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Catalytic reduction of an α,β-disubstituted alkene with sodium borohydride in the presence of tetra-*tert*-butylphthalocyanine complexes

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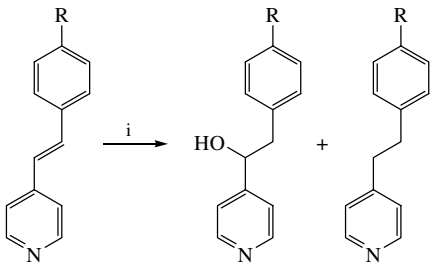
Cobalt tetra-*tert*-butylphthalocyanine was found an efficient catalyst for the catalytic reduction of 4-[(*E*)-2-phenylethenyl]-pyridine to 4-(2-phenylethyl)pyridine with sodium borohydride.

The combination of a reducing agent, molecular oxygen and a metal porphyrin is a potential catalytic system for the reductive conversion of organic compounds. In 1979, Tabushi and Koga[1] proposed the first catalytic system consisting of a substituted manganese(III) porphyrin as the catalyst and sodium borohydride as the reducing agent, which simulated the function of cytochrome P-450. The major products of reductive hydroxylation of cyclohexene included cyclohexanol and cyclohexen-2-ol. It was assumed that cyclohexene oxide was formed as an intermediate and was then reduced to cyclohexanol with sodium borohydride in the presence of manganese tetraphenylporphyrinate. The subsequent studies of this reaction[2] cast doubt that epoxides were formed in it. A mechanism was proposed for the catalytic reductive hydroxylation of alkenes involving the coordination of an alkene with manganese(II) porphyrin as the initial stage, followed by incorporation of an oxygen molecule into the carbon–metal bond. Presumably, a manganese alkylporphyrin is the key intermediate in the catalytic hydroxylation involving manganese porphyrinate. Aside from manganese porphyrin, iron(III) tetraporphyrinate[3] and cobalt(II) tetraporphyrinate[4] also showed catalytic activity in this reaction.

The structure of phthalocyanines is similar to that of porphyrins, but the former have been studied much less thoroughly with respect to reductive hydroxylation. Reductive hydroxylation was studied using styrene and α-methylstyrene as model substrates.[4–6] It was reported[4] that the reaction slowed down with alkenes with higher substitution complexity; in many cases, the yields of reductive hydroxylation decreased as well. In view of this, it was interesting to study the conditions of reductive hydroxylation for alkenes with higher substitution complexity.

We used 4-[(*E*)-2-phenylethenyl]pyridine, a heterocyclic analogue of stilbene, as the substrate. Two reaction products were obtained at room temperature in the presence of 1.5 mol% cobalt *tert*-butylphthalocyanine ($^{Bu^t}$PcCo) according to Scheme 1.

As expected, the reaction gave compound **2a**, which resulted from the reductive hydroxylation of alkene **1a**. Unexpectedly, 4-(2-phenylethyl)pyridine **3a** was also obtained, which is a product of double bond hydrogenation in compound **1a**. Note that compounds **2a** and **3a** were formed in a ratio of 1:1. An increase in the temperature to 70 °C resulted in a 1:3 ratio between compounds **2a** and **3a**. If the reaction temperature was increased to 120 °C (in 2-methoxyethanol), only compound **3a** was obtained in 37% yield. There are examples of the hydrogenation of alkenes on cobalt phthalocyanine, but less sterically



Scheme 1 *Reagents and conditions*: i, $NaBH_4$, $^{Bu^t}$PcCo, $Mg(ClO_4)_2$, O_2, 20 °C.

substituted (styrene and α-methylstyrene).[5] The presence of magnesium perchlorate increased the yield of reaction product **3a**. The highest yield of compound **3a** (78%) was achieved in the THF–ethanol solvent system in the presence of an equivalent amount of magnesium perchlorate in the reaction mixture† at 70 °C. In this case, no reductive hydroxylation product (compound **2a**) was found in the reaction mixture. Moreover, this

† *Synthetic procedure*: $Mg(ClO_4)_2$ (111.6 mg, 0.5 mmol) and $^{Bu^t}$PcCo (8.0 mg, 0.01 mmol) were added to a solution of 90.6 mg (0.5 mmol) of compound **1a** (obtained according to a published procedure[7]) in a mixture of anhydrous tetrahydrofuran (20 ml) and anhydrous ethanol (10 ml). After the reagents dissolved, $NaBH_4$ (56.7 mg, 1.5 mmol) was added and the solution was kept at 70 °C for 9 h with stirring by an air flow [after 3 and 6 h of heating, a portion of $NaBH_4$ (56.7 mg, 1.5 mmol) was added each time]. After cooling, toluene and water were added to the mixture; the organic layer was separated while the aqueous layer was extracted with toluene (2×20 ml). The solvents were evaporated *in vacuo* and the precipitate was dissolved in 0.5 M HCl. The phthalocyanine precipitated was filtered off, and a solution of NaOH was added to the filtrate to adjust pH 10. The solution was extracted with dichloromethane, and the extract was dried with K_2CO_3. The solvent was evaporated *in vacuo*, and the crystalline residue was chromatographed with chloroform on silica gel. The chloroformic solution was concentrated to give 71.5 mg (78%) of compound **3a**[8,9] as colourless crystals, mp 69–70 °C. ^{1}H NMR (200 MHz, $CDCl_3$) δ: 2.91 (s, 4H, $2CH_2$), 7.02–7.39 (m, 7H, Ph and β-Py), 8.47 (d, 2H, α-Py). MS, *m*/*z*: 183 (M^+).

Similarly, 4-[2-(4-bromophenyl)ethyl]pyridine **3b** was obtained from compound **1b** and isolated as a hydrochloride salt in 83% yield; mp 154–155 °C. ^{1}H NMR (200 MHz, [$^2H_6$]DMSO) δ: 2.98 (t, 2H, CH_2), 3.20 (t, 2H, CH_2), 7.22 (d, 2H, 4-BrC_6H_4), 7.54 (d, 2H, 4-BrC_6H_4), 7.94 (d, 2H, β-C_5H_4N), 8.82 (d, 2H, α-C_5H_4N). MS, *m*/*z*: 262 (M^+).

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reaction with compound **1b**, a 4-bromo-substituted analogue of **1a**, was carried out (Scheme 1). In this case, the yield of **3b**, an analogue of compound **3a**, was 83%.

Presumably, the mechanism of catalysis by cobalt(II) phthalocyanine is as follows: at the first stage, cobalt(II) phthalocyanine is reduced with sodium borohydride to give cobalt(I) phthalocyanine. The latter reacts with the alkene to give an alkyl σ-complex, which adds a proton from the protic solvent to give the alkane. This is supported by the fact that the reduction of styrene with $NaBH_4$ and ^{But}PcCo has been reported[5] (however, α-methylstyrene is weakly reduced in this system). To check this possibility, we performed the reaction using the procedure described† but under argon. Under these conditions, product **3a** is formed in trace amounts only. On the other hand, this reaction with compound **2a** (instead of compound **1a**) under the same conditions did not give compound **3a**. This agrees with other data[10] that α,β-disubstituted alkenes (*e.g.*, stilbene) are reduced with the sodium borohydride–iron(III) porphyrine system much less readily than mono-substituted alkenes.

An increase in the concentration of ^{But}PcCo from 1.5 to 10.0 mol% does not increase the yield of compound **3a** (all other conditions specified in the experimental section).

After the reaction, ^{But}PcCo was quantitatively regenerated from the reaction mixture (it was filtered off from aqueous solution and then purified by column chromatography on silica gel); it was used repeatedly (100 cycles) without a loss in catalytic activity. In addition to cobalt phthalocyanine, we also studied a *tert*-butyl-substituted phthalocyanine and its nickel complex as catalysts for this reaction. They displayed only weak catalytic activity: in the presence of ^{But}PcNi, the yield of compound **3a** was 11% and that in the presence of $^{But}PcH_2$ was 5%. Thus, cobalt *tert*-butylphthalocyanine is the best catalyst for this reaction.

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