

Stereochemistry of Intermolecular Radical Reactions of Unsaturated Tungsten Carbene Complexes

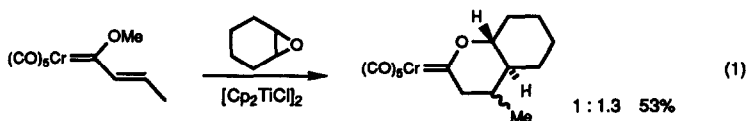
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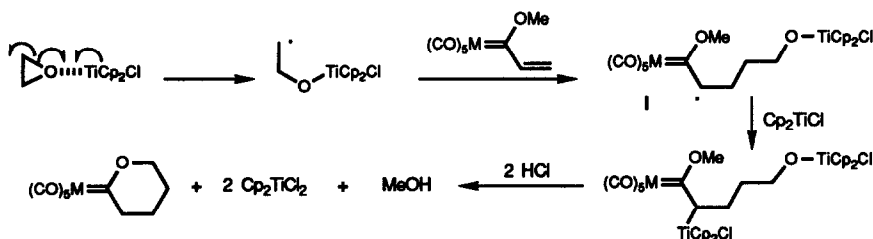
Abstract: *The stereoselectivity of radical coupling reactions between unsaturated tungsten carbene complexes and epoxides is reported. Cyclic epoxides are found to give high levels of selectivity. A model is proposed to explain the stereochemical control.*

Reactions employing radical intermediates have produced a remarkable diversity of chemistry.¹ Recently, much attention has focused on the stereochemical control of radical processes and some impressive results have been reported.² A novel approach to control radical selectivity is the use of transition metal fragments as templates to direct regiochemistry and stereochemistry through steric and or electronic effects as has been utilized in synthetic applications of nucleophilic and electrophilic additions to polyene and polyenyl organometallic complexes.³ This strategy would complement the generation of organic radicals by transition metal complexes^{4,5} and extend the chemistry of odd electron count organometallic complexes that have been isolated and characterized.⁶ We are investigating coupling reactions, cyclizations and other radical processes in metal coordinated polyene and polyenyl systems and report herein on the stereoselectivity of radical coupling reactions of tungsten carbene complexes and alkyl radicals generated from epoxides.

Recently, we reported the first coupling reactions of organic radicals with Fischer carbene complexes (e.g. eq 1).^{7,8} These reactions demonstrated that α,β -unsaturated chromium and tungsten carbene complexes efficiently trap alkyl radicals in a regioselective, frontier molecular orbital controlled, addition to the β -position. A key point was that the reactivity of unsaturated carbene complexes overcame the steric inhibition induced by β -substituents, which are known to inhibit many intermolecular radical coupling reactions.⁹ The reactions also exhibited interesting stereochemical control by forming trans-fused bicyclic systems exclusively. This is in marked contrast with unsaturated esters which produce 1:1 to 2:1 mixtures of isomers from analogous reactions.⁵ The method of Nugent and RajanBabu⁵ was employed to generate radicals by reaction of titanocene monochloride dimer with epoxides. We utilized this stoichiometric generation of alkyl radicals, rather than the typical radical chain processes,¹ due to uncertainties associated with the radical propagating abilities of the organometallic radical intermediate I shown in the overall mechanism in Scheme 1.



Scheme 1



Intrigued by the potential of carbene complexes to control stereochemistry, we investigated this further. Table I presents the results of radical coupling reactions between tungsten carbene complexes and epoxides.^{10,11} In entries 1 through 5, the product tetrahydropyranylidene complexes contain only trans ring fusions as evidenced by typical triplet of doublets coupling patterns ($J = 11, 4$ Hz) for the methine protons geminal to oxygen. The diastereoselectivity at the β -position is strongly dependent on the size of the β -substituent. The equatorial isomer is obtained as the major product when the β -substituent is phenyl, but the axial isomer predominated when the substituent is methyl. Carbene complex 3, with a large isopropyl substituent similar in size to a phenyl group,¹² yields nearly the same diastereoselectivity as 1. The selectivity also depends on the geometry of the starting vinyl carbene complex (entries 3-5). Starting with cyclopentene oxide, only two products, epimeric at the β -position, are obtained with only one cyclized to the trans tetrahydropyranylidene complex via intramolecular alcoholysis (entry 6). The modest stereoselectivity observed at the β -position in reactions with cyclohexene oxide is diminished when acyclic epoxides are utilized (entries 7-9). As expected, the stereochemistry of an acyclic epoxide is found to be lost in the radical coupling reaction (entry 9).

A model to explain the observed stereoselectivities is illustrated in Scheme 2. The selectivity for trans substitution on the cyclohexane ring is determined by the facial selectivity of approach of the carbene to the cyclohexyl radical. The relatively large carbene complexes approach exclusively from an equatorial position in contrast with small organic acceptors such as methyl acrylate which react from both equatorial and axial positions.^{5,13,14} A diaxial conformation of the cyclohexyl radical, obviously unfavored as a ground state, is unlikely as a transition state due to the resulting lack of steric interactions that would lead to β -position selectivity. The β -position stereochemistry (II vs III) is determined by the facial selectivity on the carbene component in the transition state. This selectivity will be influenced by a number of interactions and the differences in energies between potential transition state conformations are small, but staggered geometries can be assumed. The acceptor will approach the cyclohexyl radical with a large substituent ($R_L = \text{Ph, iPr}$) oriented away from the alkoxytitanium substituent as in path A. With a small β -substituent ($R_S = \text{Me}$), path B becomes dominant as steric interactions with the bulky carbene moiety prevail. In contrast, the cis substrate 5b shows essentially no preference for either transition state. The β -position stereoselectivity observed here has not been adequately addressed in the literature.^{2,14} Exclusive trans substitution in 7a,b is in accord with precedent.¹³ Intermediate radicals derived from acyclic epoxides lack any stereochemical rigidity, therefore little or no selectivity is found between the β and γ -positions.¹⁵

Scheme 2

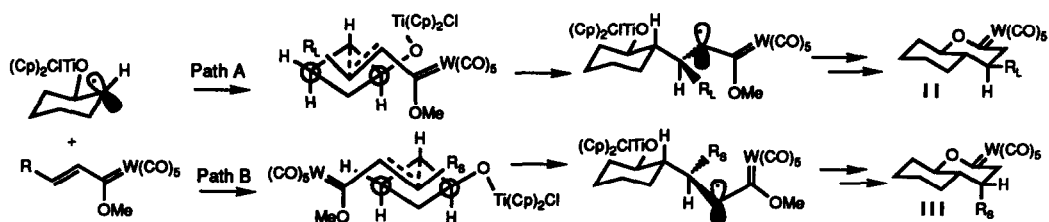


Table I. Radical Coupling of Tungsten Carbene Complexes and Epoxides

Entry	Carbene	Epoxide	Products	Ratio	Yield
1				3.5 : 1	56%
2				3.6 : 1	74%
3	100 : 0 E : Z			1 : 3.3	60%
4	50 : 50 E : Z			1 : 2.0	54%
5	12 : 88 E : Z			1 : 1.3	71%
6				1 : 1.2	54%
7				1.5 : 1	47%
8				1.4 : 1	62%
9				34 : 26 : 29 : 11	82%

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- In a typical reaction, cyclohexene oxide (1.5 equiv) and titanocene monochloride dimer (1.5 equiv) were added simultaneously via syringe pump to a solution of carbene complex cooled to -20°C. After an ethereal HCl (3 equiv) quench, the coupled adducts were obtained in addition to titanocene dichloride.
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