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Interactions of Aziridines with Nickel Complexes: Oxidative-Addition and Reductive-Elimination Reactions that Break and Make C−N Bonds

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The past several years have seen significant research attention focused on reductive-elimination reactions that form C−X bonds (where X is a heteroatom such as N, O, S, Se, or Te).[1−5] These types of reductive-elimination reactions, which were unknown a decade ago, are now well established in the Ni triad and have been incorporated into synthetically useful processes, particularly the preparation of arylamines and aryl ethers.[2] We have reported on a class of reductive-elimination reactions involving Ni that forms N−C, O−C, and S−C bonds.[3−5] An intriguing feature common to these reactions is that many of the $L_xNi(R)(X)$ complexes are isolable and thermally robust, with the elimination of R−X occurring at ambient temperature only when triggered by oxidation of Ni(II) to Ni(III) (oxidatively induced reductive elimination).[3−6] We recognized that the thermal stability of $L_xNi(R)(X)$ offered a unique opportunity to study fundamental mechanistic details of the reductive-elimination event. By preparing complexes with known stereochemistry at the reacting carbon center one could in principle follow the stereochemical course of the reaction in forming the R−X product. Herein we report the results of our investigation of reactions of several aziridines with Ni(0) and Ni(II) complexes that yield stable Ni(II) azametallacyclobutane products, the preparation of an H/D isotopic diastereomer of one azametallacyclobutane complex, and the stereochemical course of the oxidatively induced reductive elimination that reforms the aziridine on reaction with dioxygen.

Reaction of the *N*-tosylaziridines ($(p\text{-}CH_3C_6H_4SO_2)NCH_2CHR$ (**1a**, R = H; **1b**, R = Me; **1c**, R = *n*-Bu; **1d**, R = *i*-Pr)[7a−b] with (bpy)Ni(cod) (**2**; bpy = 2,2′-bipyridine; cod = 1,5-cyclooctadiene)[7c] or $(bpy)NiEt_2$ (**3**)[7d] results in elimination of cod or butane from **2** and **3**, respectively, and oxidative addition of an aziridine C−N bond to give the azametallacyclobutane complexes $(bpy)Ni(NTsCHRCH_2)$ (**4a**, R = H; **4b**, R = Me; **4c**, R = *n*-Bu; **4d**, R = *i*-Pr) as maroon solids in 50−70% isolated yields (Scheme 1).[8] In these cases, only one regioisomer is observed, with oxidative addition occurring exclusively at the least-hindered C−N bond.[9] These are the first examples of metallacycles isolated from oxidative-addition reactions of aziridines, although such azametallacyclobutanes have been invoked as intermediates in reactions involving aziridines, such as catalytic carbonylation of aziridines to give β-lactams.[10]

The structure of **4b** has been determined by X-ray crystallography (Figure 1), confirming the presence of a puckered four-membered azametallacycle (Ni−N(1)−C(2)−C(1) dihedral angle = 12.6(5)°) containing a pyramidal nitrogen; the tosyl group on N and the methyl substituent on the adjacent C are disposed in an *anti* conformation.[11] The Ni−N(1) bond distance (1.911(5) Å) is at the high end of the range found in other structurally characterized nickel amido complexes.[12] The methylene and methine protons of the azametallacycle were clearly located in a difference map, allowing for the accurate determination of their positions and consequently the two HCCH dihedral angles (*syn* = 15(5)°; *anti* = 124(6)°).

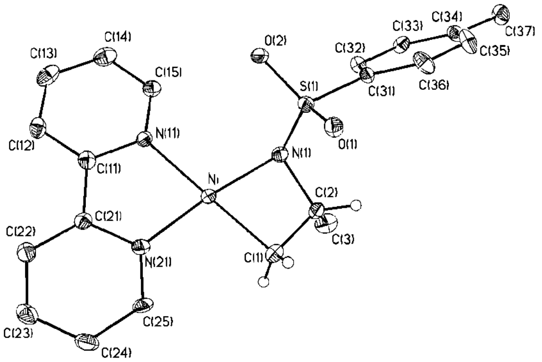
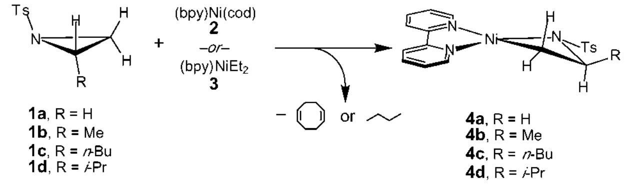


Figure 1. A perspective view of the molecular structure of **4b**. H-atoms, except those attached to C(1) and C(2), have been omitted. Selected metrical parameters: Ni−N(1) = 1.911(5), Ni−C(1) = 1.921(7), C(1)−C(2) = 1.500(9), N(1)−C(2) = 1.513(8) Å; Ni−N(1)−C(2) = 92.7(3), N(1)−C(2)-C(1) = 98.9(5), Ni−C(1)−C(2) = 92.7(4), N(1)−Ni-C(1) = 73.4(3)°.

Scheme 1



To gain mechanistic insight into the oxidative-addition process, we have followed the relative stereochemistry at the aziridine's methylene carbon center. The monodeuterated aziridine *syn*-$(p\text{-}CH_3C_6H_4SO_2)NCHDCH$-*n*-Bu (**1e**; $^3J_{HH} = 7.0$ Hz) was prepared by the Evans aziridination of *cis*-1-deutero-1-hexene,[7a] giving **1e** with >95% *syn*-stereochemistry. **1e** reacts with either **2** or **3** to give (bpy)Ni{NTsCH(*n*-Bu)CHD} (**4e**) in 60−65% yield (Scheme 2). The observed $^3J_{HH} = 4.1$ Hz for **4e** is consistent with a diastereomer having an *anti* arrangement of the methine and methylene protons in the azametallacycle and indicates that >95% inversion of stereochemistry has occurred at the methylene carbon during the oxidative-addition reaction (as determined by ^1H NMR integration). This suggests this oxidative addition proceeds via an S_N2-type mechanism involving nucleophilic attack of Ni at C and then rotation about the C−C bond followed by ring-closure to give the observed product (shown in Scheme 2).[13]

Assignment of the two methylene proton resonances in **4c** was essential for interpreting the results of the labeling experiment. Irradiation of the methine resonance of **4c** (δ 3.62) results in a 4.2% ^1H nOe intensity enhancement for the methylene proton resonating

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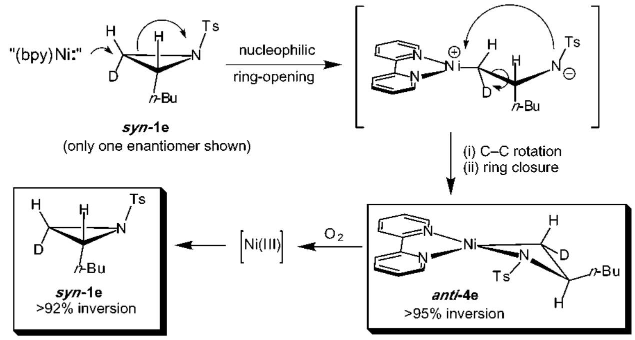
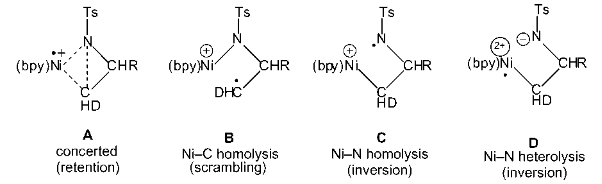
Scheme 2



Scheme 3



at δ 0.30, and a 0.8% enhancement for the methylene proton at δ -0.01, allowing for the assignment of the former as the proton *syn* to the methine H and the latter as the *anti* proton. Similar assignments follow for the methyl-substituted metallacycle **4b**, where irradiation of the methine proton at δ 3.79 results in a 2.0% nOe enhancement for the *syn* methylene proton at δ 0.44, and a 0.1% enhancement for the *anti*-H resonance at δ -0.05. As an independent confirmation, the magnitudes of the $^3J_{HH}$ for these resonances are consistent with the *syn*/*anti*-assignments made on the basis of the crystal structure of **4b**. Evaluation of the Karplus equation, relating the dihedral angle between vicinal protons and their $^3J_{HH}$, predicts couplings of 7.6 ± 0.3 Hz and 4.4 ± 0.8 Hz for the *syn* and *anti* protons, respectively, using the crystallographically determined angles (vide supra).[14] These values compare favorably with the measured couplings of 7.8 and 5.0 Hz for **4b**, and 8.3 and 4.1 Hz for **4c**.

When the azametallacyclobutane complexes **4a**−**e** are exposed to oxygen, a reaction ensues giving the free aziridines in 30−60% isolated yields.[15] These oxidatively induced reductive-elimination reactions are analogous to previously reported examples that give tertiary amines (from acyclic (bpy)Ni(R)(NR′R″) complexes) or five-membered cyclic amines (e.g., pyrrolidines and indolines) from azametallacycles.[3] In the oxidation of **4e**, the product aziridine is spectroscopically identical to its parent, **1e**, indicating the elimination that forms the C−N bond also proceeds with inversion of stereochemistry (~92% by ^{1}H NMR integration) at the methylene carbon (Scheme 2). Four scenarios for the bond-forming event are illustrated in Scheme 3. The stereochemical result is inconsistent with a concerted elimination (**A**, which would give retention at C) and one involving Ni−C homolysis to generate a primary C radical (**B**, giving scrambling). It is consistent with mechanisms involving Ni−N homolysis (**C**) or heterolysis (**D**) followed by ring-closing displacements (i.e., S_H1 or S_N2 processes), but does not allow for differentiation between these latter two mechanisms.

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Supporting Information Available: Experimental, spectroscopic, and analytical details; crystallographic details; atomic coordinates; bond angles and distances; anisotropic thermal parameters; hydrogen atom coordinates; least-squares planes; torsion angles (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) A representative procedure for the preparation of **4a**−**e** is given for **4b**. (bpy)NiEt$_2$ (**3**; 0.25 g, 0.75 mmol) was dissolved in 10 mL of THF under an inert atmosphere. To the stirring solution was added *N*-*p*-tolylsulfonyl-2-methyl aziridine (**1b**; 0.15 g, 0.71 mmol) in a THF solution. The reaction mixture was stirred at ambient temperature for 3 h, the resulting dark-red solution was filtered, and the solids were washed with 3 × 2 mL of THF. The combined filtrates were reduced in volume to ~2 mL, and the product was precipitated by slow addition of hexanes. The red precipitate was filtered, washed with 3 × 2 mL of hexanes, and dried under vacuum to afford **4b** (0.18 g, 56% yield). An analogous procedure using (bpy)Ni(cod) (**2**) as the Ni source requires longer reaction times but gives similar yields. Spectroscopic and analytical data are given in the Supporting Information.
(9) Propylene sulfide reacts with **2** to give a mixture of the thiametallacycles (bpy)Ni(SCH$_2$CHMe) and (bpy)Ni(SCHMeCH$_2$) in a 1:6 ratio. Matsunaga, P. T.; Hillhouse, G. L. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1748.
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(11) Crystal data for **4b**: $C_{20}H_{21}N_3NiO_2S$, monoclinic, $C2/c$, $a = 13.7055(13)$ Å, $b = 14.4807(14)$ Å, $c = 20.1202(19)$ Å, $\beta = 102.477(2)°$, $Z = 8$, μ(Mo Kα) = 11.22 cm^{-1}, $T = 100$ K, $V = 3898.9(6)$ Å^3, $\lambda = 0.71073$ Å, $D_c = 1.452$ mg/mm^3. Of 9679 data collected (red crystal, $2.07 \leq \theta \leq 25.10$) 3446 were independent and observed with $I > 2\sigma(I)$. All non-hydrogen atoms were anisotropically refined, and hydrogen atoms were idealized except for those attached to C(1) and C(2), which were located from the difference map and refined isotropically. $R(F) = 0.081$ and $R(wF^2) = 0.159$.
(12) In structures of terminal Ni(I) and Ni(II) amides, Ni−N ranges from 1.93 to 1.82 Å, averaging 1.88 Å. See: Mindiola, D. J.; Hillhouse, G. L. *J. Am. Chem. Soc.* **2001**, *123*, 4623 and references therein.
(13) Such a mechanism is consistent with the observed lack of reactivity of 2,3-disubstituted *N*-tosylaziridines with **2** and **3**.
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(15) A representative procedure for oxidation of **4a**−**e** is given for **4e**. A 25-mg sample of **4e** (0.05 mmol) was dissolved in 10 mL of benzene and stirred under 1 atm of O$_2$ for 1 h. GC−MS analysis of the supernatant showed only **1e** and bipyridine to be present. Solvent was removed under vacuum from the resulting heterogeneous mixture, and the aziridine **1e** (4 mg, 46% yield) was isolated by flash chromatography (silica; hexanes/EtOAc, 4:1).

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