflux. [b] Isolated yield.

## Notes and references

† Fe(tpp)$ClO_4$ and Fe(tpp)OTf were prepared according to the method described previously, see ref. 8.

‡ The products **2a**–**2f** gave satisfactory NMR, IR and high-resolution mass spectra. For example, $^1$H- and $^{13}$C-NMR data of **2a** and **2e** are as follows. **2a**: $^1$H-NMR (270 MHz, $CDCl_3$) $\delta$ 0.88 (3H, t, $J$ = 6.6 Hz), 1.18–1.35 (8H, m), 1.58 (2H, m), 2.33 (3H, s), 2.73 (2H, t, $J$ = 7.4 Hz); $^{13}$C-NMR (67.8 MHz, $CDCl_3$) $\delta$ 14.1, 22.6, 23.1, 23.7, 29.0, 29.1, 31.6, 35.7, 197.6, 199.5. **2e**: $^1$H-NMR (270 MHz, $CDCl_3$) $\delta$ 1.93 (2H, m), 2.29 (3H, s), 2.64 (2H, t, $J$ = 7.6 Hz), 2.75 (2H, t, $J$ = 7.3 Hz), 7.15–7.31 (m, 5H); $^{13}$C-NMR (67.8 MHz, $CDCl_3$) $\delta$ 23.7, 24.6, 35.0, 126.1, 128.4, 128.5, 141.3, 197.4, 199.1. The products **2g**[10a] and **2h**[6a] are compared with the literature data.

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