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Cobalt Catalysis

Markovnikov-Selective Cobalt-Catalyzed Wacker-Type Oxidation of Styrenes into Ketones under Ambient Conditions Enabled by Hydrogen Bonding

Naba Abuhafez, Andreas W. Ehlers,* Bas de Bruin,* and Rafael Gramage-Doria*

Abstract: The replacement of palladium catalysts for Wacker-type oxidation of olefins into ketones by first-row transition metals is a relevant approach for searching more sustainable protocols. Besides highly sophisticated iron catalysts, all the other first-row transition metal complexes have only led to poor activities and selectivities. Herein, we show that the cobalt-tetraphenylporphyrin complex is a competent catalyst for the aerobic oxidation of styrenes into ketones with silanes as the hydrogen sources. Remarkably, under room temperature and air atmosphere, the reactions were exceedingly fast (up to 10 minutes) with a low catalyst loading (1 mol%) while keeping an excellent chemo- and Markovnikov-selectivity (up to 99% of ketone). Unprecedently high TOF ($864 \, h^{-1}$) and TON (5,800) were reached for the oxidation of aromatic olefins under these benign conditions. Mechanistic studies suggest a reaction mechanism similar to the Mukaiyama-type hydration of olefins with a change in the last fundamental step, which controls the chemoselectivity, thanks to a unique hydrogen bonding network between the ethanol solvent and the cobalt peroxo intermediate.

Introduction

Oxidation reactions play a paramount role in chemical synthesis since they typically allow specific introduction of carbonyl or hydroxyl groups into low-functionalized starting materials en route to complex structures.[1] Among the myriad of oxidation reactions available nowadays, Wacker-type reactions have attracted increased attention since their discovery in the 60's as they lead to almost perfect atom-economy using O_2 as reagent (Figure 1, top).[2] Such reactions enable the oxidation of an olefin into the corresponding ketone or aldehyde while keeping the same number of carbon atoms in the final product.[3] The selectivity of the reaction for terminal olefins, either Markovnikov (ketone) or anti-Markovnikov (aldehyde), is exclusively controlled by the nature of the ligand coordinating to the palladium catalyst and the reaction conditions.[4] A vast number of studies have been devoted to increase the levels of sustainability of this process.[5] For instance, avoiding copper as co-catalyst, replacing the pure hazardous O_2 by air as well as searching for alternatives to the typically used acidic conditions to make these oxidations compatible with sensitive and useful functional groups are urgent requirements by academic and industrial laboratories.[6]

Alternatively, remarkable efforts have been devoted to replace the catalytically active palladium species by more benign, less expensive and more affordable first-row transition metal complexes.[7] From the many ones studied, iron catalysts have proven extremely powerful and thanks to the nature of the ligand coordinating to iron as well as the type of oxidant and fine-tuned reaction conditions, it has been possible to deliver in a selective manner either the Markovnikov ketone product or the anti-Markovnikov

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Pd- or Fe-catalyzed Wacker-type oxidation of olefins (**known**):

Co-catalyzed Wacker-type oxidation of aromatic olefins to ketones (**this work**):

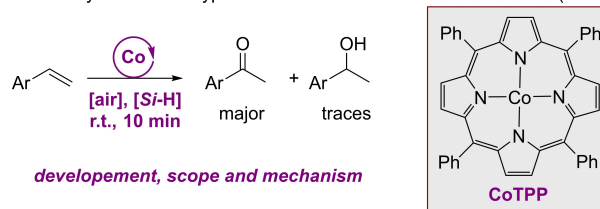*developement, scope and mechanism*

Figure 1. Wacker-type reactions under classical palladium catalysis and iron catalysis (top) and the Markovnikov-selective system with cobalt catalysis operating under ambient conditions (bottom). [O]=oxygen source, [H]=hydrogen source.
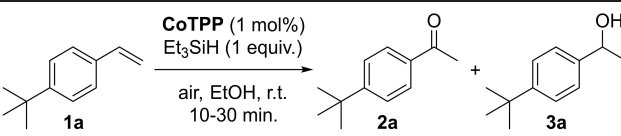
aldehyde one (Figure 1, top).[8–11] According to Che and co-workers, the aldehydes are typically obtained from iron-porphyrin catalysts with PhIO or H_2O_2 as the oxidant under an epoxide/isomerization mechanism.[8] Interestingly, Arnold, Hammer and co-workers engineered an artificial heme-metalloenzyme that operated under air with impressive turnover numbers.[9] On the other hand the Markovnikov ketone product readily forms from iron catalysts, typically iron-porphyrinoids, under ambient conditions using a hydrosilane as the hydrogen source via a radical-mediated mechanism, which is different than the one operating for aldehyde formation.[10] In these cases, the presence of μ-oxo-bridged diiron species may limit its productivity in catalysis as mononuclear species are postulated as the active species.[11] The catalyst loadings for these reactions are typically found in the range of 2.5–10 mol % and reaction times require more than 5 hours.[10,11] As such, there is room for improvement for these important reactions through the design and development of other first-row transition metal catalysts different than iron.[12]

We envisioned that cobalt-porphyrins could replace iron complexes as catalysts and eventually lead to a more reactive system since the homologous μ-oxo-bridged dicobalt species are unknown so far and cobalt-porphyrin radical chemistry compares well with that of iron.[13] Furthermore, previous reports point out that cobalt complexes display some activity in Wacker-type reactions although with low selectivity or under hazardous conditions.[14] For instance, Matsushita found that a highly sophisticated octa-chlorinated cobalt-porphyrin led to a mixture of ketone, alcohol and hydroperoxide products under a pure O_2 atmosphere and a hydrosilane source.[15] As such, a second step involving acetylation was required to obtain the desired ketone product.[16] Herein, we demonstrate that the readily available and unfunctionalized cobalt-tetraphenylporphyrin complex **CoTPP** behaves as an excellent homogeneous catalyst for the oxidation of aromatic olefins under ambient conditions of pressure and temperature, with an activity and selectivity for ketone products (Figure 1, bottom) that outperforms current, state-of-the-art iron catalysts. Besides a broad functional group tolerance encountered in the catalysis, a combination of experimental and computational studies was carried out in order to unveil the reaction mechanism, in which hydrogen bonding significantly contributes to decrease the energy barrier of the key chemo-determining step.

Results and Discussion

We initiated this study by evaluating the oxidation of 4-*tert*-butylstyrene starting material (**1a**) under conditions similar to those reported for iron catalysts but replacing the catalyst by the cobalt-tetraphenylporphyrin **CoTPP** (Table 1 and Tables S1–S2 in the Supporting Information).[10,11] By screening the reaction conditions, we discovered that 1 mol % of **CoTPP** complex enabled the oxidation of **1a** into the corresponding ketone **2a** in an excellent 96 % yield in the presence of one equivalent of Et_3SiH at room temperature

Table 1: Optimization of reaction conditions for the cobalt-catalyzed Wacker-type Markovnikov-selective oxidation of **1a** and control experimentation.[a]

Entry	Deviation from above conditions	Conv. [%][b]	2a:3a [%][b]
1	none	>99	96:4
2	2 instead of 1 equiv. of Et_3SiH	>99	96:4
3	3 instead of 1 equiv. of Et_3SiH	>99	96:4
4	$PhSiH_3$ instead of Et_3SiH	>99	87:13
5	Ph_2SiH_2 instead of Et_3SiH	>99	86:14
6	Et_2SiH_2 instead of Et_3SiH	>99	84:16
7[c]	PMHS instead of Et_3SiH	17	n.d.
8	CaH_2 instead of Et_3SiH	0	n.d.
9	H_2 instead of Et_3SiH	0	n.d.
10	EtOH with 4 % water content	>99	70:30
11	absence of **CoTPP**	0	n.d.
12	absence of Et_3SiH	0	n.d.
13	argon instead of air	25	80:20
14	DCM instead of EtOH under argon	<5 %	n.d.
15	DCM instead of EtOH under air	>99	74:26
16	with light protection (in the dark)	>99	94:6
17	addition of **1a** as the last reagent	91	87:13
18	50 °C and 2 equiv. of Et_3SiH	>99	96:4
19	0 °C instead of r.t.	16	100:0

[a] Reaction conditions: **1a** (0.325 mmol), Et_3SiH (0.325 mmol), **CoTPP** (0.00325 mmol), EtOH (1 mL), dodecane (0.081 mmol), room temperature, air atmosphere, 10 or 30 minutes. [b] Conversion of **1a** and yields of **2a** and **3a** GC and GC-MS using dodecane as the internal standard. [c] Reaction performed at 100 °C. PMHS = polymethylhydrosiloxane, n.d. = not determined.

under air after 30 minutes in ethanol solvent (Table 1, entry 1). This corresponds to an initial turnover frequency of 864 h^{-1} (see Supporting Information), which is a twelve-fold increase when compared to the most active iron catalyst reported so far.[11] Interestingly, the alcohol side-product **3a** reached only 4 % and no evidence for formation of other side-products such as hydroperoxide or aldehydes was obtained. A kinetic study indicated that the reaction was completed in only 10 minutes with the formation of **2a** being directly correlated to the consumption of the substrate **1a** (Figure S1 in the Supporting Information). The presence of excess of Et_3SiH (2 or 3 equivalents) did not change the chemo and regioselectivity of the reaction (Table 1, entries 2–3). Other hydrosilane sources such as $PhSiH_3$, Ph_2SiH_2 and Et_2SiH_2 were not as effective and the alcohol side-product reached 13–16 % yield (Table 1, entries 4–6). The slight increased formation of alcohol side-products with these silanes is likely the result of an increased reducing character that could help in the reduction of the ketone to the alcohol side-product.[17] Using PMHS (PMHS = polymethylhydrosiloxane) as hydrosilane led to 15 % yield of **2a** and similar reactivity (17 %) was obtained at 100 °C under air atmosphere (Table 1, entry 7). Replacing Et_3SiH by CaH_2 or H_2 completely inhibited the catalysis (Table 1, entry 8–9). Because the presence of water increases the

reactivity and Markovnikov-selectivity in some iron-porphyrin-catalyzed Wacker-type reactions,[11] we replaced the pure and dry ethanol solvent by a mixture of ethanol/water (96:4). In this scenario, 30% alcohol was formed with 70% ketone product being obtained (Table 1, entry 10).

Control experiments indicated that the presence of all reagents and catalysts was required for the observed reactivity (Table 1, entries 11–12). Under argon atmosphere in place of air, the conversion of the starting material **1a** significantly dropped to 25% (Table 1, entry 13), indirectly indicating that the O_2 from air is the source of oxygen in the reaction as found elsewhere for iron-porphyrin catalysts.[10,11] Because the ratio of ketone/alcohol (80:20) observed in this experiment (Table 1, entry 13) compares well with that obtained with 4% water content (70:30, Table 1, entry 10), we assume that the presence of traces of air and/or water in the reagents and/or the solvent are the oxygen source for explaining the non-negligible reactivity under argon atmosphere (Table 1, entry 13).[18] As a matter of fact, the catalysis performed with dichloromethane as the solvent under argon atmosphere led to a higher decrease of yield (5%, Table 1, entry 14) when compared to the reaction performed under air conditions (>99% conversion of **1a** with 74% formation of ketone **2a**, Table 1, entry 15).[18]

We also noted that the reaction was insensitive to light as the same outcome was observed in the dark (Table 1, entry 16). However, the reaction was sensitive to the order of addition of reagents because adding the substrate **1a** as the last reagent to the reaction vessel led to a slight decrease in both conversion (91%) and selectivity (**2a**:**3a**=79:12, Table 1, entry 17). Similar observations were made for iron-porphyrin catalysts exhibiting Markovnikov selectivity.[11] Using free-base tetraphenylporphyrin and Co(OAc)$_2$·4H$_2$O, respectively, as eventual catalysts led to no reactivity and full recovery of the starting material **1a** (see Supporting Information). We also noted that the catalysis was tolerant to 50°C in the presence of 2 equivalents of Et$_3$SiH (Table 1, entry 18).[19] However, at 0°C the catalysis led only to a 16% conversion towards ketone **2a** (Table 1, entry 19). The robustness of the catalysis was addressed by performing an experiment with 0.001 mol% of **CoTPP** catalyst, reaching a turnover number value of 5,800 (see Supporting Information for more details). As a proof-of-concept, we addressed the stability of the **CoTPP** catalyst by recovering it after one reaction and using it up to two times affording full conversion and 96% ketone formation the first time and 93% ketone formation the second time (see Supporting Information), thus showing the ability of **CoTPP** catalyst to be reused and recycled.

Next, the scope of the cobalt-catalyzed oxidation of C=C bonds was addressed. For styrene derivatives **1a**–**1l**, full conversions were reached in 10 minutes with very high selectivities observed for ketone **2** over the alcohol side-product **3** (Scheme 1). For instance, alkyl-containing styrenes **1a**–**1b** were oxidized into their corresponding methyl ketones **2a** and **2b** in 91% and 88% isolated yields, respectively. Unfunctionalized styrene **1c** delivered acetophenone **2c** in 96% selectivity and 82% isolated yield. Halides such as fluoride, chloride and bromide were
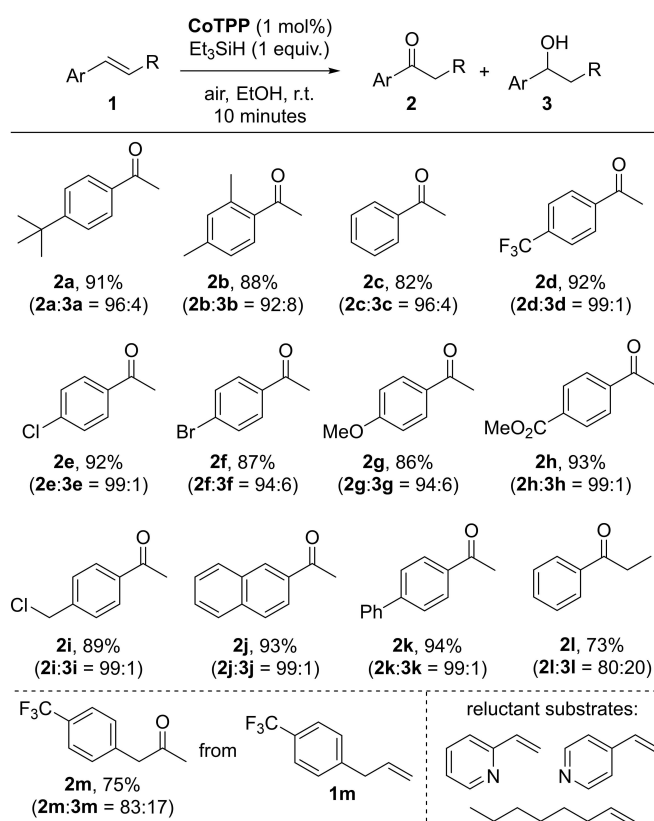
Scheme 1. Evaluation of olefin derivatives in the **CoTPP**-catalyzed oxidation into ketones under ambient conditions.

tolerated as shown in the synthesis of ketones **2d**–**2f** with high selectivity (up to 99%) and isolated yields in the range of 87–92%. Ether- and ester-containing ketones **2g** and **2h** were obtained in 86% and 93% isolated yields. Of high relevance is the fact that alcohol side-products **3d**–**3h** did not reach more than 6%. 4-Vinylbenzyl chloride (**1i**) delivered exclusively the 4-acetylbenzyl chloride (**2i**) in 89% yield. Polyaromatic substrates were also compatible as shown in the synthesis of 2-acetonaphthone (**2j**) and 4-acetylbiphenyl (**2k**) in >93% yield with no trace formation of alcohol **3j** and **3k**, respectively. The reactions are not only compatible with terminal aromatic olefins, but also with internal ones. For instance, the 1,2-di-substituted *trans*-β-methylstyrene furnished propiophenone (**2l**) in a remarkable 80% selectivity and 73% isolated yield. This case is the only one in which the cobalt-catalyzed oxidation afforded up to 20% of alcohol **3l** as side-product. These observations highlight that the **CoTPP** catalyst outperforms the reactivity and Markovnikov-selectivity of previous iron catalyst systems for the oxidation of aryl olefins into ketones.[10,11] Importantly, the reaction was amenable to upscaling as demonstrated in the gram-scale synthesis of **2a** in 85% isolated yield (0.97 g) starting with 1.04 g of styrene derivative **1a** (see Supporting Information). The reaction performed with heteroaromatic 2-vinylpyridine and 4-vinyl-pyridine, respectively, led to no reactivity, strongly suggesting that the pyridine binds to an in situ formed

Co(III)-porphyrin species as reported elsewhere,[20] which is relevant for mechanistic considerations (see below). Interestingly, the allyl-containing substrate **1m**, which contains the electron-withdrawing CF₃ group, reacted efficiently under cobalt catalysis provided that the temperature was raised to 70°C during 16 hours and that 2 equivalents of PhSiH₃ were used (Scheme 1). In this case, the corresponding ketone product **2m** formed in 83% selectivity and it was isolated in 75% yield. The side-product alcohol **3m** was formed in 17% yield and no other side-products were detected, which is in stark contrast with previous reports with iron-porphyrin catalysts that produced up to five additional side-products with low selectivity for **3m** (38%).[11] Unfortunately, a low reactivity was observed for allyl derivatives bearing other substitution patterns (see Supporting Information for more details). No reactivity was observed for the highly inert aliphatic olefins and related substrates (see Supporting Information for more details).[21]

In order to better understand the origin for such excellent selectivity, we submitted the ketone product (**2c**) and the side-product alcohol (**3c**), respectively, to the optimal reaction conditions under cobalt catalysis (Figure 2A, top). In both cases, the starting materials were fully recovered, indicating that (i) the alcohol is not an intermediate towards the formation of the ketone via dehydrogenation and (ii) the alcohol is formed during the course of the catalysis via an irreversible side reaction that does not involve the ketone most likely following the Mukaiyama-type mechanism for the cobalt-catalyzed hydration of olefins.[22] On the other hand, the reaction carried out in the presence of a radical scavenger such as TEMPO [TEMPO = (2,2,6,6-tetramethylpiperidin-1-yl)oxyl] significantly suppressed catalyst activity with trace formation of the ketone product **2a** (Figure 2B, top). This finding strongly suggest that the catalysis undergoes a radical-based reaction mechanism.[23,24] The epoxidation/isomerization pathway[8] was ruled out as regards of the absence of reactivity found for styrene oxide (**4**) under the cobalt-catalyzed reaction conditions (Figure 2C, top). To gain further insights on the precise action mode of the **CoTPP**-catalyzed oxidation of **1a**

into ketone **2a**, we performed UV/Vis titration studies by adding aliquots of Et₃SiH from 0 to 10 equivalents to a solution of **CoTPP** in ethanol (Figures S3 in the Supporting Information). A new absorbance peak appeared at 430 nm near to the main Soret absorbance band at 410 nm. UV/Vis analysis of the reaction mixture performed after the initial 5 minutes of the catalysis featured only the absorbance band at 430 nm (Figure S4 in the Supporting Information), thereby supporting formation of cobalt(III)-porphyrin species during the oxidation process.[25] Because of the short lifetime of the active species, we did not manage to get relevant information from NMR and EPR spectroscopy studies. On the other hand, kinetic studies applying the initial rate method indicated that the reaction is first order in both **CoTPP** and Et₃SiH reagent, whereas it is zero order in substrate **1a** (Figure 2D, bottom). As such, the formation of the initial cobalt-hydride species seems to be the rate-determining step of the catalytic cycle. This is similar to the cobalt species evaluated in the reactions dealing with hydrogen transfer to nitrile- or acetate-substituted olefins[26] as well as previous reports dealing with cobalt-porphyrin hydride species.[27] A simplified, postulated reaction mechanism is proposed in Scheme 2, in which the olefin reacts in a chemo-selective manner with the hydride cobalt species leading to a cobalt-alkyl intermediate that might react with dioxygen forming the corresponding alkyl-peroxo cobalt species. This intermediate further rearranges affording the methylketone final product and the cobalt-hydroxo species that undergo reaction with the silane reagent to regenerate the active cobalt-hydride species, which is the rate-determining step of the catalytic cycle. Such reaction mechanism resembles the Mukaiyama-type hydration of olefins, which uses typically Co(acac)₂ as the pre-catalyst and leads to alcohols, but with a change here in the step that controls the chemoselectivity towards the ketone product.[22]

Taking the above-stated mechanistic information into consideration, DFT calculations were performed in order to qualitatively understand the regio- (Markovnikov) and chemo-selectivity (ketone formation) as well as the oxidation state at cobalt in the catalytic cycle once the cobalt-
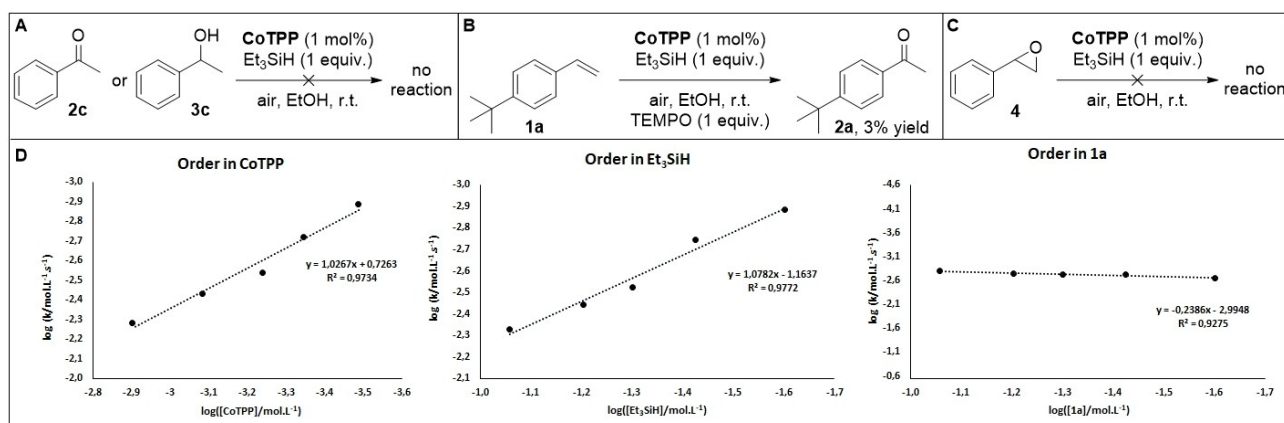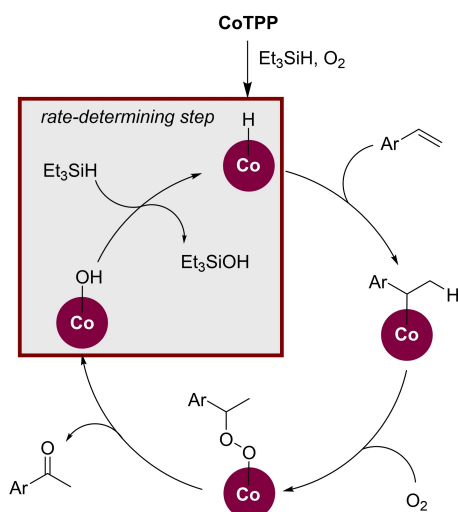

Figure 2. Selected control experiments for mechanistic understanding (**A–C**, top) and detailed kinetic study for identifying the order of reagents for the Wacker-type oxidation of *para-tert*-butylstyrene **1a** (**D**, bottom).

Scheme 2. Postulated, simplified reaction mechanism for the **CoTPP**-catalyzed oxidation of olefins to ketones in the presence of dioxygen and Et₃SiH (for the sake of clarity, the tetraphenylporhpyrinato ligand around the cobalt center is displayed as a purple circle).

hydride is formed (see Supporting Information for more details). As a model substrate, unfunctionalized styrene was employed and the phenyl groups in **CoTPP** were not considered for efficiency reasons (Figure 3). Based on the above reported observations and analogous to previous iron-porphyrin hydride species that catalyze silane-mediated oxidation reactions of olefins,[10,11] the catalytic cycle was considered to begin with Co(III)porphyrin-hydride species **A** originating from the oxidation of Co(II)porphyrin in the presence of hydrosilane. The olefin substrate can approach

to the hydride of **A** from the same face resulting in the formation of the pre-complex **B** ($\Delta G°_{298K} = -2.3$ kcal mol⁻¹). Then, the cobalt-coordinated hydrogen atom is transferred to the terminal carbon of the styrene substrate with a low barrier of $\Delta G^{\ddagger} = +2.6$ kcal mol⁻¹ to form the Markovnikov closed contact radical pair **C** (**B**→**C**, $\Delta G°_{298K} = -6.0$ kcal mol⁻¹). It is noticeable that the formation of the anti-Markovnikov biradical **C′** (**B**→**C′**, $\Delta G°_{298K} = +15.9$ kcal mol⁻¹) is energetically uphill explaining the observed regioselectivity of the reaction (see Supporting Information for more details). Recombination of the radical pair **C**→**D** yields -12.7 kcal mol⁻¹ to form the alkyl adduct **D**. Alternatively, in the presence of molecular dioxygen, O₂ can bind easily ($\Delta G°_{298K} = -5.5$ kcal mol⁻¹) on the back side of the carbon radical part of the radical pair (**C**) to form an alkyl peroxo-cobalt(II) radical pair (**E**). Rotation around the (Ph)C–C bond allows combination of the O radical with the Co(II) moiety under Co–O bond formation to build the peroxo Co(III) complex **F** ($\Delta G°_{298K} = -14.4$ kcal mol⁻¹). In other words, **D** easily undergoes homolysis followed by interception of the alkyl radical by O₂ towards formation of the intermediate **F**. Formation of the π-π adduct between acetophenone product and the Co(III)-hydroxy complex (**G**, $\Delta G°_{298K} = -52.0$ kcal mol⁻¹) may then proceed via a synchronous H-transfer/O–O splitting pathway with an activation barrier of moderate $\Delta G^{\ddagger} = +24.5$ kcal mol⁻¹. Release of the ketone product and reaction of Co(III)-hydroxy complex with the Et₃SiH silane rebuilds the Co(III) hydride (**A**), which is the rate-determining step of the mechanism in agreement with the kinetic studies (see above). In fact, the oxidation of the silane is found theoretically to have the highest barrier of the whole process. Attack of the silicon by the cobalt bound hydroxide
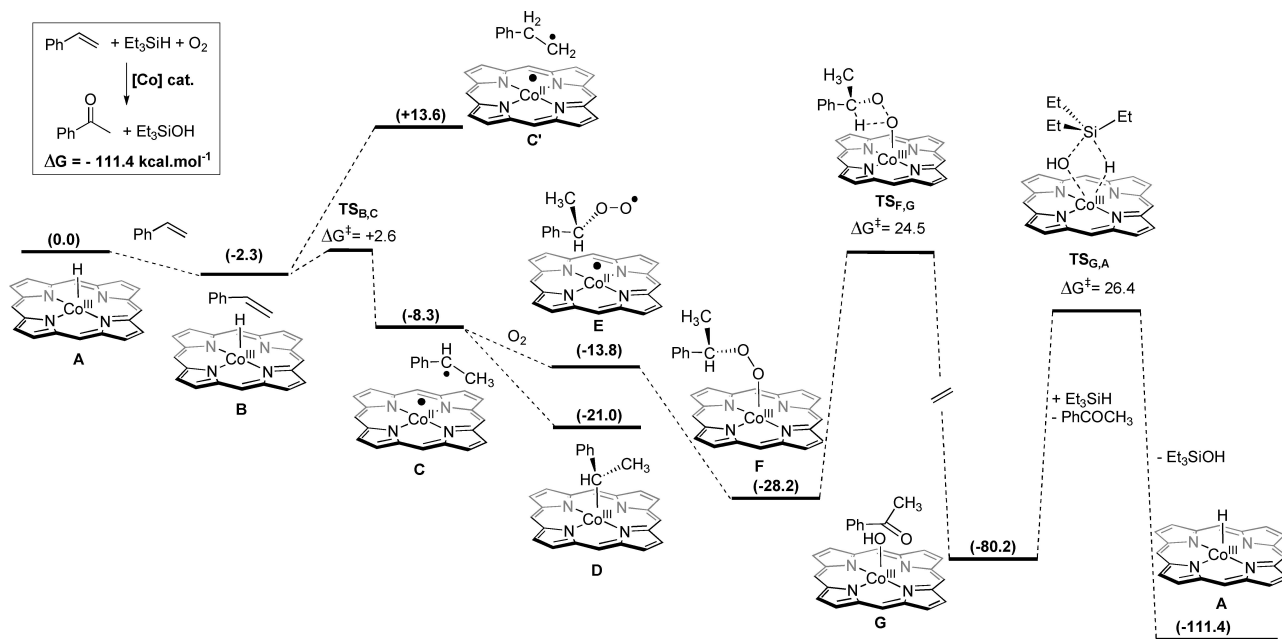

Figure 3. Reaction mechanism for the cobalt-catalyzed Markovnikov selective formation of ketone from styrene according to DFT calculations. Values in brackets correspond to the free energies ($\Delta G°_{298K}$) in kcal mol⁻¹.

($d_{Si-O} = 1.924$ Å) with simultaneous transfer of the hydride ($d_{Co-H} = 1.590$ Å) via a five coordinated silicate-like structure (**TS$_{G,A}$**, Figure 3) proceeds with a free energy barrier of 26.4 kcal mol^{-1}. This gas-phase value might be a bit smaller in solution. Also, the reaction might then proceed in a more stepwise manner, which is hard to simulate due to charge separations in the gas phase. Nevertheless, this catalyst regeneration step closes the catalytic cycle and adds another -31.2 kcal mol^{-1} to the total driving force, thus resulting in a total amount of -111.4 kcal mol^{-1} Gibbs free energy for the aerobic oxidation of styrene with Et$_3$SiH affording acetophenone and Et$_3$SiOH under cobalt catalysis (frame, Figure 3).[28] Moreover, we detected formation of almost stoichiometric amounts of Et$_3$SiOEt and traces of Et$_3$SiOH at the end of the catalysis. This observation is reminiscent of those observed mechanistically for the iron-catalyzed Wacker-type oxidation of olefins involving a postulated mechanism similar to this one.[10,11] Additionally, to qualitatively evaluate whether the reactive Co–H species will react preferentially with the olefin substrate or with the oxygen, we performed the catalysis at different concentrations. For instance, a 4-fold more diluted reaction behaved equal to the optimal conditions whereas a 2-fold concentrated one led to 65 % conversion with the same selectivity (Table S2 in the Supporting Information). These results indirectly indicate that the amount of oxygen solubilized in the ethanol solution during the reaction is relevant. On the other hand, performing the reaction with one bar of pure O$_2$ instead of air led to the same reactivity as the optimal conditions (Table S1 in the Supporting Information). Consequently, in this case of study, the Co–H species prefers to react with the olefin substrate rather than with the dioxygen, further supporting the DFT-computed mechanism.

Alternatively, because ethanol is used as the solvent for the catalysis, we anticipated that ethanol could possibly facilitate the proton transfer in the chemo-determining step **F→G** (Figure 4). Indeed, a hydrogen bond can be formed between EtOH and the peroxo cobalt complex, which is only slightly exergonic by $+2.3$ kcal mol^{-1} (**F′**). Via a six membered transition state, the acetophenone is formed readily together with the hydroxo-cobalt(III) complex (**G**) with a moderate barrier $\Delta G^{\ddagger}$ of 19.3 kcal mol^{-1}. A single ethanol molecule involved in the transition state significantly decreases the energy barrier by 5.2 kcal mol^{-1} upon comparing **TS$_{F,G}$** (Figure 3) and **TS$_{F′,G}$** (Figure 4). Presumably, a more extended hydrogen bonding network would result in an even lower barrier. The hydroxo-cobalt(III) complex (**G**) can then easily be reduced to the hydride by the silane. Such hydrogen bonding effect was indirectly evidenced by the complete lack of reactivity encountered when the catalysis was performed in a non-polar solvent such as toluene that is not able to be involved in hydrogen bonding (Table S1 in the Supporting Information). In fact, it cannot be ruled out that in non-alcoholic solvents the step from species **F** to **G** might become the rate-determining step, with a much higher barrier than **G** to **A** in absence of a protic solvent to stabilize the transition state. Note that protic solvents such as hexafluoroisopropanol (p$K_a = 9$), water (p$K_a = 14$), and isopropanol (p$K_a = 16.5$) led to lower conversions of olefin **1a**:
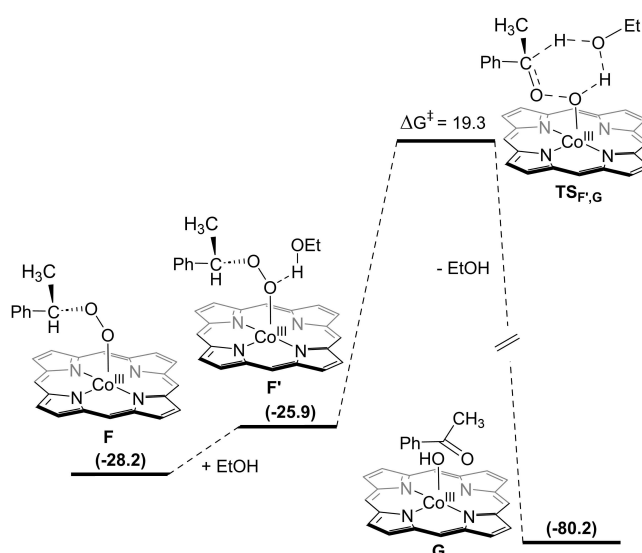

Figure 4. DFT-computed pathway for the chemo-determining step from **F** to **G** considering one molecule of ethanol. Values in brackets correspond to the free energies (ΔG°_{298K}) in kcal mol^{-1}.

15 %, 34 % and 68 %, respectively (Table S1 in the Supporting Information). The reactivity of **CoTPP** in the oxidation of the olefin **1a** using methanol (p$K_a = 15.5$) as the solvent compared well with that obtained using ethanol (p$K_a = 15.9$) albeit the formation of the alcohol side-product **3a** raised to 12 % (Table S1 in the Supporting Information). As such, there is a very narrow window of operational pK_a for the success of the transformation thanks to the hydrogen bonding effect. Moreover, there was a negligible kinetic isotope effect and no deuterium incorporation in **2a** was observed upon performing the catalysis with deuterated ethanol, further ruling out that the **F→G** step is the rate-determining one (Figure S2 in the Supporting Information).

Conclusion

In summary, we have demonstrated that the readily available **CoTPP** complex displays an unprecedented activity and selectivity towards ketone formation when applied in the Wacker-type oxidation of styrene derivatives. Thanks to the Et$_3$SiH reagent (source of hydrides) operating under air (source of oxygen) at room temperature, the reactions delivered up to 99 % ketone formation for the best cases with alcohol side-products typically below 5 %, which outperforms previous first row transition metal catalysts.[10,11] The catalysis is compatible with a number of relevant functional groups and performed well also with internal aromatic olefins and with electron-withdrawing allyl ones. A combination of control experiments, UV/Vis, kinetics and DFT calculations shed light on the reaction mechanism in which radical species are involved in a Co(III)/Co(II) manifold catalytic cycle where the formation of Co–H species is the rate-determining step. Of particular relevance is the ability of the ethanol solvent to participate in the

catalytic cycle by decreasing the energy associated to the transition state of the chemo-determining step via an unprecedented hydrogen bonding network. Whether ethanol plays the same role in similar iron-porphyrin catalysis as well as many first-row metal catalysis in general,[10–15] including important olefin functionalizations,[13a,29] might be of interest for the further design of more powerful first-row metal-based catalysts. As such, this contribution highlights the unique role of the solvent within the secondary coordination sphere of the catalyst,[30] which is of paramount importance for the future development of sustainable catalysts as remote events far from the active site can play a pivotal role for controlling catalyst reactivity as enzymes do.[31] Future efforts will be devoted to the design of superior cobalt catalysts to enlarge the substrate scope of such transformation.

Supporting Information

Experimental procedures, and compound characterization data as well as computational details that support the findings of this study are available in the online version of this paper in the accompanying Supporting Information.

Acknowledgements

Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: cobalt · ketone · olefin · oxidation · porphyrin

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