

present catalyst can be transformed readily into chiral catalysts of defined structure.

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Supplementary Material Available: Details of improved preparations of $[\text{Ti}(\text{Cp}^*)_2\text{Cl}_2]$, $[\text{Ti}(\text{Cp}^*)_2(\text{H}_2\text{O})_2](\text{CF}_3\text{SO}_3)_2$, and $[\text{Ti}(\text{Cp}^*)_2(\text{O}_2\text{CCF}_3)_2]$, details on performance of the catalyses, and a second-order plot for Diels-Alder catalysis (3 pages). Ordering information is given on any current masthead page.

New Copper(I)-Catalyzed Reactions of Oxaziridines: Stereochemical Control of Product Distribution

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The reactions of oxaziridines with various metals, notably iron, have been investigated since those heterocycles were first reported by Emmons in 1957.¹ In general, single-electron transfer effects N-O bond cleavage to afford nitrogen-centered radical/alkoxide pairs, which typically undergo protonation and β -scission or radical rearrangement reactions. Given the similarity of these reactions to radical-mediated reactions of *N*-chloroalkylamines² and contemporary interest in nitrogen-centered radicals in synthesis,³ an

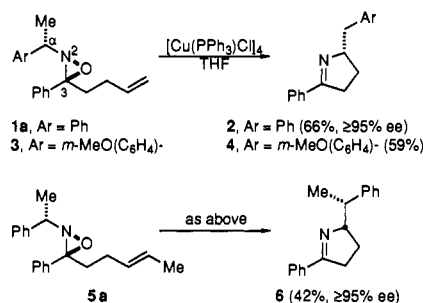
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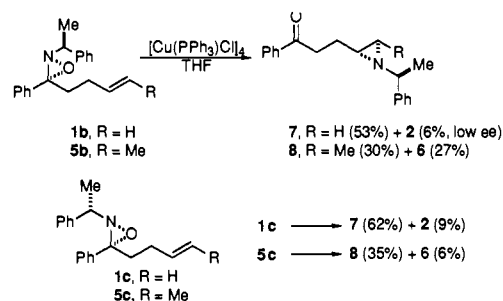
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(3) Some recent references include the following: (a) Tokuda, M.; Yamada, Y.; Takagi, T.; Sugimoto, H.; Furusaki, A. *Tetrahedron Lett.* **1985**, *26*, 6085-6088. (b) Newcomb, M.; Deeb, T. M. *J. Am. Chem. Soc.* **1987**, *109*, 3163-3165. (c) Dicks, P. F.; Glover, S. A.; Goosen, A.; McClelland, C. W. *Tetrahedron* **1987**, *43*, 923-934. (d) Tokuda, M.; Yamada, Y.; Takagi, T.; Sugimoto, H.; Furusaki, A. *Tetrahedron* **1987**, *43*, 281-296. (e) Karady, S.; Corley, E. G.; Abramson, N. L.; Weinstock, L. M. *Tetrahedron Lett.* **1989**, *30*, 2191-2194. (f) Newcomb, M.; Deeb, T. M.; Marquardt, D. J. *Tetrahedron* **1990**, *46*, 2317-2328. (g) Newcomb, M.; Marquardt, D. J.; Deeb, T. M. *Tetrahedron* **1990**, *46*, 2329-2344. (h) Newcomb, M.; Marquardt, D. J.; Kumar, M. U. *Tetrahedron* **1990**, *46*, 2345-2352. (i) Boivin, J.; Fouquet, E.; Zard, S. Z. *Tetrahedron Lett.* **1990**, *31*, 85-88. (j) Boivin, J.; Fouquet, E.; Zard, S. Z. *Tetrahedron Lett.* **1990**, *31*, 3545-3548. (k) Boivin, J.; Fouquet, E.; Zard, S. Z. *J. Am. Chem. Soc.* **1991**, *113*, 1055-1057. (l) Newcomb, M.; Esker, J. L. *Tetrahedron Lett.* **1991**, *32*, 1035-1038. (m) Newcomb, M.; Weber, K. A. *J. Org. Chem.* **1991**, *56*, 1309-1313. (n) Boivin, J.; Fouquet, E.; Zard, S. Z. *Tetrahedron Lett.* **1991**, *32*, 4299-4302. (o) Newcomb, M.; Chau, H. *Tetrahedron Lett.* **1992**, *33*, 6493-6496. Nitrogen radical intermediates have also been implicated in the intramolecular addition of hydroxylamines to olefins, but this mechanism has been questioned: (p) House, H. O.; Manning, D. T.; Melillo, D. G.; Lee, L. F.; Haynes, O. R.; Wilkes, B. E. *J. Org. Chem.* **1976**, *41*, 855-863. (q) Oppolzer, W.; Siles, S.; Snowden, R.; Bakker, B. H.; Petrzilka, M. *Tetrahedron Lett.* **1979**, 4391-4394. (r) Ciganek, E. *J. Org. Chem.* **1990**, *55*, 3007-3009. (s) Holmes, A. B.; Smith, A. L.; Williams, S. F.; Hughes, L. R.; Lidert, Z.; Swithenbank, C. *J. Org. Chem.* **1991**, *56*, 1393.

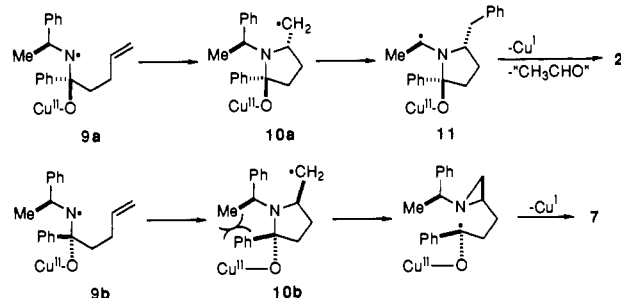
Scheme I



Scheme II



Scheme III



investigation of the intramolecular addition reactions of radicals generated from chiral oxaziridines⁴ was undertaken. Here, we report (1) conditions to effect N-O cleavage under nonaqueous, neutral conditions; (2) two remarkable, highly stereoselective reaction pathways for oxaziridine-derived radicals yielding enantiomerically enriched pyrrolines or aziridines, respectively; and (3) that the stereochemistry of the starting oxaziridine profoundly affects the course of its reaction.

A survey of several organometallic reagents showed that $[\text{Cu}(\text{PPh}_3)\text{Cl}]_4$ in THF could conveniently effect the formation of nitrogen-centered radicals from oxaziridines.⁶ Therefore, a 3-butenyloxaziridine **1'** was dissolved in degassed THF with 5 mol

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(5) Churchill, M. R.; Bezman, S. A.; Osborn, J. A.; Wormald, J. *Inorg. Chem.* **1972**, *11*, 1818-1825.

(6) Depending on the structure of the starting oxaziridines, this reagent can effect N-O homolytic processes leading to C → N alkyl migration, α -cleavage, or allylic H-atom abstraction. All of these processes are consistent with the intervention of nitrogen radicals or related species. Wang, Y.; Peng, X.; Gülgeze, B.; Aubé, J. Unpublished work from these laboratories.

(7) The oxaziridines used in this study were prepared from the corresponding ketone via formation of the imine using (*S*)- α -methylbenzylamine and subsequent oxidation with *m*-CPBA. The structures were determined by NMR spectroscopy and the known⁸ stereochemical course of imine oxidation reactions (see supplementary material). All new compounds were fully characterized and gave satisfactory ¹H and ¹³C NMR, IR, MS, and HRMS or elemental analytical data.

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% [Cu(PPh₃)Cl]₄ (Scheme I). Reflux (ca. 7 h) followed by concentration and chromatography led to the isolation of pyrroline (*S*)-**2** in 66% yield and ≥95% ee. The optical purity of the product and its absolute configuration were determined by ¹H NMR chiral solvation studies⁹ and chemical correlation.¹⁰ The analogous transformation of *rac*-**3** → *rac*-**4** (59%) established the origin of the C-5 arylmethyl substituent in the pyrroline products, and the isolation of stereochemically homogeneous **6** (42%, [α]_D -96.0° (*c* = 1.0, ethanol) was indicative of a high level of diastereoselectivity with respect to the alkene component.¹² In each case, the reaction mixture also included a 10–25% yield of the 3-butenyl or 3-pentenyl phenyl ketone corresponding to the starting oxaziridine.

The high level of stereoselectivity obtained in the formation of **2** and **6** was surprising in light of results obtained in other nitrogen radical cyclization reactions.^{3a,d,g,o} To gain some insight into the source of stereochemical control, the diastereomeric oxaziridine **1b** was submitted to the same reaction conditions as above (Scheme II). We were astonished to find that aziridine **7** was formed as a single diastereomer in 53% yield, accompanied by only a small amount of the expected **2** in low optical purity.^{13,14} The relative configuration of **7** was established by X-ray crystallography. Similar treatment of **1c** also afforded **7** as the major product. This demonstrated that the change in the C- α /C-3 relative stereochemistry (which is the same in **1b** or **1c**) and not the C- α /N-2 relationship (identical in **1a** and **1b**) was responsible for the observed product distributions. Oxaziridines **5b** and **5c** behaved similarly, albeit with lower selectivity.

A mechanistic outline consistent with these results is shown in Scheme III. Single-electron transfer^{1,15} (SET) to oxaziridines **1a** or **1b/1c** should give rise to radical/alkoxide pairs **9a** or **9b**, respectively (the copper(II) ion generated during the SET step is depicted as the counterion for bookkeeping purposes). The high ee of the final product **2** requires that the cyclization **9a** → **10a** take place with high diastereoselectivity, either in a kinetic or thermodynamic sense. The radical center in **10a** then initiates ipso attack upon the aryl ring followed by 1,4-aryl migration to afford nitrogen-stabilized radical **11**;¹⁶ formal loss of the elements of Cu(I) (available for another catalytic cycle) and acetaldehyde leads to **2**. Radical **9b** should add to the olefin with the same sense of intraannular selectivity to afford **10b**. In this case, however,

the transition state required for phenyl transfer is disfavored, possibly due to steric interactions between the α -methyl substituent and the pyrrolidine phenyl substituent. Instead, **10b** undergoes bond reorganization, ultimately resulting in aziridine **7**. The absolute and relative stereochemistries of products **2**, **7**, and **6a** are consistent with the observed face selectivities of the olefin addition reactions.

The two reaction types reported herein constitute new departures in the use of oxaziridines for the stereoselective synthesis of heterocyclic compounds. In addition, these results provide a remarkable demonstration of the effect of stereochemistry on the fate of reactive intermediates.¹⁷

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Supplementary Material Available: Details of the synthesis and structure elucidations of oxaziridines **1a–c** and X-ray crystallographic data for the LAH reduction product of compounds **6**¹² and **7** (33 pages). Ordering information is given on any current masthead page.

(17) For an example of rotamer control of product distribution in a radical-mediated reaction, see: Snieckus, V.; Cuevas, J.-C.; Sloan, C. P.; Liu, H.; Curran, D. P. *J. Am. Chem. Soc.* 1990, 112, 896–898.

Formation of Cyclic Acetylene Complexes from the Reactions between Cycloalkeno-1,2,3-selenadiazoles and $[(\eta^5\text{-C}_5\text{H}_5)\text{Mo}(\text{CO})_2]_2^1$

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Whereas cycloalkynes containing five, six, and seven carbon atoms are kinetically unstable compounds only observed as transient species, they may be stabilized by complexation to metal atoms. In 1964 Wilkinson et al. observed the Co₂(CO)₈-mediated transformation of octafluorocyclohexa-1,3-diene to (hexafluorohex-1-yn-3-ene)Co₂(CO)₆,² and more general methodologies for stabilizing cycloalkynes have been established by the Bennett (eq 1),³ Buchwald (eq 2),⁴ and Chisholm groups (eq 3).⁵ A ring closure route involving pre-coordinated triple bonds has been reported by Schreiber et al.⁶

Attractive precursors for the thermal generation of such cycloalkynes, and cycloalkenyne, are 4,5-cycloalkeno-1,2,3-selenadiazoles, I.⁷ We, and others, have studied the reactions of selenadiazoles with transition metal complexes and shown that they are able to form a series of compounds dependent upon the nature of the 4,5-substituents and the transition metal complex.⁸

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(5) Chisholm, M. H.; Foltz, K.; Huffman, J. C.; Lucas, E. A. *Organometallics* 1991, 10, 535.

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(7) (a) Meier, H.; Zeller, K. P. *Angew. Chem., Int. Ed. Engl.* 1975, 14, 32. (b) Meier, H.; Voigt, E. *Tetrahedron* 1972, 28, 187. (c) Buhl, H.; Seitz, B.; Meier, H. *Tetrahedron* 1977, 33, 449. (d) Peterson, H.; Kolshorn, H.; Meier, H. *Angew. Chem., Int. Ed. Engl.* 1978, 17, 461.

(9) Pirkle, W. H.; Rinaldi, P. L. *J. Org. Chem.* 1978, 43, 4475.

(10) An authentic sample of (*R*)-**2** was prepared from *N*-Boc-phenylalanyl¹¹ (1) KO-*t*-Bu, (EtO)₂P(O)CH₂C(O)Ph, THF; (2) H₂, Pd/C, acetone; (3) trifluoroacetic acid and shown to have [α]_D + 83.8° (*c* = 1.0, ethanol) (cf. [α]_D -82.8° (*c* = 1.0, ethanol) for (*S*)-**2** as prepared according to Scheme I).

(11) Fehrentz, J.-A.; Castro, B. *Synthesis* 1983, 676–678.

(12) Pyrroline **6** was reduced with LAH to afford its *cis*-pyrrolidine derivative, the structure of which was elucidated by X-ray crystallography (supplementary material). The ee was ascertained by chiral solvation studies and the absolute configuration assigned in analogy to **2**.

(13) For a single example of a related reaction, see: Schmitz, E.; Janisch, K. *Chem. Heterocycl. Compds. (Engl. Transl.)* 1976, 12, 1432–1439; *Khim. Geterosikl. Soedin.* 1974, 12, 1629–1638.

(14) Some recent examples of olefin aziridination reactions include: Evans, D. A.; Woerpel, K. A.; Hinman, M. M.; Faul, M. M. *J. Am. Chem. Soc.* 1991, 113, 726–728. (b) Lowenthal, R. E.; Masamune, S. *Tetrahedron Lett.* 1991, 32, 7373–7376 (see ref 11). (c) Evans, D. A.; Faul, M. M.; Bilodeau, M. T. *J. Org. Chem.* 1991, 56, 6744–6746.

(15) A variety of intermediates related to those suggested in Scheme III can also be envisioned, such as copper-associated radicals or copper-containing metalocycles; future work will attempt to differentiate between these various possibilities.

(16) For some examples of the addition of radicals to arenes and radical-mediated ipso substitution, see: (a) Surzur, J.-M.; Stella, L. *Tetrahedron Lett.* 1974, 2191–2194. (b) Ishibashi, H.; Nakamura, N.; Ito, K.; Kitayama, S.; Ikeda, M. *Heterocycles* 1990, 31, 1781–1784. (c) Ishibashi, H.; So, T. S.; Okochi, K.; Sato, T.; Nakamura, N.; Nakatani, H.; Ikeda, M. *J. Org. Chem.* 1991, 56, 95–102. (d) Lauk, U.; Dürst, D.; Fischer, W. *Tetrahedron Lett.* 1991, 32, 65–68. (e) Curran, D. P.; Liu, H. *J. Am. Chem. Soc.* 1991, 113, 2127–2132. (f) Bertrand, M. P.; Surzur, J.-M.; Oumar-Mahamat, H.; Moustrou, C. *J. Org. Chem.* 1991, 56, 3089–3097. (g) Curran, D. P.; Abraham, A. C.; Liu, H. *J. Org. Chem.* 1991, 56, 4335–4337. (h) Curran, D. P.; Morgan, T. M.; Schwartz, C. E.; Snider, B. B.; Dombroski, M. A. *J. Am. Chem. Soc.* 1991, 113, 6607–6617. (i) Motherwell, W. B.; Pennell, A. M. K. *J. Chem. Soc., Chem. Commun.* 1991, 877–879. (j) Bowman, W. R.; Heaney, H.; Jordan, B. M. *Tetrahedron* 1991, 47, 10119–10128.