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Tandem C(sp^2)–OMe Activation/C(sp^2)–C(sp^2) Coupling in Early Transition-Metal Complexes: Aromatic C–O Activation beyond Late Transition Metals

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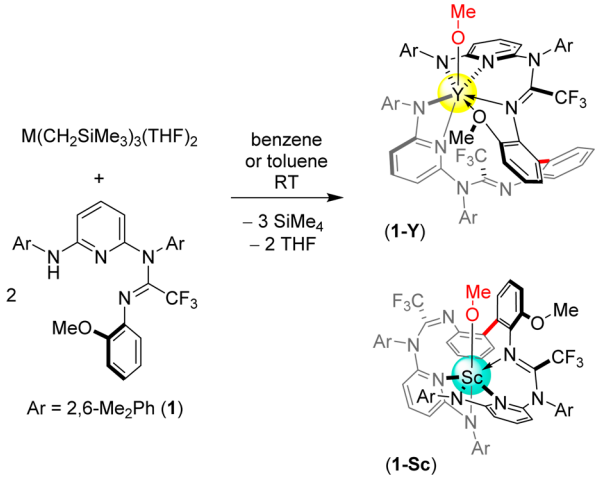
Supporting Information

ABSTRACT: We report on combined structural, kinetic, and computational studies unraveling the mechanism of a unique, highly selective intramolecular C(sp^2)–OMe cleavage/C(sp^2)–C(sp^2) coupling tandem reaction in group 3 metal (Y and Sc) complexes of amidine-amidopyridinate ligands. The latter process represents a rare stoichiometric model of the nonredox cleavage of inert C(sp^2)–O bonds relevant to cross-coupling reactions of aromatic ethers catalyzed by late transition metals.

Selective C–O bond cleavage constitutes a pivotal step in modern, challenging metal-catalyzed processes such as cross-couplings[1] and hydrogenation[2] of aromatic ethers. Thermodynamically more stable (BDE_{298}(C(aryl)–OMe bond) = 101 kcal·mol^{-1})[3] than aryl halides (BDE_{298}(C(aryl)–X bonds, where X = I, Br, Cl) = 67–97 kcal·mol^{-1}), aromatic ethers are usually chemically inert and do not undergo regular activation protocols. Nonetheless, a number of C–O bond cleavage reactions have been reported recently.[4] Also, in connection with recent progress of Kumada–Tamao–Corriu[1] and related cross-coupling,[5] several late transition-metal-based (typically Ni and Rh)[6] systems have been shown to insert competently into C(sp^2)–O bonds following regular oxidative addition. Yet, the actual mechanism of C(sp^2)–O bond activation–cleavage is still debated. Thus, cleavage of C(sp^2)–O bonds in Ni-catalyzed reactions that does not involve an oxidative addition step has been proposed.[7] On the other hand, to our knowledge, there is no example of selective cleavage of C(sp^2)–O bonds of aromatic ethers with complexes of early transition metals, despite their high oxophilic character.[8,9] Herein, we report such an unprecedented reactivity in group 3 metal (Y and Sc) complexes of amidine-aminopyridinate ligand systems[10] that are methoxy substituted at the imino-phenyl group.

Treatment of Y(CH$_2$SiMe$_3$)$_3$(THF)$_2$[11] with 1 equiv of proligand **1** at room temperature in benzene or toluene resulted in the unexpected formation of the methoxy-yttrium complex **1-Y** that incorporates a new dianionic biphenyl-centered ligand, while half of the yttrium precursor remained intact. Accordingly, a 2:1 reaction between **1** and Y(CH$_2$SiMe$_3$)$_3$(THF)$_2$ yielded quantitatively **1-Y** (Scheme 1). The room-temperature ^{1}H, ^{13}C{^{1}H}, and ^{19}F{^{1}H} NMR spectra of **1-Y** were all in agreement

Scheme 1. Formation of Complexes 1-M (M = Y, Sc) from 1 and M(CH$_2$SiMe$_3$)$_3$(THF)$_2$[a]



[a]Activated MeO groups and the C–C bond formed are shown in red.

with a C_1-symmetric structure (see Figures S10–S12, respectively). In particular, the ^{19}F{^{1}H} NMR spectrum of **1-Y** displayed two resonances of equal intensities from the two nonequivalent CF$_3$ groups. Similar reactions between **1** and Sc(CH$_2$SiMe$_3$)$_3$(THF)$_2$ (at either 1:1 or 2:1 ratios) resulted in the formation of the analogous **1-Sc** as major product (~60% yield), along with three other minor species (most likely isomers of **1-Sc**, *vide infra*).[12]

The molecular structures of complexes **1-Y** and **1-Sc** in the solid state are shown in Figures 1 and 2, respectively, and the structure refinement data are given in Table S1. Due to differences in the ionic radii of these metals (Y^{3+} (CN = 6): 0.90 Å vs Sc^{3+} (CN = 6): 0.75 Å),[13] these complexes feature dissimilar geometries and organizations of the newly formed biphenyl-centered ligands about the metal centers. In **1-Y**, the pendant (unactivated) OMe group of the ligand is coordinated to yttrium together with five nitrogen atoms of the two amidopyridinate and one amidine fragments and a methoxy

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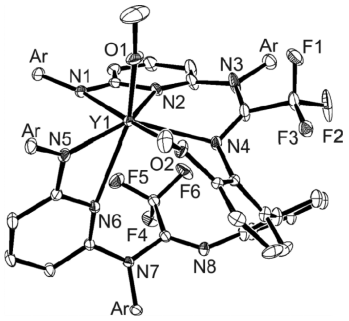


Figure 1. Molecular solid-state structure of **1-Y** (all hydrogen atoms and the four 2,6-dimethyl-phenyl groups (Ar) are omitted for clarity; thermal ellipsoids drawn at the 50% probability). Selected bond distances (Å) and angles (deg): Y(1)−N(1), 2.421(2); Y(1)−N(2), 2.374(3); Y(1)−N(4), 2.647(2); Y(1)−N(5), 2.337(2); Y(1)−N(6), 2.681(2); Y(1)−O(1), 2.022(2); Y(1)−O(2), 2.465(19); N(1)−Y(1)−O(1), 96.89(8); N(5)−Y(1)−N(2), 149.09(8).

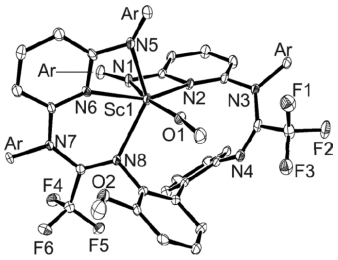
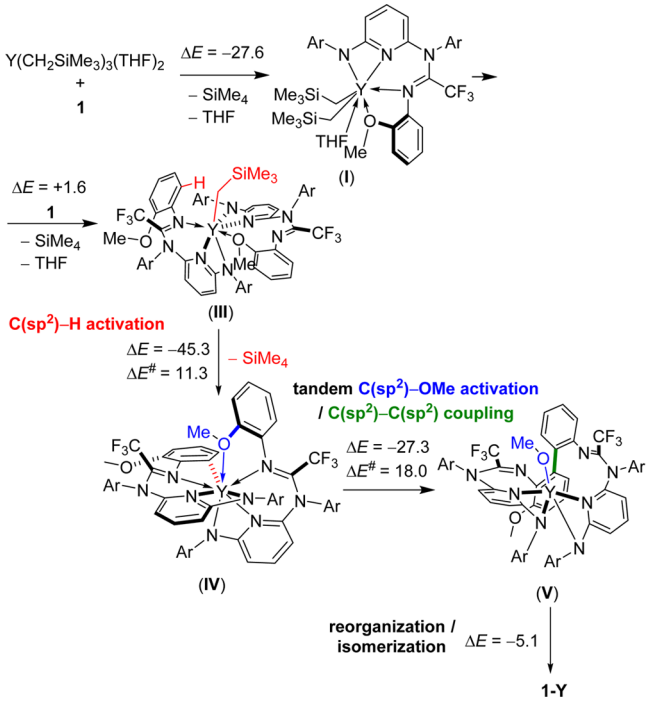


Figure 2. Molecular solid-state structure of **1-Sc**·(benzene) (all hydrogen atoms and the four 2,6-dimethyl-phenyl groups (Ar) are omitted for clarity; thermal ellipsoids drawn at the 50% probability). Selected bond distances (Å) and angles (deg): Sc(1)−N(1), 2.258(5); Sc(1)−N(2), 2.281(5); Sc(1)−N(5), 2.223(5); Sc(1)−N(6), 2.175(4); Sc(1)−N(8), 2.369(5); Sc(1)−O(1), 1.873(4); N(1)−Sc(1)−O(1), 160.24(18); N(5)−Sc(1)−N(2), 107.38(18).

group, thus building up the formal coordination number to 7. In contrast, in the six-coordinate analogue **1-Sc**, the pendant OMe group of the ligand lays out of the coordination sphere of the metal. The corresponding Y(1)−N(ligand) and Y(1)−O(methoxide) bond distances in **1-Y** are longer than those in **1-Sc** by 0.10−0.17 Å, which is also in line with the ionic radius of these metals.[13] In **1-Y**, the Y(1)−N(1), Y(1)−N(2), and Y(1)−N(5) bond distances (2.421(2), 2.374(3), and 2.337(2) Å, respectively) are in the same range of the Y−N bonds (2.343−2.491 Å) observed in related yttrium complexes of amidine-amidopyridinate ligands,[10] while the Y(1)−N(4) and Y(1)−N(6) bond distances (2.647(2) and 2.681(2) Å, respectively) are somewhat longer. This latter fact could stem from a particular steric situation about the seven-coordinate yttrium center surrounded by a bulky and sterically congested ligand. The covalent Y(1)−O(1) and the coordinate Y(1)−O(2) bonds in **1-Y** (2.022(2) and 2.465(19) Å, respectively) compare well with those found in related yttrium complexes of N-based ligands (2.067−2.247 and 2.385−2.401 Å, respectively).[10,14] In **1-Sc**, the corresponding Sc(1)−N(ligand) and Sc(1)−O(OMe) bond distances (2.175(4)−2.369(5) and 1.873(4) Å, respectively) are in the normal range or very close to those (2.028−2.389 and 1.882−2.100 Å, respectively) reported for scandium complexes of N-based ligands.[15]

Intrigued by the mechanism of this process, we conducted additional experimental and theoretical studies. First, a possible mechanism for the formation of **1-Y** was assessed computationally using DFT methods (see the Supporting Information (SI) for details). Of several computed pathways (Figure S23), the most plausible one, based on thermodynamic and kinetic grounds, is presented in Scheme 2. The highly exothermic and

Scheme 2. Simplified Representation of the Most Favored Computed Pathway for the Formation of 1-Y from 1 and $Y(CH_2SiMe_3)_3(THF)_2$ (Ar = 2,6-$Me_2C_6H_3$)[a]



[a]Energy values (E + ZPE) are given in kcal·mol^{-1}. For the more detailed computed mechanism, see the SI.

low-energy-demanding formation of the cyclometalated intermediate **IV** from the parent monoalkyl bis(ligand) **III** via intramolecular C(sp^2)−H activation reaction is anticipated to occur under mild conditions (e.g., at relatively low temperature). The transition state for the subsequent intramolecular tandem C(sp^2)−OMe activation/C(sp^2)−C(sp^2) coupling process was located (Figure 3). An activation barrier of 18 kcal·mol^{-1} (with respect to **IV**) was calculated in this case, suggesting that this

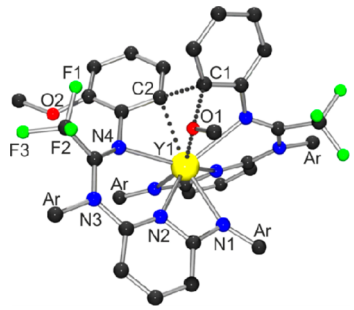


Figure 3. Computed structure of the four-center $TS_{IV\rightarrow V}$ (all hydrogen atoms and the four 2,6-dimethyl-phenyl groups (Ar) are omitted for clarity). Selected bond distances (Å) and angles (deg): C(1)−C(2), 2.057; C(2)−Y(1), 2.396; O(1)−Y(1), 2.459; O(1)−C(1), 1.700; C(2)−Y(1)−O(1), 64.05; Y(1)−C(2)−C(1), 85.76; O(1)−C(1)−C(2), 88.21.

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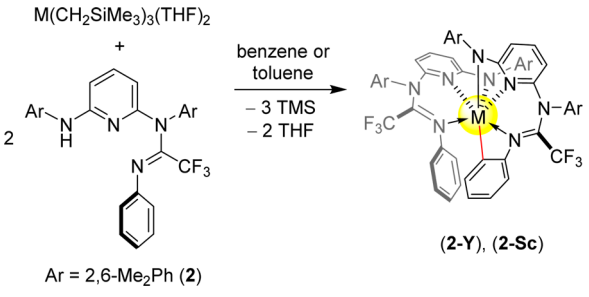
process should be relatively slow and could be monitored by NMR spectroscopy.

Monitoring by ^{1}H NMR spectroscopy the 2:1 reaction between **1** and $Y(CH_2SiMe_3)_3(THF)_2$ in toluene-d_8 in the −50 to −30 °C range indicated rapid consumption of the metal precursor (disappearance of the signals from the CH_2 and $SiMe_3$ groups) and concomitant elimination of 3 equiv of $SiMe_4$. Yet, the nature of the metal-containing species formed at this stage could not be established due to broadening and overlapping of resonances in this temperature range.

When the temperature of the reaction mixture was raised up to −10 °C, only five sets of resonances belonging to **1-Y** and four other species became observable in the $^{19}F\{^{1}H\}$ NMR spectra. After ∼20 h at this temperature, the signals from the four intermediates completely disappeared, and only the signals from **1-Y** remained both in the ^{1}H and $^{19}F\{^{1}H\}$ NMR spectra, indicating full and selective conversion. Kinetic monitoring of this transformation process of the four intermediates into **1-Y** by $^{19}F\{^{1}H\}$ NMR spectroscopy (Figure S13), as a function of $[Y]_0$ and temperature, allowed estimation of the pseudo-first-order rate constants and corresponding activation parameters (Table S2). Although the obtained kinetic data did not allow either unequivocal matching the kinetic steps with the calculated mechanism or establishing the exact nature of the intermediates that preceded the formation of **1-Y**, several key observations should be highlighted: (a) the independence of the determined rate constants from $[Y]_0$ concentration (Figure S29) and the near-zero values of the activation entropy $\Delta S^{\ddagger}$ are both indicative of intramolecular processes;[16] (b) the experimentally determined activation enthalpy $\Delta H^{\ddagger}$ values of 19.5(7)−21.7(1) kcal·mol^{-1} (Figure S30) for the two consecutive reactions leading straight to the formation of **1-Y** are very close to the computed $\Delta E^{\ddagger}$ value (18 kcal·mol^{-1}) for the barrier of the intramolecular $C(sp^2)$−OMe activation/$C(sp^2)$−$C(sp^2)$ coupling tandem reaction (**IV** → **V**, Scheme 2).

To get a better clue about the nature and stability of the actual intermediates involved in the formation of **1-Y**, we synthesized the MeO-free proligand **2** and investigated its reactivity toward $M(CH_2SiMe_3)_3(THF)_2$ (M = Y, Sc). The corresponding reactions, monitored by ^{1}H and $^{19}F\{^{1}H\}$ NMR spectroscopy in toluene-d_8 in the −50 to −10 °C temperature range, proceeded very rapidly and cleanly to afford the cyclometalated isostructural complexes **2-Y** and **2-Sc** (Scheme 3; see Figure S19 for **2-Y**),[17] respectively, with concomitant release of 3 equiv of $SiMe_4$. Both compounds were isolated and characterized by NMR spectroscopy,[18] X-ray crystallography (Figures S2 and S3, respectively), and combustion analysis. Those compounds, which are direct structural analogues of the mixed-ligand intermediate **IV** (Scheme 2), did not undergo further reactivity; i.e., they are stable in aromatic hydrocarbon solutions up to 100 °C for hours.

Scheme 3. Formation of Cyclometalated Complexes 2-M (M = Y, Sc), Analogues of IV, from 2 and $M(CH_2SiMe_3)_3(THF)_2$



These observations are in agreement with the proposed intermediacy of the mixed-ligand cyclometalated complex of type **IV** in the formation of **1-Y** and **1-Sc**. The presence of the MeO substituent in the imino-phenyl part of the ligand apparently plays a crucial role for enabling further reactivity of the system and eventually prompting the $C(sp^2)$−OMe activation/$C(sp^2)$−$C(sp^2)$ coupling step. More, it appears that for complex **1-Sc**, which incorporates a smaller metal ion and is therefore more susceptible to steric environment changes, the isomerization of intermediates of type **V** into the final product may feature a substantial activation barrier; the latter hypothesis is in line with the experimental observation of several products (isomers)[12] in the reaction of **1** with $Sc(CH_2SiMe_3)_3(THF)_2$ yielding **1-Sc** (*vide supra*).

In conclusion, we have established an original multistep mechanism for coupling of the amidine-amidopyridinate ligand in the coordination sphere of early transition metals, through a series of selective cyclometalative $C(sp^2)$−H bond activation steps and a so far unprecedented tandem $C(sp^2)$−OMe activation/$C(sp^2)$−$C(sp^2)$ coupling process that operates via a corresponding highly ordered transition state. These findings point out that other mechanisms of $C(sp^2)$−OMe bond cleavage beyond those affecting the oxidation state of the metal center may operate under appropriate conditions.[1b] In this regard, alternative reaction pathways offering kinetically favorable concerted C−O bond/coupling steps could be sought and potentially implemented in transition-metal-catalyzed transformations of aromatic alkyl ethers.[19] Apparently, there is in the system reported herein an intimate interplay of electronic and steric effects of the substituents on the ligand backbone. Future work will be aimed at analyzing comprehensively the role of these substituents (alkoxy, imido, pyridine, aromatic rings, CF_3-group) to understand how exactly this transformation is executed as well as the prospective impact of this methodology.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b01877.

Synthetic procedures, NMR characterization data, details of DFT computations and kinetic data (PDF)

Crystallographic data (CIF)

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Notes

The authors declare no competing financial interest.

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(16) The following additional experiments were carried out to evidence that conditions did not affect the fate of the reaction: (a) the synthesis of **1-Y** from **1** and $Y(CH_2C_6H_4(o\text{-}NMe_2))_3$ in toluene-d_8 under regular conditions; (b) synthesis of **1-Y** from **1** and $Y(CH_2SiMe_3)_3(THF)_2$ in THF-d_8 or in pyridine-d_5 solution at −50°C−RT; note however that, due to the instability of the yttrium-trisalkyl precursor in these solvents, quantitative formation of **1-Y** was not achieved; (c) synthesis of **1-Y** from **1** and $Y(CH_2SiMe_3)_3(THF)_2$ in toluene-d_8 in the presence of stoichiometric amounts of additional donors (2-MeO-naphthalene) and redox reagents (ferrocene, TEMPO).

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(18) The characteristic signals from the ipso-carbons of the ortho-metalated groups M−(*o*-Ph) were observed in the $^{13}C\{^{1}H\}$ NMR spectra of **2-Y** and **2-Sc** (δ 181.7 (d, $^{1}J_{C-Y}$ of 28 Hz) and 182.2 ppm, respectively).

(19) For a recent example of the DFT modeling of an intramolecular redox-free mechanism of the Kumada−Tamao−Curriu reaction, see: Ogawa, H.; Minami, H.; Ozaki, T.; Komagawa, S.; Wang, C.; Uchiyama, M. *Chem. - Eur. J.* **2015**, *21*, 13904.

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