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Room Temperature Ring-Opening Metathesis of Pyridines by a Transient Ti≡C Linkage

Brad C. Bailey, Hongjun Fan, John C. Huffman, Mu-Hyun Baik,* and Daniel J. Mindiola*

Department of Chemistry, Molecular Structure Center and School of Informatics, Indiana University, Bloomington, Indiana 47405

Received March 7, 2006; E-mail: mbaik@indiana.edu; mindiola@indiana.edu

Cleavage of the carbon−nitrogen bond of pyridine, an N-heterocycle of remarkable stability, is difficult, and only a few well-defined homogeneous examples of this potentially useful transformation have been documented.[1−3] This chemical paradigm is particularly attractive given its relevance to important industrial processes such as hydrodenitrogenation (HDN), a reaction in which *N*-heterocycles present in petroleum or coal-based liquids are catalytically converted to NH_3 and nitrogen-free carbon−hydrogen based products.[4] As a result, understanding the mechanism by which strong C−N bonds of aromatic substrates such as pyridine can be cleaved offer an excellent opportunity to improve or develop more efficient HDN catalysts.[5] To date, the work by Wolczanski[1] and Wigley[2] comprise the scarce examples of well-defined homogeneous HDN models for mild C−N bond cleavage of pyridine. One common step to C−N bond cleavage of pyridine, in either case, was η^2-(N,C) activation[1,2,6] of the substrate by a highly reducing group 5 metal center. Subsequent reduction[1] or alkyl migration[2] of the latter precursors resulted in ring-opening of the N-heterocycle.

We report the facile and nonreductive C−N activation and cleavage of pyridine by a transient titanium alkylidyne (PNP)Ti≡C^{t}Bu (PNP = N[2-P(CHMe$_2$)$_2$-4-methylphenyl]$_2^-$).[7] Activation of the C−N bond in pyridine involves a unique process, a ring-opening metathesis (ROM) step invoking the [2 + 2] cycloaddition of the aromatic C═N bond across a reactive Ti≡C^{t}Bu linkage. The combination of synthesis, isotopic labeling, and theoretical studies allowed for understanding this rare transformation in which the aromatic ring of the N-heterocycle is cleaved.

As an attempt to trap the elusive alkylidyne (PNP)Ti≡C^{t}Bu,[7] the titanium alkylidene−alkyl complex (PNP)Ti═CH^{t}Bu(CH$_2$^{t}Bu) (**1**),[7] was treated with neat pyridine at room temperature for 12 h, to afford quantitative formation of the azametallabicyclic complex (PNP)Ti(C(^{t}Bu)CC$_4$H$_4$NH) (**2a**) and extrusion of CH$_3$^{t}Bu (Figure 1).[8] Compound **2a** displays two low-field ^{13}C NMR resonances at 245 and 217 ppm as well as four sp^2-CH resonances amid those seen for the aryl C−H's of the pincer ligand. Complete assignment of all six carbon environments in the bicyclic ring in **2a** was aided by HMQC and HMBC NMR experiments.[8] The ^{31}P NMR spectrum reveals two sets of doublets (J_{P-P} = 48 Hz), while ^{1}H NMR displays only one ^{t}Bu group and five multiplets integrating each to one proton thus consistent with a C_1 symmetric molecule. When the reaction was carried out in pyridine-d_5, the latter five resonances vanish in the ^{1}H NMR spectrum of (PNP)Ti(C(^{t}Bu)CC$_4$D$_4$ND), **2a**-d_5, but are clearly observable in the ^{2}H NMR spectrum without ^{2}H scrambling into the ancillary PNP ligand. Stronger evidence for the correct ^{1}H and ^{13}C NMR assignment in **2a** originates from derivation of the pyridine. When (PNP)Ti═CH^{t}Bu(CH$_2$^{t}Bu) was dissolved in neat 4-picoline, C−N bond rupture rapidly ensues to afford (PNP)Ti(C(^{t}Bu)CC$_4$H$_3$MeNH), **2b**. ^{1}H, ^{13}C, and ^{31}P NMR spectroscopic data of **2b** reveal a similar pattern and symmetry to **2a**.[8]

To conclusively elucidate the connectivity in **2a** and **2b**, single-crystal X-ray diffraction studies were conducted. Among the many

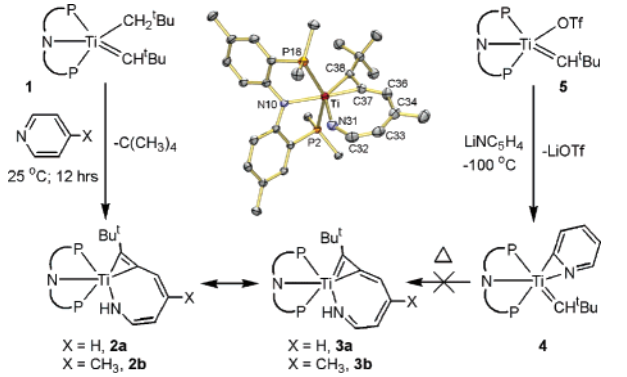

Figure 1. Ring-opening metathesis of pyridine and 4-picoline by a transient titanium alkylidyne. The molecular structure of complex **2b** depicts thermal ellipsoids at the 50% probability level. ^{i}Pr methyls and H-atoms have been excluded for clarity. Selected bond lengths (Å) and angles (deg): Ti−N31, 1.982(8); Ti−N10, 2.193(6); Ti−C38, 2.010(2); Ti−C37, 2.010(2); Ti−P18, 2.6145(7); Ti−P2, 2.6100(7); C38−C37, 1.330(3); C37−C36, 1.430-(3); C36−C34, 1.368(3); C34−C33, 1.427(3); C33−C32, 1.367(3); C32−N31, 1.362(3); C38−Ti1−C37, 38.63(8); P18−Ti−P2, 145.73(2); Ti−C37−C36, 150.3(6); Ti−N31−C32, 143.1(6).

salient features observed in the molecular structures of **2a**[8] and **2b** is the azametallabicyclic ring formation resulting from the ring-opening of pyridine (Figure 1).[8] The structure of **2b** exposes a seven-three-metallabicyclic framework fused perpendicularly to an unperturbed planar pincer-type ligand. The metrical parameters in the structure of **2a** are consistent with a dianionic alkene (C38−C37, 1.330(3) Å) ligand possessing a pendant −CH═CH═CH═CH−NH amide arm N-bound to the metal center. X-ray structural data are therefore not consistent with contribution from **3**, an alternate resonance bearing an η^2-vinyl with a parent imine arm coordinated to titanium (Figure 1).

Examination of the volatile components in the **1** → **2a** conversion reveals CH$_3$^{t}Bu to be the only product, suggesting that α-H abstraction precedes C−N bond activation. To better understand C−N bond cleavage, we explored several possible reaction pathways using high-level density functional theory at the B3LYP/cc-pVTZ(-f) level of theory[9] using the Jaguar program suite.[10] The most plausible pathway is shown in Figure 2. Initial α-H abstraction is predicted to be rate determining with an activation free energy of 27.8 kcal/mol, which gives rise to transient (PNP)Ti≡C^{t}Bu (**6**). The latter displays a short Ti−C bond distance of 1.749 Å and a Mayer bond order of 2.49 (Figure 2),[11] consistent with a Ti−C triple bond motif. Complex **6** readily coordinates pyridine to form the intermediate (PNP)Ti≡C^{t}Bu(py) (**7**) in an overall exergonic process with a thermodynamic driving force of 13.3 kcal/mol. Conversion to the azametallacyclobutene **8** involves a formal [2 + 2] cycloaddition of the C−N bond of pyridine across the Ti≡C linkage. Our calculations locate an "early" transition state **7-TS** for this process with a C−C separation of 2.373 Å, which has a barrier of 12.7 kcal/mol associated with it (Figure 2). Intermediate

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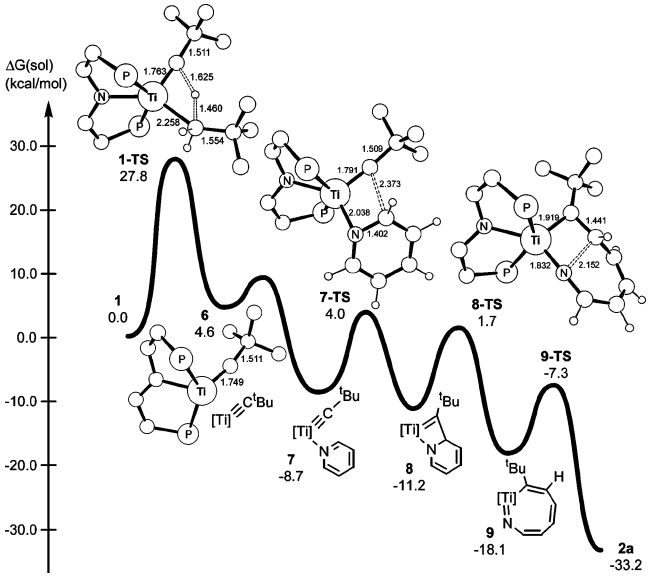

Figure 2. Proposed mechanism of the ROM of pyrdine. Only core structures are shown for illustration. All energies are solution phase free energies, and all bond lengths are given in Å. [Ti] represents the (PNP)Ti framework, and solvation calculations were carried out at the optimized gas-phase geometry employing the dielectric constant of $\epsilon = 2.379$ (pyridine).

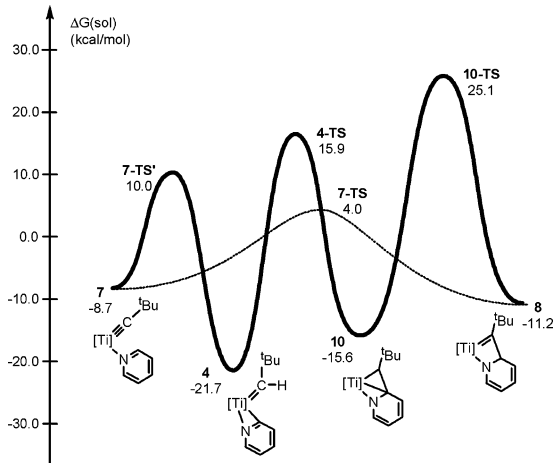

Figure 3. Proposed mechanism of the ROM of pyrdine. All energies are solution phase free energies. The dotted line represents the conversion of **7** directly to **8**, as also depicted in Figure 2.

8 is amenable to ROM with a barrier of 12.9 kcal/mol to afford the ring-expanded titanium imide intermediate **9**, which rapidly yields the ring contracted product **2a** upon proton shift.

In view of the previously reported reactivity of the alkylidyne intermediate toward C−H activation,[7] we considered another mechanistic possibility. After initial coordination of pyridine to give intermediate **7**, one could envision orthometalation to afford an η^2-(N,C) pyridyl complex **4** (Figure 3), which could subsequently undergo ring expansion concomitant with C−C bond formation to produce intermediate **10**. The latter would rearrange to **8** thus unavoidably producing complex **2a** as the final product. Wigley and co-workers reported a similar case involving the migratory insertion of an alkyl into an η^2-pyridyl.[2b,c] Our calculations indicate that the C−H activation is possible and involves the transition state **7-TS′** with an activation barrier of 18.7 kcal/mol from intermediate **7** (Figure 3). The η^2-(N,C) pyridyl complex **4**, however, is very stable at −21.7 kcal/mol relative to reactant **1**. Consequently, the C−C coupling and H-migration steps are associated with very high activation barriers of 37.6 and 46.8 kcal/mol relative to the stable intermediate **4**, respectively, essentially disqualifying this seemingly plausible route.

To experimentally test the computational prediction that the orthometalation of pyridine is not a viable pathway to **2a**, we prepared the η^2-(*N,C)* pyridyl complex **4** independently via direct transmetalation of $LiNC_5H_4$[12] with (PNP)Ti=CH^{t}Bu(OTf) (**5**)[13] at −100 °C (Figure 1).[8] The combination of ^{1}H, ^{13}C, ^{31}P, and HMQC NMR experiments is in accordance with **4** having a terminal alkylidene (^{13}C NMR: 276 ppm, $J_{C-H} = 91$ Hz) as well as an (N,C)-η^2-pyridyl ligand (^{13}C NMR for the pyridyl α-C: 217 ppm, $J_{C-P} = 12$ Hz).[8] Complex **4** is thermally unstable but can be readily isolated upon immediate workup of the reaction mixture at low temperatures. As suggested by the calculated reaction profile in Figure 3, thermolysis of complex **4** does not produce **2a** (25 °C, 24 h, Figure 1),[8] hence further supporting the notion that C−H activation of pyridine is not likely the first step along the C−N bond rupture process.

Based on all these observations we propose that ROM of pyridine is promoted by transient (PNP)Ti≡C^{t}Bu. Systems such as (PNP)-Ti≡C^{t}Bu offer an excellent opportunity to interrogate reaction mechanisms surrounding specific elementary steps such as aromatic C−N activation and cleavage by M−C multiply bonded linkages,[5] since both steps have tremendous implications toward important processes such as HDN. A detailed study surrounding the mechanistic aspects of this reaction will be published in due course.

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Supporting Information Available: Experimental preparation and reactivity (compounds **1**−**4**), crystallographic data (compounds **1** and **2**), computational details, all calculated structures, energies, and additional discussion. This material is available free of charge via the Internet at http://pubs.acs.org.

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