Catalysis

Reaction Pathways and Redox States in α-Selective Cobalt-Catalyzed Hydroborations of Alkynes

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Abstract: Cobalt(II) alkyl complexes supported by a mono-anionic NNN pincer ligand are pre-catalysts for the regioselective hydroboronation of terminal alkynes, yielding the Markovnikov products with α:β-(E) ratios of up to 97:3. A cobalt(II) hydride and a cobalt(II) vinyl complex appear to determine the main reaction pathway. In a background reaction the highly reactive hydrido species specifically converts to a coordinatively unsaturated cobalt(I) complex which was found to re-enter the main catalytic cycle.

The burgeoning field of base metal catalysis has been stimulated by novel reactivity patterns and their potential in catalytic transformations.[2] Compared to noble metals, the propensity of cobalt compounds to engage in one-electron redox processes has been found as a distinctive difference, such as the tendency of cobalt(II) alkyl or hydride complexes to be readily convertible into the corresponding cobalt(I) complexes.[3] Cobalt(II) hydrides[4,5]—often postulated as transient species—are thought to be key intermediates in the functionalization of C–C multiple bonds as well as hydride transfer reactions.[6] On the other hand, coordinately unsaturated cobalt(I) complexes have been efficiently employed in small molecule or inert bond activations[3b,7] as well as catalytic transformations.[6]

Cobalt-mediated hydrometallation reactions provide a convenient access to synthetically useful reagents,[3a,9] and in particular the catalytic hydroboration of alkynes allows for the synthesis of alkenyl boronates and related species.[10] In case of terminal alkynes, the potential formation of three different isomers with either α-, β-(Z)- or β-(E)-configuration necessitates control of regio- and stereoselectivity. Chirik and co-workers established bis(imino)pyridine cobalt complexes as effective catalysts for the stereodivergent hydroboration of terminal alkynes to (Z)-configured alkenyl boronates, which stem from a syn-hydrometallation step of an alkynyl boronate intermediate.[11] For the cobalt-mediated synthesis of (E)-alkenyl boronates, both an isolated α-dimine cobalt(II) hydride complex[5] and a bench-stable cobalt(II) coordination polymer[12] have been recently reported.

The α-selective hydroboration of terminal alkynes to produce α-borylated alkenes provides access to valuable reagents for the synthesis of 1,1b-disubstituted, terminal alkenes, a common structural motif in a range of bioactive compounds.[13] Current synthetic methods include a Ni-catalyzed hydroalumination procedure,[14] NHC-Cu-mediated hydroboration reactions with diboron reagents in the presence of tert-butoxide salts,[13,15] as well as a Pd-catalyzed hydrometallation approach,[16] requiring elevated reaction temperatures of 80°C. In view of the structural relevance of α-borylated, terminal alkenes, the need for further synthetic strategies under mild conditions seems apparent.

Based on our previous work on boxmi[7] complexes in catalytic transformations,[16] we chose the synthesis of alkyl complexes RboxmiCoCH2SiMe3 (1) as starting point for our investigation (Scheme 1).

Treating dialkyl precursor (tmeda)Co(CH2SiMe3)2 (tmeda = N,N,N’,N’-tetramethylethylenediamine) with equimolar amounts of protio-ligand Rboxmi-H provided facile access to cobalt(II) high-spin complexes 1 in quantitative yields. The molecular structure of the four-coordinate distorted tetrahedral precatalyst 1b was established by X-Ray diffraction, with all Co-N and Co-C23 bond lengths being in good agreement with similar 3d metal boxmi high-spin complexes.[16b,19] The cobalt complexes 1 were found to be

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Scheme 1. Left: Synthesis of cobalt(II) alkyl complexes 1. Right: Molecular structure of 1b (boxmiCoCH2SiMe3, 1b) in the solid-state. Displacement ellipsoids set at 30% probability level, hydrogen atoms omitted for clarity, only one of two independent molecules shown. Selected bond lengths [Å] and angles [°], values for the second independent molecule are given in square brackets: Co–C23 1.963(7) [1.981(7)], Co–N1 1.905(6) [1.891(6)], Co–N2 1.963(6) [1.947(5)], Co–N3 1.929(6) [1.917(6)], N2-Co-C23 134.5(3) [130.7(3)], N1-Co-N3 135.3(2) [160.1(2)].

1a (R = H, R’ = Ph)
1b (R = H, R’ = Pr)
suitable precatalysts for the selective hydroboration of alkynes. In a first assay, we reacted 1-ethynyl-4-fluorobenzene (2a) with two equivalents pinacolborane (HBPin) in the presence of 2.5 mol% $^{11}$PboxmiCoCH$_2$SiMe$_3$ (1a), finding the selective formation of mono-borylated products 3a in a remarkable ratio of $\alpha$:3a:$\beta$-($E$)-3a = 8:1 (Figure 1, top).

Notably, the resulting synthetically useful, branched regioisomer $\alpha$-3a as main product is in stark contrast to previously reported procedures for cobalt-catalyzed hydroborations, all of which favor the linear anti-Markovnikov products with ($E$)-[13] or ($Z$)-selectivity.[11,12] As monitored by in situ $^{19}$F NMR spectroscopy (Figure 1, bottom), the $c$-$T$ profile for the hydroboration by alkyl complex 1a features a distinct sigmoidal course, indicating a significant induction period prior to the reduction process.

Upon treatment of the alkyl complexes 1 with an excess of pinacolborane, slow consumption of HBPin and the emergence of the O-bond metathesis product Me$_3$SiCH$_2$BPin were detected. From a mass balance point of view, the rise of the latter implies the presence of a cobalt hydride complex (Scheme 2, middle), the instability of which precluded its isolation.[21] However, the reaction of $^{11}$PboxmiCoCH$_2$SiMe$_3$ with pinacolborane in the presence of an internal alkyne, namely 1-phenyl-1-propyne, resulted in the generation of vinyl complex 4 (Scheme 2, top) which confirms the in situ generation of a cobalt hydride complex. More importantly, the reaction outcome also renders this insertion reaction a probable elementary step in the catalytic cycle for the cobalt-catalyzed hydroboration. Although alkyne insertions into a cobalt hydride bond are frequently postulated for various transformations,[20] the isolation of catalytically relevant cobalt(II) vinyl complexes remains scarce. This is in stark contrast to the fact that the fundamental feasibility of this transformation has long been known, in fact also for terminal alkynes.[21] Notably, a Markovnikov-selective hydrometallation step was very recently proposed to facilitate the cobalt-catalyzed sequential hydrogenation/hydrohydrodiation of terminal alkynes.[22] There was no evidence for the formation of a cobalt boryl species or the occurrence of an oxidative addition step as discussed for similar catalysts.[11,23]

The $d^6$ low-spin vinyl complex 4 adopts a distorted square-planar coordination sphere with all bond metrics being in the expected range[19] (Figure 2, left). In solution, well-resolved paramagnetic $^1$H and $^{13}$C NMR spectra with comparatively small shift dispersions are consistent with the $C_2$ symmetry of the pincer complex in agreement with other square-planar cobalt(II) compounds (SI).[24]

All attempts to isolate the hydrido species failed, due to its selective but irreversible transformation, formally resulting from H$_2$ elimination, to a coordinatively unsaturated cobalt(I) complex 5 (Scheme 2, bottom).[5,6]

The molecular structure of cobalt(I) complex 5 was determined by X-ray diffraction to be dimeric in the solid-state (Figure 2, right). With the cobalt centers positioned slightly above the boxmi ligand plane, additional weak interactions of the metal to a $C$-$C$ double bond of the neighboring boxmi ligand are observed ($d = 2.029$ Å and 2.047 Å) and give rise to a distorted tetrahedral coordination sphere around the cobalt centers. With T-shaped geometries being scarce,[7c,26] this form of dimerization constitutes a hitherto not observed stabilization mode for this type of complex, as the majority of coordinatively unsaturated cobalt(I) compounds is further stabilized by additional arene,[7b,26] carbon monoxide,[34] or nitrogen ligands[35] or undergo ligand rearrangements upon dimerization.[27]

The magnetic moment of complex 5 was found to be $\mu_{\text{eff}} = 5.07$ $\mu_B$ at room temperature in solution, indicating a moderate antiferromagnetic coupling between the two cobalt centers, Accordingly, an antiferromagnetic coupling constant of $J_{\text{CC}} = -54$ cm$^{-1}$ was derived from solid-state (SQUID) experiments (see SI). A strong temperature-dependence of the paramagnetic $^1$H NMR spectra was observed, resulting in a non-Curie and coalescence behavior. As a consequence, the signal number is diminished from 32 in the low temperature limit, which is consistent with a nonsymmetric dimer, to eight at elevated temperatures which can be attributed to a reversible dynamic dissociation giving the monomeric form dominating at elevated temperatures (see SI).

Apart from the absence or presence of an internal alkyne, both vinyl species 4 and the cobalt(I) species 5 were prepared...
The feasibility of this elementary reaction within the given context and its importance for the catalytic process (Scheme 3c).

Based on these findings, a catalytic cycle consisting of reversible alkyne insertion into a cobalt(II) hydride and subsequent product release via $\pi$-bond metathesis is proposed for the cobalt-catalyzed hydroboration of alkynes (Scheme 4).

To probe the synthetic potential of the cobalt-catalyzed hydroboration of terminal alkynes a screening of differently substituted boxmi ligands and reaction conditions established the phenyl-substituted complex 1a as the most efficient pre-catalyst, allowing catalyst loadings as low as 0.5 mol% for full conversion within 6 h at room temperature (Table 1, for details see SI).

With these optimized conditions in hand, we explored the applicability of the cobalt-catalyzed method and subjected a variety of alkynes to the Markovnikov-selective hydroboration with the phenyl-substituted alkyl complex 1a (Scheme 5, top). Both electron-withdrawing substituents (3a,c,d) and the presence of ortho-substituents (3h,l,m) appeared to be beneficial for high $\alpha/\beta$ ratios (up to 97:3), thereby matching the selectivities obtained from previous approaches.[15] Regarding terminal alky alkenes, cyclohexyl derivative 2n turned out to be detrimental to a satisfactory enrichment of the $\alpha$-isomer, whereas only sluggish hydroboration was observed for the trimethylsilyl substituted alkyne 2o. In the case of ester, cyan, or nitro groups being attached to an aryl alkyne, slow conversions of the substrate were accompanied by the formation of insep-
arable side products (see SI), preventing the pure isolation of the target compounds. As mentioned above, internal alkynes (2p) were also tolerated in this cobalt-catalyzed hydroboration protocol, albeit with inverted α:β selectivity. In addition, compound α-3p was obtained as the major product from the catalytic conversion of 3-phenyl-1-propyne with pinacolborane, demonstrating the tendency of propargylic substrates to form the respective internal alkene derivatives (see SI for details).

The facile access to the respective α-isomers in the case of aryl alkynes prompted us to apply this cobalt-based method in the synthesis of a biologically active compound with the given structural core motif (Scheme 5, bottom). Reacting the readily accessible alkyne 2q in the presence of precatalyst 1a with pinacolborane yielded the borylated alkene 3q in a selectivity of 97.3:3, allowing for the isolation of the 1,1-disubstituted alkene α-3q in 46% yield. Following a literature procedure,[19] this compound can be converted in two steps into Bexarotene, a pharmaceutical for the treatment of cutaneous T-cell lymphomas[20].

In conclusion, the boxmi-cobalt(II) alkyl complexes effectively catalyze the Markovnikov-selective hydroboration of terminal alkynes, furnishing the respective branched aryl alkynyl boronate esters in moderate to good yields (α:β ratio up to 97.3). The facile accessibility of a coordinatively unsaturated cobalt(I) compound demonstrates the marked one-electron redox chemistry of 3d metal complexes, an off-cycle reactivity in the case at hand but opening up new perspectives for future applications in homogeneous catalysis.

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Conflict of interest

The authors declare no conflict of interest.

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