thenium complex, **1**, products of N-H activation are observed for every amide tested whereas reactions are seen for the iron complexes, **2** and **3**, with amides a-c only. Increasing reaction times and temperatures for **1** are required as the acidities of the amides[10] are decreased: quantitative reaction with triflamide (g) occurs immediately at room temperature, trifluoroacetamide (a) requires heating at 50 °C for 40 min, difluoroacetamide (b) requires 20 h at 50 °C, and acetamide (d) requires heating at 50 °C for 36 h. The stabilities, also, of the products correlate with the amide acidity; quantitative yields of **1a** and free benzamide are obtained in the reaction of 2 equiv of trifluoroacetamide with **1e**. Although **1** and **2** are known to activate C-H bonds of arenes and alkanes to form stable products,[11] N-H activation products, only, are observed despite the high concentration of solvent (THF) C-H bonds and the presence of "activated" C-H bonds (e.g., the C-H bonds of acetamides b, d, and f).

The mechanism(s) of product (**1a-g**, **2a-c**, **3a-c**) formation is (are) unclear. Two possible limiting pathways (there are certainly other possibilities) for the reactions of **1**, **2**, and **3** with amides are (1) reductive elimination (photochemically driven for **2**[12]) to form zerovalent M(diphosphine)$_2$ followed by oxidative addition of the H-N bond and (2) bimolecular reaction (protonolysis) with amide. As the reaction of amides with **2** occurs with photochemical activation only, reductive elimination of H_2 is apparently required. However, intermediates resulting from C-H bond activation may be generated on the path to product formation. When an amide-d_2 (trifluoroacetamide or triflamide) is employed in the reaction with **1**, the product hydride resonance disappears and no deuterium is found in the elimination product, naphthalene.[13] This indicates that neither direct protonation of the M-C bond by the amide nor scrambling between amide N-H(D) and Ru-H bonds occurs. Furthermore, the rates at which **1** reacts with g and a ($t_{1/2}$ <2 and 20 min, respectively, at 25 °C) are much faster than the reported rate of naphthalene reductive elimination from **1** ($t_{1/2} \cong$ 300 min at 65 °C).[10b] These results lead us to favor a bimolecular reaction pathway consisting of a rate-determining, regiospecific protonation (possibly trans to the M-C bond) at the metal center followed by rapid arene elimination for the reactions of a and g with **1**. For the less acidic amides, pathways involving initial reductive elimination are kinetically competent and must be considered possible. When **1** reacts with excess g, dihydrogen (D_2 when g-d_2 is used) is evolved and a new product, tentatively identified as *cis*-Ru(dmpe)$_2$(NHSO$_2$CF$_3$)$_2$,[14] is produced.

The Ru(dmpe)$_2$(NHCOR)(H) products undergo rapid ($t_{1/2}$ < 3 min) exchange of amido groups but not through a reductive elimination/oxidative addition sequence. For example, reaction of **1a** with 1 equiv of ^{15}N-a immediately produces an equimolar mixture of ^{15}N-labeled and natural abundance ^{14}N **1a**, as shown by the coupling of the hydride and the N-H resonances in the ^{1}H NMR spectrum. Conversely, reaction of **1a** with an excess of a-d_2 over a 2-week period shows no exchange of deuterium for protium at the hydride resonance. Similar results are obtained when either ^{15}N- or D-labeled **1a** is equilibrated with unlabeled a. These results are consistent with a simple ligand-exchange process which may be associative or dissociative; due to the low dielectric constants of the solvents employed, the associative pathway seems most probable.

In summary, products of formal N-H bond activation result from the thermal reactions of amides with *cis*-RuH(naphthyl)(dmpe)$_2$ and FeH(C$_6$H$_4$PPhCH$_2$CH$_2$PPh$_2$)(dppe) and from the photochemical reactions of *cis*-FeH$_2$(dmpe)$_2$ and amides. Alcohols, water, and simple amines do not undergo analogous reactions, suggesting that the design of late transition metal catalyzed hydroaminations may be achieved more readily by using amides as ammonia synthetic equivalents. Our current efforts are directed at clarification of the mechanistic aspects of amide N-H activation and at the exploitation of N-H activation in hydroamination catalysis.

Acknowledgment. We thank the National Institutes of Health (GM39417-02) for support of this work.

Supplementary Material Available: Experimental details of the isolation of compound **3a** and the attempted isolation of compound **2a** and NMR data for compounds **1b-g**, **2a-c**, and **3a-c** (4 pages). Ordering information is given on any current masthead page.

(10) Representative pK_a's: trifluoroacetamide (a), pK_a = 6.3 (water);[10a] trifluoromethanesulfonamide (g), pK_a = 6.3 (water);[10b] acetamide (d), pK_a = 25.5 (DMSO).[10a] (a) Bordwell, F. G. *Pure Appl. Chem.* **1977**, *49*, 963. (b) Trepka, R. D.; Harrington, J. K.; Belisle, J. W. *J. Org. Chem.* **1974**, *39*, 1094. We have not been able to find appropriate pK_a values in THF.

(11) (a) Baker, M. V.; Field, L. D. *J. Am. Chem. Soc.* **1987**, *109*, 2825. (b) Tolman, C. A.; Ittel, S. D.; English, A. D.; Jesson, J. P. *J. Am. Chem. Soc.* **1978**, *100*, 4080.

(12) Bergamini, P.; Sostero, S.; Traverso, O. *J. Organomet. Chem.* **1986**, *299*, C11.

(13) Less than 5% C$_{10}$H$_7$D detected by GC/MS.

(14) NMR data. *cis*-Ru(CF$_3$SO$_2$NH)$_2$(dmpe)$_2$ in THF-d_8. ^{31}P{^{1}H}: δ 38.6, t, J_{P-P} = 24 Hz, 2 P; δ 54.1, t, J_{P-P} = 24 Hz, 2 P; ^{31}P{^{1}H off-resonance}: δ 38.6, t; δ 54.1, t. ^{19}F: δ -71.5, s. ^{1}H: PCH_3, δ 1.26 and 1.31, br, 24 H; PCH_2, δ 1.4, br, 8 H, no other peaks observed.

Endocyclic Restriction Test: Evaluation of Transition-Structure Geometry for an Aryl Bromide-Alkyllithium Exchange Reaction

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The endocyclic restriction test provides an approach for the evaluation of transition-structure geometry that is applicable to nonstereogenic atoms and thereby can provide information that can be used to distinguish between alternative mechanisms.[1-6] In this communication we report an investigation of this approach for a formal nucleophilic substitution at bromine and use our results to evaluate the mechanisms for the aryl bromide-alkyllithium exchange reaction. To the best of our knowledge, this is the first report of an experimental evaluation of transition-structure geometry for a formal substitution at bromine.

Treatment of *o*-bromophenethyl iodide **1** with 1.8 equiv of *tert*-butyllithium at -98 °C in tetrahydrofuran followed by addition of methanol gives the products **3-9** in the yields indicated along with 10% recovered **1**.[7] The products of interest, **3-5**, are considered to arise after initial conversion of **1** to (*o*-bromophenethyl)lithium (**2**). The *o*-bromoethylbenzene (**3**) is from protonation of **2** by methanol, the *o*-bromophenethyl bromide (**5**) from bromine-lithium exchange of **2**, and the phenethyl bromide (**4**) from intra- or intermolecular rearrangement of **2** to *o*-lithiophenethyl bromide (**10**) prior to protonation by methanol.[9]

An intermolecular pathway for a monomeric unit in the conversion of **2** to **10** was established by the double labeling exper-

(1) For substitution at carbon: Tenud, L.; Farooq, S.; Seibl, J.; Eschenmoser, A. *Helv. Chim. Acta* **1970**, *53*, 2059.

(2) For substitution at sulfur: Hogg, D. R.; Vipand, P. W. *J. Chem. Soc. C* **1970**, 2142. Kampmeier, J. A. *ACS Symp. Ser.* **1978**, *No. 69*, 275. Andersen, K. K.; Malver, O. *J. Org. Chem.* **1983**, *48*, 4803. Andersen, K. K.; Chumpradit, S.; McIntyre, D. J. *J. Org. Chem.* **1988**, *53*, 4667. Beckwith, A. L. J.; Boate, D. R. *J. Chem. Soc., Chem. Commun.* **1986**, 189.

(3) For an early suggestion of this approach for iodine, see: Drury, R. F.; Kaplan, L. *J. Am. Chem. Soc.* **1972**, *94*, 3982.

(4) For substitution at nitrogen: Beak, P.; Basha, A.; Kokko, B. *J. Am. Chem. Soc.* **1984**, *106*, 1511. Beak, P.; Basha, A.; Kokko, B.; Loo, D. *J. Am. Chem. Soc.* **1986**, *108*, 6016.

(5) For substitution at oxygen: Beak, P.; Loo, D. *J. Am. Chem. Soc.* **1986**, *51*, 3834.

(6) For general discussion, see: Minkin, V. I.; Olekhnovich, L. P.; Zhdanov, Y. A. *Molecular Design of Tautomeric Compounds*; D. Reidel Publishing Co.: Dordrecht, Holland, 1988.

(7) Seebach, D.; Neumann, H. *Chem. Ber.* **1974**, *107*, 847. Neumann, H.; Seebach, D. *Chem. Ber.* **1978**, *111*, 2785.

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(9) An intramolecular reaction within a radical cage is also ruled out by these results. The possibility that electron transfer precedes formation of an ate complex or an S$_N$2 transition structure cannot be ruled out but is not necessary. The lack of bromide incorporation into **5** rules out formation of this product by bromide displacement on **1**.

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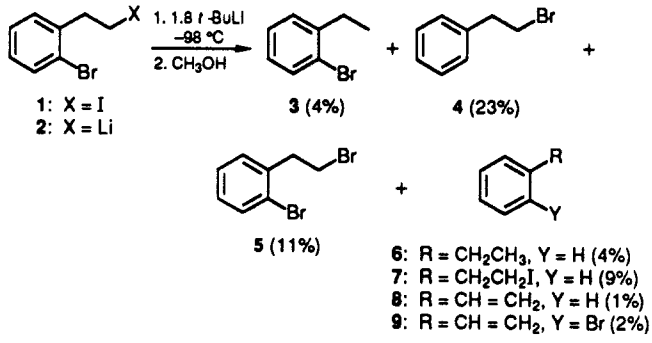
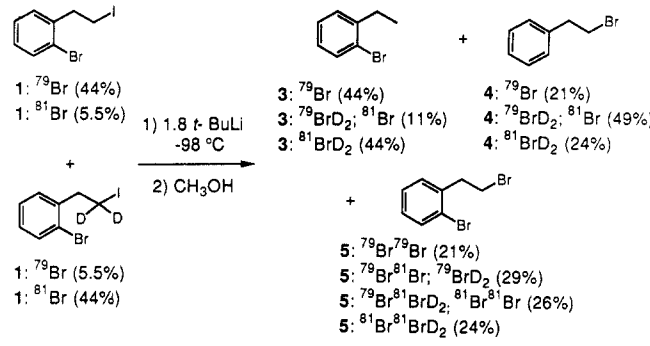
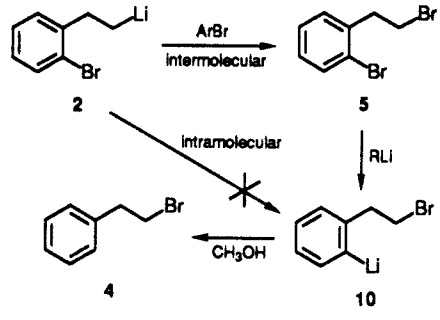


iment involving an equimolar mixture of **1**-^{79}Br and **1**-^{81}BrD$_2$ with minor amounts of **1**-^{81}Br and **1**-^{79}BrD$_2$ as shown. Analysis of the products by GC/MS shows **3** to be unscrambled, **4** to be fully scrambled, and **5** to be partially scrambled. When the reaction of labeled **1** is carried out in the presence of unlabeled lithium bromide, no incorporation of unlabeled bromide into **4** or **5** is observed.

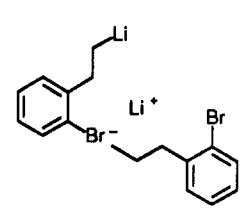


The significant result is that **2** is converted to **10** by an intermolecular process via **5**; the transfer of bromine from the aryl carbon to the methylene carbon apparently cannot proceed intramolecularly within the endocyclic restriction of a five-membered ring.



Four mechanisms have been suggested for the bromine–lithium exchange reaction: (1) a four-center process; (2) a stepwise process initiated by single electron transfer; (3) formation of an ate complex, and (4) an S_N2 reaction.[8] Reaction by the four-centered reaction should be possible intramolecularly for the conversion of **2** to **10**, so the present results do not support that mechanism in this case. Reaction by the pathway usually invoked for a single electron transfer which could be intermolecular would involve formation of an aromatic radical anion which expels bromide followed by bromide escape and capture by the alkyl radical of another molecule to give a radical anion that loses an electron to provide **5**. In this case incorporation of external bromide should be found in **4** and **5**. Since that was not observed, this version of the single electron transfer process is not consistent with our observations.[9]

The intermolecular conversion of **2** to **10** is consistent with a transition structure that requires the carbons entering and leaving the bromine to be at a large bond angle. This disposition of the carbons would be expected for apical substituents in the 10-Br-2 transition structure of either an ate complex or an S_N2 reaction shown as **11** and **12**, respectively.[8,10,11] Further tests utilizing homologues and systems in which a defined large angle between the alkyllithium and the aryl bromide is enforced are under way. The present results can be taken to support a mechanism of bromine–lithium exchange for the conversion of **2** to **10** that proceeds via an ate complex or S_N2 process, to discount the four-center mechanism, and to make a radical mechanism unnecessary.[12] The generality of this conclusion will be tested by investigation of other systems.



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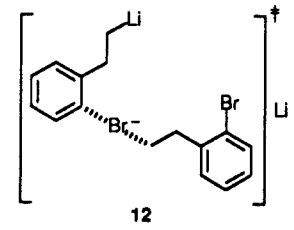

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Acknowledgment. We are grateful to the National Institutes of Health and National Science Foundation for financial support.

Supplementary Material Available: Experimental details of the syntheses and reactions of labeled **1** (10 pages). Ordering information is given on any current masthead page.

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(12) This analysis is for the monomeric unit of an organolithium reagent which probably exists as an aggregate. An intraaggregate reaction for **2** which would be intermolecular by the double-labeling criterion and could involve a formal seven-membered ring in which the carbons might not be fully apically arranged is possible but is discounted by our preliminary observation that the reaction is also intermolecular in (*o*-bromophenyl)-*n*-pentyl iodide, a system in which a monomeric unit could rearrange by an eight-membered ring. That result also reinforces the conclusion about the four-center mechanism based on **2**.

Secondary Structure Nucleation in Peptides. Transition Metal Ion Stabilized α-Helices†

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It is unusual for monomeric peptides less than 20 residues in length to adopt an α-helical conformation in aqueous solution.[1] Formation of α-helices in disordered polypeptides is a classical nucleation event, with the energetically unfavorable formation of the first turn being rate limiting.[1,2] A few studies have been aimed at promoting α-helix formation by introducing conformational constraints in peptides.[3] These approaches often require

† This paper is dedicated to the memory of Professor Emil T. Kaiser.

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