plicability to the evergreen problem concerning mass spectrometric rearrangements of $C_7H_8^{\bullet+}$ isomers.[4]

Acknowledgment. We thank Professor J. E. Bartmess for helpful discussions. We are also indebted to a referee for suggesting that a two-state model would be consistent with the formation of $\mathbf{2}^{\bullet+}$ and $\mathbf{3}^{\bullet+}$ from $\mathbf{1}^{\bullet+}$. The research at the University of Tennessee was supported by the Division of Chemical Sciences, Office of Basic Energy Sciences, U.S. Department of Energy (Grant No. DE-FG05-88ER13852). This work was supported at Syracuse University by the National Science Foundation and aided through technical assistance by Ms. Karla A. Villarica.

Intermolecular Radical Reactions of Unsaturated Chromium and Tungsten Carbene Complexes

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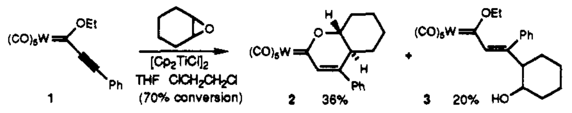
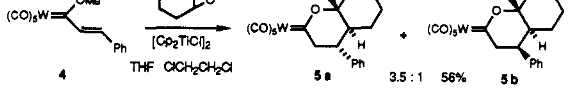
The use of radicals in organic synthesis has seen phenomenal development as chemists have found methods to control their reactivity.[1] While radical reactions can be performed under mild conditions and are tolerant of a variety of functional groups, reaction stereoselectivity and functionalization of product radicals remain as important areas of research.[2] A potentially powerful solution to these concerns is the use of transition metals to template radical reactions in order to control stereoselectivity and functionalization. Although transition-metal complexes have been utilized to generate organic radicals[3,4] and odd-electron-count organometallic complexes have been isolated and characterized,[5] radical reactions on metal-coordinated unsaturated ligands have not been explored in synthetic terms. In fact, for most organometallic species with applications to organic synthesis, only even-electron processes such as nucleophilic and electrophilic addition have been investigated.[6] We have initiated a program to examine coupling reactions, cyclizations, and other radical processes in metal-coordinated polyene and polyenyl systems and report herein the first intermolecular radical coupling reactions of carbene complexes and alkyl radicals.

Radical additions to α,β-unsaturated chromium and tungsten carbene complexes were chosen for study after considering the highly electrophilic nature of Fischer carbene complexes,[7] the relative nucleophilic behavior of alkyl-substituted radicals,[1] analogy to the reactivity of α,β-unsaturated esters, and the synthetic utility of Fischer carbene complexes.[7] Although most synthetically useful radical reactions are performed as chain processes,[8] we utilized stoichiometric generation of alkyl radicals and trapping by unsaturated Fischer carbene complexes. The generation of alkyl radicals by reaction of titanocene monochloride dimer and epoxides developed by Nugent and RajanBabu was most successful.[4] Simultaneous syringe pump addition of cyclohexene oxide (1.5 equiv) and titanocene monochloride dimer (1.5 equiv) to a solution of carbene complex **1** cooled to −20 °C followed by quenching with ethereal HCl (3 equiv) provided adducts **2** and **3** (eq 1).[9] The dihydropyranylidene complex **2** was a single isomer containing a trans-fused ring junction as evidenced by the coupling of the methine proton geminal to oxygen (3.78 ppm, td, J = 11.9, 4.1 Hz). Acyclic alcohol **3** was also a single isomer.[10] Although modest in yield, the key importance of these products is that they demonstrate the first coupling of an organic radical with a carbene complex.[11]

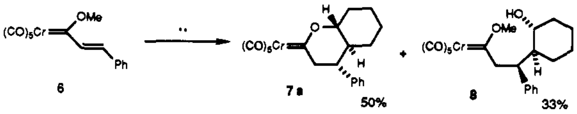


(1)

Reaction of styrenyl carbene **4** was more successful, providing the adducts **5a** and **5b** (3.5:1 by ^{1}H NMR) in 56% yield (eq 2). Again, the ring fusions were only trans[12] and the product ratio reflects the equatorial and axial phenyl group isomers, respectively. Chromium carbene complexes are equally effective in the radical coupling reactions as demonstrated by complex **6** (eq 3). Interestingly, product **8** did not cyclize under the reaction conditions, but readily cyclized upon subsequent treatment with catalytic sodium methoxide, providing the isomer of **7a**.



(2)



(3)

Abstraction of allylic hydrogen atoms by the alkyl radicals is not a concern as the propenyl complexes provided similar results (eqs 4, 5, 7). The modest stereoselectivity observed at the β-position in the reaction of tungsten complex **9** and cyclohexene oxide (eq 4) is diminished when an acyclic epoxide is used (eqs 7, 8). In a direct comparison between carbene complexes and esters in radical coupling reactions, reaction of excess methyl crotonate substrate (10 equiv) at room temperature provided a

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[1] For reviews, see: (a) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*; Pergamon: New York, 1986. (b) Giese, B. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 553. (c) Barluenga, J.; Yus, M. *Chem. Rev.* **1988**, *88*, 487.

[2] For example, see: RajanBabu, T. V. *Acc. Chem. Res.* **1991**, *24*, 139. (b) Giese, B. *Angew. Chem., Int. Ed. Engl.* **1989**, *28*, 969. (c) Porter, N. A.; Scott, D. M.; Rosenstein, I. J.; Giese, B.; Veit, A.; Zeitz, H. G. *J. Am. Chem. Soc.* **1991**, *113*, 1791. (d) Hamon, D. P. G.; Razzino, P.; Massey-Westropp, R. A. *J. Chem. Soc., Chem. Commun.* **1991**, 332. (e) Curran, D. P.; Shen, W.; Zhang, J.; Heffner, T. A. *J. Am. Chem. Soc.* **1990**, *112*, 6738. (f) Spellmeyer, D. C.; Houk, K. N. *J. Org. Chem.* **1987**, *52*, 959.

[3] For example, see: (a) Thoma, G.; Giese, B. *Tetrahedron Lett.* **1989**, *30*, 2907. (b) Pattenden, G. *Chem. Soc. Rev.* **1988**, *17*, 361. (c) Branchaud, B. P.; Meier, M. S. *J. Org. Chem.* **1989**, *54*, 1320. (d) Sustmann, R.; Altevogt, R. *Tetrahedron Lett.* **1981**, *22*, 5167. (e) Bullock, R. M.; Samsel, E. G. *J. Am. Chem. Soc.* **1987**, *109*, 6542. (f) Tada, M.; Inoue, K.; Okabe, M. *Chem. Lett.* **1986**, 703. (g) Molander, G. A.; Kenny, C. *J. Am. Chem. Soc.* **1989**, *111*, 8236.

[4] (a) Nugent, W. A.; RajanBabu, T. V. *J. Am. Chem. Soc.* **1988**, *110*, 8561. (b) RajanBabu, T. V.; Nugent, W. A. *J. Am. Chem. Soc.* **1989**, *111*, 4525. (c) RajanBabu, T. V.; Nugent, W. A.; Beattie, M. S. *J. Am. Chem. Soc.* **1990**, *112*, 6408. (d) RajanBabu, T. V.; Nugent, W. A. *Chem. Scr.* **1989**, *29*, 439.

[5] For reviews of metal-centered radicals, see: (a) *Organometallic Radical Processes*; Trogler, W. C., Ed.; Elsevier: New York, 1990. (b) Astruc, D. *Acc. Chem. Res.* **1991**, *24*, 36. (c) Baird, M. C. *Chem. Rev.* **1988**, *88*, 1217. (d) Stiegman, A. E.; Tyler, D. R. *Comments Inorg. Chem.* **1986**, *5*, 215. (e) Espenson, J. H. *Prog. Inorg. Chem.* **1983**, *30*, 189. (f) Drago, R. S. *Coord. Chem. Rev.* **1980**, *32*, 97. (g) Kochi, J. K. *Organometallic Mechanisms and Catalysis*; Academic Press: New York, 1978.

[6] Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, 1987.

[7] For reviews on the chemistry of Fischer carbene complexes, see: (a) Wulff, W. D. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: New York, 1990; Vol. 5. (b) Wulff, W. D. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press Inc.: Greenwich, CT, 1989; Vol. 1. (c) *Advances in Metal Carbene Chemistry*; Schubert, U., Ed.; Kluwer Academic Publishers: Hingham, MA, 1989. (d) Wulff, W. D.; Tang, P.-C.; Chan, K.-S.; McCallum, J. S.; Yang, D. C.; Gilbertson, S. R. *Tetrahedron* **1985**, *41*, 5813. (e) Dötz, K. H.; Fischer, H.; Hofmann, P.; Kreissel, F. R.; Schubert, U.; Weiss, K. *Transition Metal Carbene Complexes*; Verlag Chemie: Deerfield Beach, FL, 1984. (f) Dötz, K. H. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 587.

[8] Curran, D. P. *Synthesis* **1988**, 417, 489.

[9] All new compounds were fully characterized by ^{1}H NMR, ^{13}C NMR, and infrared spectroscopy, and elemental composition was established by combustion analysis and/or high-resolution mass spectroscopy.

[10] The cyclic carbene complexes were found to be much more stable compared to the acyclic hydroxycarbene complexes.

[11] For reactions of carbene anions with epoxides, see: Lattuada, L.; Licandro, E.; Maiorana, S.; Molinari, H.; Papagni, A. *Organometallics* **1991**, *10*, 807.

[12] The proton geminal to the alkoxy substituent appeared as a triplet of doublets (J = 11.1, 4.4 Hz) at 4.09 ppm in the ^{1}H NMR spectrum.

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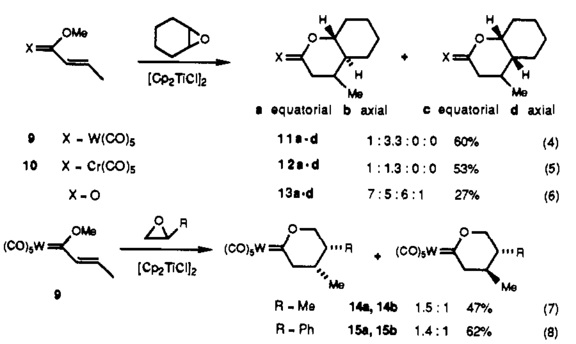
low yield of a 7:5:6:1 mixture of epimeric trans- and cis-fused products (eq 6). Thus, the carbene complexes **9** and **10** are superior radical traps compared to methyl crotonate in terms of reactivity, stereoselectivity, and yield.[13,14]



Central to this comparison is the β-substituent, which is known to inhibit intermolecular radical coupling reactions of unsaturated esters.[15] The principle organic radical acceptors containing substituents at the reacting center that readily participate in intermolecular radical coupling reactions are vinyl nitro compounds and unsaturated diesters.[16,17] The reactivity of unsaturated carbene complexes overcomes the steric inhibition induced by the β-substituent, allowing reaction at lower temperatures and in a nearly 1:1 ratio of substrate and radical, whereas the organic analogues generally require ratios of 10:1.[1,4,8] Therefore, these reactions can serve to construct functionalized carbene complexes and, potentially, serve as synthons for β-substituted esters.[13,17b,18]

The reaction mechanism involves generation of a β-alkoxy radical, addition to the unsaturated carbene complex, and trapping of a novel metal carbene α-radical by a second equivalent of titanocene monochloride. In terms of regioselectivity, the β-position of an α,β-unsaturated carbene complex proves to be more reactive toward alkyl radicals than the carbene carbon; no products arising from addition to the carbene carbon have been isolated. This contrasts with nucleophilic addition reactions where competing addition to both the carbene carbon and β-carbons has been observed.[19,20] Thus, the softer nature of alkyl radicals provides a regioselective reaction to functionalize the β-position. The exclusive formation of trans-fused bicyclic systems is in stark contrast with organic esters, which produce 1:1 or 2:1 mixtures of isomers.[4] This reflects selective equatorial reaction of the cyclohexyl radical with the carbene complexes due to the greater steric demands of the complexes as compared to esters.[21] The origins of the modest β-diastereoselectivity are under study and are possibly related to the nature of the radical acceptor as evidenced by the lower stereoselectivity of the less electrophilic, but equally effective, chromium carbene complexes. Note that at least 90% of the titanium can be recovered from these reactions by filtration of the bright red microcrystalline Cp_2TiCl_2 formed upon quenching with ethereal HCl.

In summary, we have demonstrated the first intermolecular couplings of organic radicals and unsaturated Fischer carbene complexes which proceed in good yields with excellent diastereoselectivity for trans ring junctions when cyclic epoxides are used, provide modest diastereoselectivity at the position β to the carbene, and serve as synthons for β-substituted esters. Current experiments will address the nature of the intermediate metal carbene α-radicals, enhance the diastereoselectivity of the reactions, test the potential for intramolecular reactions, and explore other metal-templated radical reactions.

Acknowledgment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the UCLA Academic Senate, Committee on Research, for support of this research.

Supplementary Material Available: General experimental procedure and spectral and analytical data for compounds **2**, **3**, **5a,b**, **7a,b**, **8**, **11a,b**, **12a,b**, **13a–d**, **14a,b**, and **15a,b** (4 pages). Ordering information is given on any current masthead page.

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(13) It should be noted that the product carbene complexes can be oxidized with ceric ammonium nitrate to provide esters and lactones, thus demonstrating the equivalence of the metal carbene complexes and the organic carbonyl compounds. (a) Casey, C. P.; Boggs, R. A.; Anderson, R. L. *J. Am. Chem. Soc.* **1972**, *94*, 8947. (b) Dötz, K. H.; Fügen-Köster, B.; Neugebauer, D. *J. Organomet. Chem.* **1979**, *182*, 489.

(14) An analogous test reaction employing methyl cinnamate failed to provide any coupled product.

(15) (a) Giese, B. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 771. (b) Giese, B.; Lachhein, S. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 967.

(16) For example, see: (a) Barton, D. H. R.; Togo, H.; Zard, S. Z. *Tetrahedron* **1985**, *41*, 5507. (b) Scott, D. M.; McPhail, A. T.; Porter, N. A. *Tetrahedron Lett.* **1990**, *31*, 1679.

(17) For β-substituted unsaturated nitrile acceptors, see: (a) Giese, B.; Kopping, B.; Chatgilialoglu, C. *Tetrahedron Lett.* **1989**, *30*, 681. (b) Giese, B.; Harnisch, H.; Lachhein, S. *Synthesis* **1983**, 733.

(18) However, β-unsubstituted vinyl carbene complexes are so reactive that extensive polymerization occurs in the reaction.

(19) (a) Casey, C. P.; Brunsvold, W. R. *J. Organomet. Chem.* **1974**, *77*, 345. (b) Casey, C. P.; Brunsvold, W. R. *Inorg. Chem.* **1977**, *16*, 391. (c) Fischer, E. O.; Kalder, H. J. *J. Organomet. Chem.* **1977**, *131*, 57.

(20) For recent examples of selective reaction, see: (a) Macomber, D. W.; Hung, M.-H.; Madhukar, P.; Liang, M.; Rogers, R. D. *Organometallics* **1991**, *10*, 737. (b) Wulff, W. D.; Wang, S. L. B. *J. Am. Chem. Soc.* **1990**, *112*, 4550.

(21) Interestingly, reaction of **9** with cyclopentene oxide also only produces trans-substituted products.

Stereoelectronic Effects on the Stabilities of Anions and Radicals Derived from 2-Benzoylperhydropyrimidines

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The rate of removal of either a proton or a hydrogen atom from a C–H bond adjacent to a nitrogen or oxygen atom has been shown by theory and experiment to be subject to stereoelectronic control because of interactions of the lone pairs on these atoms with the carbanion or carbon-centered radical being formed. The size of the destabilizing interactions in carbanion formation will depend on the dihedral angle between the p (or sp^3) orbital of the carbanion and the lone-pair orbital on nitrogen or oxygen, being maximal when the angle is 0° and minimal when it is 90°.[1] In radical formation these interactions are stabilizing because of the formation of a three-electron bond.[2] The stereoelectronic theory has been supported by the observation of rate retardations in the removal of a proton[1] and rate accelerations in the removal of a hydrogen atom.[3] But these effects are small, and there is a paucity of thermodynamic information concerning their size.[4] In this paper we present quantitative thermodynamic information on these questions.

The α-dimethylamino group in $PhCOCH_2NMe_2$ increases the acidity of acetophenone in DMSO by 1.8 kcal/mol because of

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(1) Hine and Dalsin (Hine, J.; Dalsin, P. D. *J. Am. Chem. Soc.* **1972**, *94*, 6998–7002) observed a 5-fold rate retardation for α-deprotonation by MeO^- in MeOH of methyl 1,3-dioxolane-2-carboxylate relative to methyl cyclopentanecarboxylate.

(2) (a) Wolfe, S.; Schlegel, H. B.; Whangbo, M. H.; Bernardi, F. *Can. J. Chem.* **1974**, *52*, 3787–3792. (b) Baird, N. C. *J. Chem. Educ.* **1977**, *54*, 291–293. (c) Pasto, D. J.; Krananansky, R.; Zercher, C. *J. Org. Chem.* **1987**, *52*, 3062–3072.

(3) (a) Hayday, K.; McKelvey, R. D. *J. Org. Chem.* **1976**, *41*, 2222–2223. (b) Malatesta and Ingold (Malatesta, V.; Ingold, K. U. *J. Am. Chem. Soc.* **1981**, *103*, 609–614) observed an 8.8-fold rate acceleration for abstraction of the C-2 α-hydrogen atom from 1,3-dioxolane by the t-BuO$^\bullet$ radical, relative to abstraction of the α-hydrogen atom in tetrahydrofuran. (c) Beckwith and Easton (Beckwith, A. I. J.; Easton, C. J. *J. Am. Chem. Soc.* **1981**, *103*, 615–619) observed that the C-2 axial hydrogen atom in *cis*-2-methoxy-4,6-dimethyl-1,3-dioxane was abstracted by the t-BuO$^\bullet$ radical 8.7 times more readily than the equatorial C-2 hydrogen atom in the trans isomer.

(4) It has been shown, however, that destabilization of the pyrazolide ion by four-electron repulsions between the electrons on the adjacent nitrogen atoms causes pyrazole to be 3.6 kcal/mol less acidic in the gas phase and 1.8 kcal/mol less acidic in DMSO than imidazole.[5]

(5) Taft, R. W.; Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 463–469.

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