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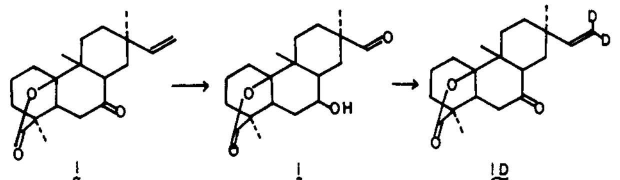

i i 1D

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(30) This work was supported by the National Science Foundation (PCM 74-07924) and by a grant from the Eli Lilly Co. The Bruker HX 270 facility is supported by NIH Grant No. 1-P07-PR00798 from the Division of Research Resources.

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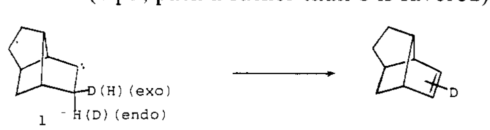
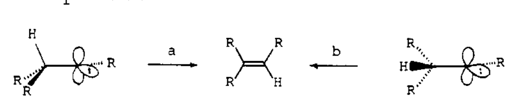
4-*tert*-Butyl-2,2-dimethylcyclohexylidene. A Surprising Lack of Stereoselectivity in a 1,2-Hydrogen Shift to an Alkylcarbene

Sir:

Recently it was reported that the exo/endo-H migratory ratio in brexan-5-ylidene **1** was 138 (eq 1).[1] Examination of models indicates that **1** is sufficiently distorted so that the exo H is much closer to alignment with the empty p orbital on the carbene center than is the endo H. Thus the migratory ratio greatly favoring exo-H migration might be interpreted as an affirmation of a number of theoretical predictions which state that the hydrogen which migrates is that which aligns with the empty p orbital (eq 2, path a rather than b is favored).[2] Our

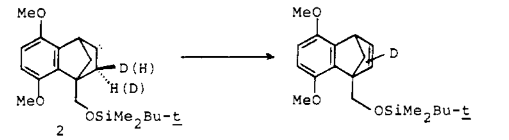


(1)



(2)

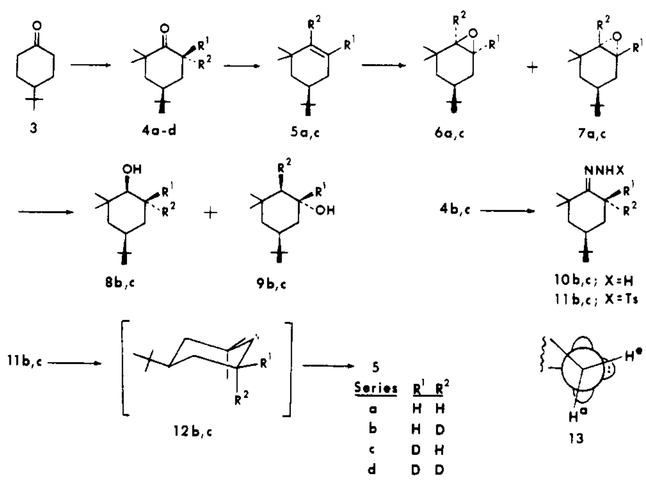
more recent work indicated, however, that cautious interpretations of the elegant experimental work of Nickon and his coworkers were in order, since, in an apparently unbiased[3] bicyclo[2.2.1]carbene **2** (eq 3), the exo-H/endo-H preference was 13 (at 190 °C).[4] Thus it might be that factors other than stereoelectronic control are operative in bicyclo[2.2.1]carbene systems.



(3)

To investigate stereoelectronic control of 1,2-H shifts in alkylcarbenes without the attendant ambiguities described above, we chose the substituted cyclohexylidene **12** as the reactive intermediate to be studied. Inspection of a Dreiding model of **12** indicates that this conformationally rigid carbene[5] has the axial hydrogen atom (H^a) ~10° away from alignment with the empty orbital and the equatorial hydrogen (H^e) is ~10° away from alignment with the sp^2 orbital as shown by the Newman projection **13.** Thus this system appeared to be an excellent choice to probe the question of stereoelectronic control of 1,2-H shifts in alkylcarbenes.

The synthesis of the carbene precursors **11** began with 4-*tert*-butylcyclohexanone (**3**), which was converted in 40%



overall yield to ketone **4a**[6] via Coates' procedure[7] of reduction-alkylation of the *n*-butylthiomethylene derivative of **3.**[8] Olefin **5a**[9] was obtained in 65% overall yield from **4a** by the thermolysis (525 °C) of a pentane solution of the acetates of the alcohols derived from the $LiAlH_4$ reduction of **4a.** Epoxidation of **5a** with MCPBA in chloroform solution gave a 1:4 mixture of cis and trans epoxides **6a** and **7a** (85%), which was reduced with $LiAlD_4/AlCl_3$ (2.5/1 mol ratio)[10] in ether to give alcohols **8b** and **9b** in quantitative yield. Alcohol **8b**[6] was obtained pure (41% from the epoxides) by careful fractional crystallizations from hexane of the *p*-nitrobenzoates of **8b** and **9b,** followed by hydrolysis (KOH/MeOH). Brown oxidation[11] of **8b** gave **4b** (83%), with $d_0{:}d_1{:}d_2$ = 2:98:0.[12a] Ketone **4a** was converted to **4d** ($d_0{:}d_1{:}d_2$ = 1:5:94) by a series of exchange reactions using DO^-/D_2O/THF, and **4d** was then transformed into **4c** ($d_0{:}d_1{:}d_2$ = 5:95:0)[12b] through the above-described series of reactions, except that the epoxides **6c** and **7c** were opened by $LiAlH_4/AlCl_3$.

Our attempts to generate **11b** and **11c** by reaction of ketones **4b** and **4c** with *p*-toluenesulfonyl hydrazide were thwarted because all such reactions, under a variety of conditions, led to extensive loss of deuterium.[13] We discovered, however, that reaction of **4b** and **4c** with distilled, anhydrous hydrazine[14] in refluxing methanol for 18 h gave hydrazones **10b** and **10c** (70%) with no exchange. Treatment of **10b** with 1 equiv of *n*-BuLi in ether at −78 °C and then addition of the resulting solution to tosyl chloride (1.4 equiv) in THF at −78 °C gave a mixture containing two major components, one of which was

Table I. Relative Yields of Olefins via the Bamford-Stevens Route from Ketones **4b,c**[a]

Starting ketone	Relative yields olefins[b] 5a	5b	5c	Migratory ratio of a/e
4b (D^a)	7.1[c]	41.3	51.6	0.80 (D/H)[e]
4c (D^e)	5.2[d]	25.0	69.8	2.8 (H/D)

[a] Results tabulated are averages of at least two duplicate runs which agreed to better than 5% of the value being determined. [b] The ratio of **5a**/(**5b** + **5c**) was determined mass spectrometrically. The ratio of **5b**/**5c** was determined by ^{1}H NMR (100 MHz); see ref 15. [c] This value corresponds to 5% H/D exchange from **4b.** [d] This value corresponds to 0% H/D exchange from **4c.** [e] This value was obtained in both the absence and presence of 8 equiv of TMEDA in the thermolysis of the lithium salt of the tosyl hydrazone.

11b (~70%) and the other which we suspect to be the bis(tosyl)hydrazone derivative. Rapid chromatography on silica gel (contact time ~5 min) gave the pure tosylhydrazone (70%), but with ~20% H-D exchange. Because of this exchange problem, we carried out the Bamford-Stevens reaction on the above-described mixture by adding a second equivalent of *n*-BuLi at −78 °C. The resulting solution was warmed to room temperature, concentrated, and evacuated at 40 °C (10 μ). The solid residue was suspended in dry, degassed cyclohexane and rapidly heated to 155 °C by immersing a sealed tube containing the mixture in an oil bath. The decomposition was complete in 5 min. A simple aqueous extraction, followed by removal of the cyclohexane and chromatography on alumina (pentane), gave a mixture of **5a–c** in yields of 40–50%. Table I shows the relative yields of the olefins which were arrived at mass spectrometrically and by ^{1}H NMR.[15] A similar sequence of steps starting with **4c** gave the data also shown in Table I.[16]

The data in Table I can now be used to determine the H^a/H^e migratory ratio, assuming that the deuterium isotope effect is the same for both axial and equatorial positions.[17,18] This leads to an isotope effect of 1.9 and a surprisingly small migratory ratio, H^a/H^e of 1.5. To test whether or not equilibration between a chair and twist-boat conformation might be the cause of the low selectivity, we used ketone **4a** as a model for **12.** We established that the ^{1}H NMR spectrum of **4a** was invariant from −70–110 °C (the temperature at which the Bamford-Stevens reaction is relatively rapid), indicating a single major (chair) conformer.[19] Control experiments which involved partial decompositions of the lithium salts of **11b** and **11c** established that these did not interconvert, as would be expected.

These data thus show minimal stereoselectivity in 1,2-H shifts in alkylcarbenes. It is interesting to note also that these results agree with the results of Seghers and Shechter[21] for 1,2-phenyl migration to a cyclohexylidene center but do not coincide with the least motion calculations carried out recently, in which there was "an overwhelming preference" [2g] for axial H migration in cyclohexylidene. We have investigated these rearrangements using semiempirical molecular orbital methods and the results are described in the following paper.

Acknowledgment. Grateful acknowledgment is made to the Robert A. Welch Foundation (F-573) for support of this work.

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(13) Even under strictly aprotic conditions (aside from the reagents) such as anhydrous THF, deuterium loss was extensive (~75%). It also noted that recovered ketone, in a reaction terminated prior to completion, had *not* lost deuterium.
(14) Anhydrous hydrazine stored over potassium hydroxide pellets led to ~20% exchange, and thus storage over KOH was avoided.
(15) At 100 MHz in deuteriochloroform solution, the olefinic protons in **5a** exhibited an AB quartet centered at δ 5.49 (J_{AB} = 10.0 Hz, ν_{AB} = 15.6 Hz), with the downfield doublet (R^1) split cleanly into doublets of doublets (J_{AC} = 4.9 Hz, J_{AD} = 1.9 Hz) owing to coupling with the pseudoaxial and equatorial protons of the methylene unit α to the double bond. The upfield doublet (R^2) was broadened into narrow, ill-resolved multiplets. The determination of the ratio of **5b** to **5c** involved planimetric integrations of multiple scans at a sweep width of 250 Hz of the A and B portions of the above-described AB quartet. Subtraction from each portion of the amount of d_0 (**5a**) present (determined by mass spectrum) then led directly to the ratio of **5b** to **5c.**
(16) It should be noted that the Bamford-Stevens reaction carried out on the partially exchanged **11b** or **11c** isolated by rapid column chromatography gave results essentially the same as those in Table I, but with greater uncertainty, since a d_0/d_1 ratio of 20/80 corresponds to d_0 (which has two olefinic protons) contributing 33% of the absorption in the olefinic region in the NMR. Since this must be subtracted to obtain the absorption due to d_1 material, an appreciable uncertainty arises in the derived migratory aptitudes.
(17) If x = deuterium isotope effect and y = the migratory ratio of H^a/H^e, then from the last column the following equations can be derived: $xy = 2.8$ and $y/x = 0.8$. This leads to $x = 1.9$ and $y = 1.5$.
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(19) In acetone-d_6 at 100 MHz, the α-axial proton (R^2 in **4a**) is sufficiently deshielded to be observed cleanly: δ 2.61 (d of d of d, J_{gem} = 14.3 Hz, J_{a-a} = 13.2 Hz, J_{a-e} = 5.7 Hz), where coupling is observed with the axial and equatorial protons on the β-methylene unit. The assignments were confirmed by observation of the spectra of **4b** and **4c.** These coupling constants are in excellent agreement with those determined for the analogous protons in **3**,[20] indicating that the *gem*-dimethyl groups at the 2 position in **4** do not appreciably change the conformation of **4** relative to **3.**
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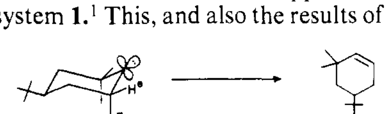
Masked Stereoelectronic Control of 1,2-Hydrogen Shifts to an Alkylcarbene Center. A MINDO/3 and MNDO Study

Sir:

Recently we reported that little stereoelectronic control of 1,2-H shifts to a carbene center was apparent in the cyclohexylidene system **1.**[1] This, and also the results of Seghers and



1 $H^a/H^e = 1.5$

Shechter,[2] appeared to sharply contradict the theoretical considerations of a number of groups,[3] who stated that axial or axial-like (i.e., toward the empty orbital) migration should