

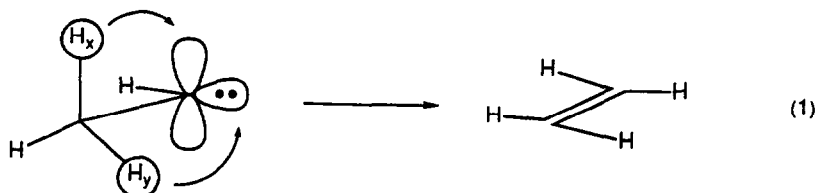
Hydrogen Rearrangements in Carbenes. Inherent H_{ax}/H_{eq} Migration Ratios in Thermal and Photic Bamford-Stevens Reactions.

Alex Nickon,* Alfred G. Stern, and Martin C. Ilao

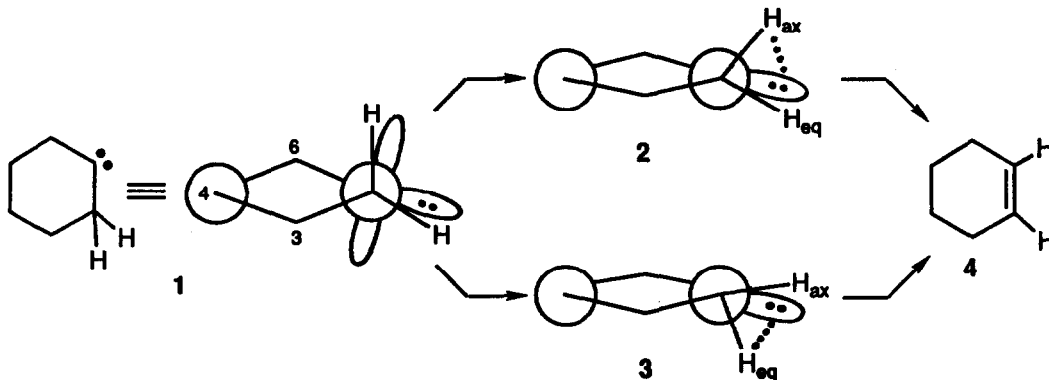
Department of Chemistry, The Johns Hopkins University, Baltimore, MD 21218-2685

Abstract: Singlet carbenes were generated from doubly labeled homobrexanones by thermolysis and by photolysis of their *p*-tosylhydrazone lithium salts. The carbenes undergo competitive 1,3-insertion and 1,2-H shift. After correction for k_H/k_D isotope effects the inherent H_{ax}/H_{eq} shift ratios were 1.7 for the carbene generated thermally and 1.2 for the carbene obtained photically. The six-membered ring in the homobrexane skeleton cannot adopt a boat shape, so these ratios are free of any chair-boat ambiguities.

Hydrogen shifts in singlet carbenes have received abundant attention from theoreticians.^{1,2} For example, about 20 different computational treatments have been reported for the rearrangement of methyl carbene to ethylene (Eq. 1) and have predicted activation energies (E_a) that range from about 0-27 kcal/mol.^{2b-m} With regard to stereochemistry, most³ of these calculations predict a lower E_a for shift of H_x than for shift of H_y .⁴



Theoreticians have also focussed on cyclohexylidene (1), because axial H and equatorial H adjacent to the carbene carbon possess, respectively, bond and orbital alignments similar to those typified by H_x and H_y in Eq. 1. According to computations by Bodor and Dewar^{2b} and by Altmann, Tee, and Yates,^{2f} a high H_{ax}/H_{eq} shift preference in 1 was to be expected.

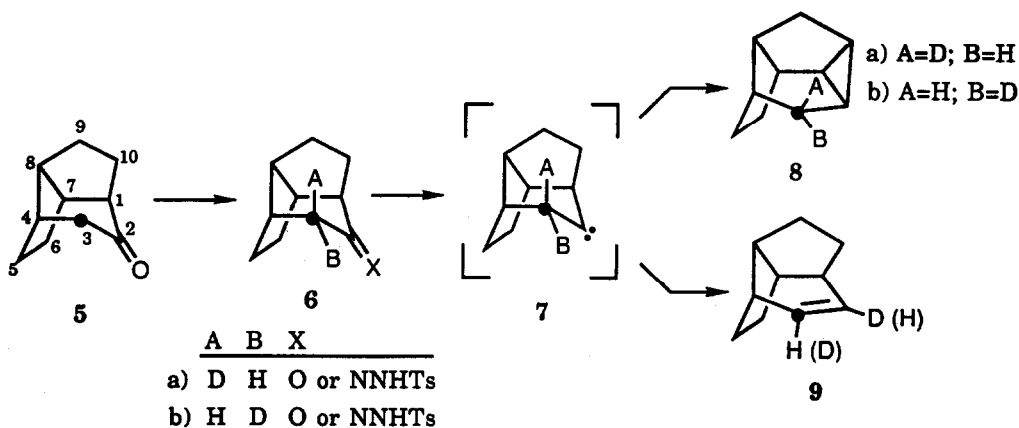


The first experiments dealing with the H_{ax} vs H_{eq} issue were published by Shechter and co-workers, who examined substituted cyclohexylidenes involving competitive migrations of *tert*-H vs *sec*-H. They generated their carbenes by thermolysis of *p*-tosylhydrazone salts (Bamford-Stevens reaction) and reported a preference for H_{ax} over H_{eq} shift.⁵ However, the magnitude of this preference could not be reliably quantified because of uncertainties about the influence of the bystander substituent in the *tert*-H vs *sec*-H competition and also about the possible role of boat-like conformations. To circumvent the first uncertainty, Kyba and John studied *sec*-H vs *sec*-D competition in thermolysis (155°C) of an epimeric pair of *p*-tosylhydrazone salts.⁶ They arrived at an H_{ax}/H_{eq} migration ratio of 1.5 (after correction for a k_H/k_D isotope effect, estimated at -1.9).

This unexpectedly low *ax*/*eq* preference contravened the prevailing theoretical predictions;^{2b,f} however, subsequent MNDO and MINDO/3 calculations by Kyba^{2h} and *ab initio* treatments by Evanseck and Houk²ⁱ accommodated that experimental result.⁷ According to these later calculations the H_{ax}/H_{eq} selectivity is low because both transition states strikingly resemble each other: viz., non-migrating groups adopt a flat, alkene-like disposition, and the migrating H is bent toward the erstwhile vacant orbital (cf. 2 and 3). Purportedly, the E_a needed to achieve this flattened geometry for H_{ax} shift (i.e. 1 \rightarrow 2) and for H_{eq} shift (i.e. 1 \rightarrow 3) are virtually the same, notwithstanding the distinctly different initial alignments in 1.⁸

Does the experimental ratio of 1.5 mean that starting orbital alignments are unimportant? Or could this low *ax*/*eq* ratio arise from some other feature of the substrate or of the experimental methodology? For example, chair \rightleftharpoons twist boat interconversion drastically alters the alignments between C—H bonds and carbenic orbitals and therefore could obfuscate interpretation. Possible intervention by boats has been suggested by Seghers and Shechter⁵ and also by Kyba and John⁶ but has not been resolved conclusively. The issue is problematic because boats could play a role at any stage of the thermal Bamford-Stevens sequence (tosylhydrazone salt, diazohydrocarbon, or carbene). And in the tosylhydrazone salt, possible *E-Z* isomerization about C=N could, through allylic 1,3-strain, also influence chair-boat populations.⁹

In view of the importance of an unambiguous experimental H_{ax}/H_{eq} ratio as a benchmark for theorists and for analysis of more complicated cyclohexylidenes, we undertook to study a system free of chair-boat and other ambiguities. Such a system is homobrexan-2-one (5), in which the 6-membered ring cannot convert to a twist boat because of constraint by the two ethano bridges.



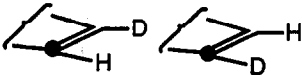
We synthesized ketone **5** labeled fully with ^{13}C at C-3 ($\bullet = ^{13}\text{C}$) by a reported route¹⁰ except for our use of $\text{Me}_3\text{Si}^{13}\text{CN}$ in place of the natural abundance reagent.¹¹ Labeled **5** was converted to the axial-d analog **6a** ($\text{X}=\text{O}$) and also to equatorial-d epimer **6b** ($\text{X}=\text{O}$) by highly selective H/D exchanges developed earlier,^{10,11} and each was converted to its corresponding *p*-tosylhydrazone ($\text{X} = \text{NNHTs}$) under conditions that preserved D stereochemistry (see later for proof). Each tosylhydrazone was treated with *t*-BuLi (~ 1 eq), and the dry Li salt was heated (neat) to generate the respective carbene (**7**). The volatile products consisted essentially of tetracyclic hydrocarbon **8** (from 1,3-insertion) and alkene **9** (from H or D shift) in a 3:1 ratio.

The tetracycle from each precursor was separated and purified, and each showed a distinct ^2H NMR spectrum. In **8a** (from **6a**) a strong deuterium doublet (coupling with ^{13}C , $J \sim 20\text{Hz}$) appeared at δ 1.98 and a weak doublet at δ 1.43. Tetracycle **8b** (from **6b**) showed the same two doublets, but with reversed intensities (weak at 1.98; strong at 1.43). Clearly, the chemical shift of D in **8** depends on its configuration. Importantly, in each tetracycle the relative intensity of the weak doublet corresponded virtually quantitatively to the amount of d_2 species plus the small proportion of epimeric d_1 species in the precursor tosylhydrazone. These NMR results establish unequivocally that D has not altered its stereochemical integrity at any stage of the sequence $6(\text{X}=\text{NNHTs}) \rightarrow 7 \rightarrow 8$, either by epimerization or by any internal H or D transfers at the Li salt stage.¹²

With assurance that initial D stereochemistry is completely intact in transient carbene **7**, consider now isomerization of **7** to alkene **9** by H or D shift. In the ^1H NMR of the hydrocarbon mixture, the vinyl H attached to ^{13}C (by virtue of its large, one-bond coupling, $J_{\text{HC}} = 158 \text{ Hz}$) is readily distinguished from the other vinyl H.¹³ After correction for d_0 species the proportions of the two monodeuterated alkenes are as summarized in the Table. These proportions reflect not only ax vs eq competition, but also H/D isotope effects. By making the usual assumption^{6,14} that isotope effects are equal for axial and equatorial shift we evaluated and corrected for $k_{\text{H}}/k_{\text{D}}$ and arrived at $\text{H}_{\text{ax}}/\text{H}_{\text{eq}} \sim 1.7$ (see Table). Furthermore, as no $\text{H}_{\text{ax}}/\text{H}_{\text{eq}}$ ratios are available for carbenes generated photochemically, we also conducted parallel studies of irradiation of the Li salts (Hg lamp, Pyrex filter) and found $\text{H}_{\text{ax}}/\text{H}_{\text{eq}} \sim 1.2$. These numbers are free of possible conformational ambiguity, and we recommend them as the inherent $\text{H}_{\text{ax}}/\text{H}_{\text{eq}}$ migration ratios, to be used for analysis of more complicated cases.¹⁵

Finally, we stress that when ax/eq ratios are obtained by H vs D competitions, the presumption is made that $k_{\text{H}}/k_{\text{D}}$ isotope effects are equal for the two pathways. Although this presumption is reasonable, it is yet to be validated. In this connection, note that unusually high H/D isotope effects have recently been reported for

Axial/Equatorial Migration Ratios in Thermolysis and Photolysis of Homobrexan-2-one *p*-Tosylhydrazone Li Salts.

Precursor ($\text{X}=\text{NNLiTs}$)	Conditions	Alkenes 9 (Rel. Amt's) 	Isotope Effect $k_{\text{H}}/k_{\text{D}}$	Migration Ratio $\text{H}_{\text{ax}}/\text{H}_{\text{eq}}$
6a	Thermolysis 120-160°C neat	1 : 1.32	2.3	1.73
6b		1 : 4.00		
6a	Photolysis 25°C, pentane	1 : 1.14	1.3	1.17
6b		1 : 1.58		

some carbenes generated by photolysis.¹⁶ And note also that a large dissimilarity (factor of 4.4!) in isotope effect has been found for axial and equatorial trajectories in a photo-induced retro rearrangement of a cyclohexene \rightarrow a cyclohexylidene.¹¹

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- However, see MINDO/3 and MNDO treatments by Kyba^{2h} and various levels of ab initio calculations.²ⁱ
- The commonly accepted model for CH₂: in its lowest singlet state (notation ¹A₁) has both nonbonding electrons in an in-plane sp²-like orbital and was proposed by Hoffman et al.^{2a} Some researchers favor a model in which these spin-paired electrons individually occupy sp³-like orbitals. See Sironi, M.; Raimondi, M.; Cooper, D. L.; Gerratt, J. *J. Chem. Soc. Faraday Trans. 2* **1987**, *83*, 1651-1661.
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- Their calculated values of E_a differed widely among computational methods. But within a given method the E_a for H_{ax} and H_{eq} shift were about equal.
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