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EFFECT OF REMOTE HETEROATOM SUBSTITUENTS ON STEREOCHEMISTRY IN 1,2 H MIGRATION TO DIVALENT CARBON. EVIDENCE FOR "NEGATIVE" HYPERCONJUGATION OF CARBENE LONE PAIR

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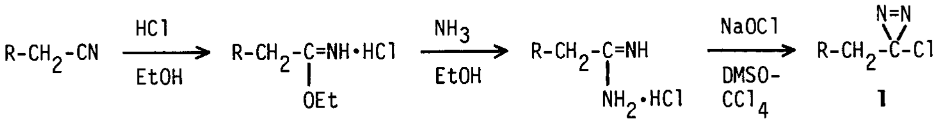
Abstract. Aryloxymethylchlorocarbene generated by photolysis of the corresponding diazirine afforded α-aryloxy-β-chloroalkene. The thermodynamically less stable Z-products are the major isomers and its content becomes dominant as more electron-withdrawing groups are introduced on phenyl ring.

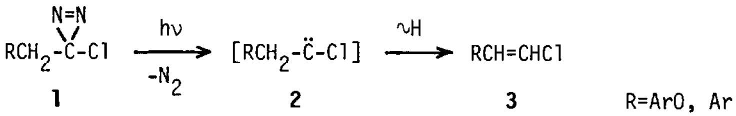
In contrast to the intensive study lavished upon the effect of substituents directly bound to, or conjugated with, the carbene center on carbene reactivity, only scant information is available concerning that of substituents which are insulated from direct conjugation with the carbenic carbon.[1,2] This is rather surprising in view of the fact that effect of remote substituents has been extensively and systematically studied for its companion 6-electron species, the carbenium ion. In the course of examining the effect of remote heteroatom substituents on the reactivity of carbene, we have discovered that β-aryloxy group affects the stereochemistry of 1,2 H migration in aryloxymethylchlorocarbene (**2**) in a manner which cannot be explained in terms of the steric and electronic effects thus far advanced. The results are interpreted as providing evidence for hyperconjugation of the carbene lone pair and the low-lying C-O σ* orbital of β-aryloxy group.

3-Chloro-3-aryloxymethyldiazirines (**1**, R=OAr) were synthesized by Graham's oxidation of the corresponding amidines which were prepared from the corresponding nitriles, as outlined in Scheme I. The diazirines were purified by silica-gel chromatography just before irradiation. That no alkenes were formed during the work-up was easily checked by NMR. The diazirine (**1**) thus obtained was photolyzed in cyclohexane with a 300-W high-pressure Hg lamp at 0 °C until all of the diazirine was destroyed. A Corning CS-052 filter in cutoff at 350 nm was used in order to avoid product isomerization.[3] The photolysis products were almost exclusively α-aryloxy-β-chloroalkenes (**3**, R=ArO, 70∿80%), which are apparently arising from a 1,2 H shift in the photolytically generated aryloxymethylchlorocarbene (**2**). In all of the cases examined, the stereoselection in the formation of the chloroalkene is great as summerized in the Table. Unexpectedly, the thermodynamically unstable Z-products, as evidenced by a 3∿4 Hz vicinal



$$R\text{-}CH_2\text{-}CN \xrightarrow[EtOH]{HCl} R\text{-}CH_2\text{-}\underset{OEt}{\underset{|}{C}}\text{=}NH\cdot HCl \xrightarrow[EtOH]{NH_3} R\text{-}CH_2\text{-}\underset{NH_2\cdot HCl}{\underset{|}{C}}\text{=}NH \xrightarrow[DMSO\text{-}CCl_4]{NaOCl} R\text{-}CH_2\text{-}\overset{N=N}{\overset{\vee}{C}}\text{-}Cl$$

1



$$\mathrm{RCH_2\text{-}\overset{N=N}{C}\text{-}Cl} \xrightarrow[-N_2]{h\nu} \mathrm{[RCH_2\text{-}\ddot{C}\text{-}Cl]} \xrightarrow{\sim H} \mathrm{RCH{=}CHCl}$$

1 **2** **3** R=ArO, Ar

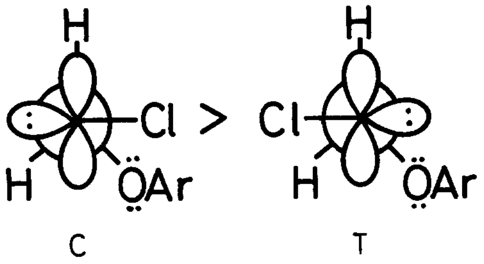
Table Stereoselection in 1,2 H Migration of Methylchlorocarbene (**2**)

	Aryloxymethylchlorocarbene (**2**, R=OAr)			Arylmethylchlorocarbene (**2**, R=Ar)		
	3, %			**3**, %		
Ar	E	Z	E/Z	E	Z	E/Z
4-$MeOC_6H_4$	24.4	75.6	0.32	93.9	6.1	15.4
4-MeC_6H_4	19.0	81.0	0.23	92.1	7.9	11.6
C_6H_5	19.0	81.0	0.23	85.1	14.9	5.7
4-ClC_6H_4	16.8	83.2	0.20	84.2	15.8	5.3
3,5-$Cl_2C_6H_3$	11.0	89.0	0.12	——	——	——
3,4-$Cl_2C_6H_3$	——	——	——	84.4	15.6	5.4
4-$NO_2C_6H_4$	7.9	92.1	0.09	——	——	——

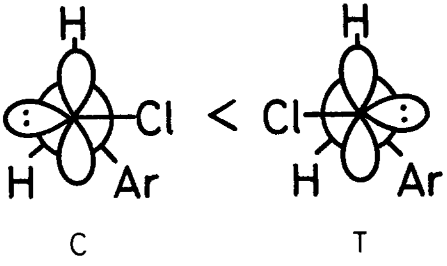
coupling constant in the ^{1}H NMR spectrum, are the major isomers. This is in a marked contrast with that observed[4] for arylmethylchlorocarbenes (**2**, R=Ar), where E-chloroalkenes are the major 1,2 H migration products, as included in the Table for comparison. One more intriguing trend observed in the Table is that Z-alkene increased as more electron-withdrawing groups are introduced on the phenyl ring.

Origins of the Z stereoselection observed in these H migrations are quite interesting. Such a dominant Z migration stereoselectivity caused by β-alkoxy substituents of carbene is not unprecedented, regardless of the generation method and precursor structure. For example, Kirmse and Buschhoff[5] observed predominant formation of Z-methoxyalkene in the 1,2 H shift of β-methoxyalkylcarbenes generated photolytically from diazo compounds. More recently Pirrung and Hwu[6] reported almost exclusive formation of Z-chloroenol silyl ether from β-siloxychlorocarbenes generated from dihalide by dehalogenation with n-butyl lithium. This indicates that conformation of precursor molecule, e.g., diazirine, is not a crucial factor.

It is generally accepted[7] that H migration occurs from the singlet state of carbene. The mechanism of 1,2 H shift involves an electrophilic pull of hydride through the vacant p orbital of the singlet carbene, starting from approximate carbene conformers *C* and *T* for formation of Z and E alkenes, respectively. The stereochemistry of 1,2 H migration will be then determined by the relative populations of the conformers, which are affected by steric as well as elecctrostatic factors. For example, steric repulsion between carbenic substituent (Cl) and β-substituents (ArO or Ar) is a dominant factor in *C* conformers, whereas electrostatic repulsion between the carbene lone pair and β-substituents becomes more effective in *T* conformers. The dominant formation of E isomer from arylmethylchlorocarbene (**2**, R=Ar) suggests that steric factors are crucial in this carbene. A marked change in stereoselection observed for aryloxymethylchlorocarbene (**2**, R=OAr) can, then, be interpreted by assuming that the repulsion between the carbene



Carbene 2 : R=OAr



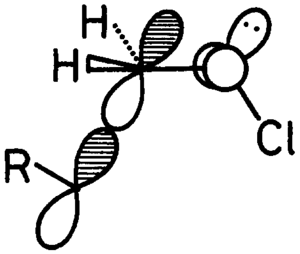
Carbene 2 : R =Ar

lone pair and the lone pair at the aryloxy oxygen dominates steric effects, which should disfavor the conformer C. This seems quite reasonable since such repulsion is absent for arylmethylchlorocarbene system. In the conformer C, however, reverse electrostatic repulsion acting between the lone pairs of chlorine and ether oxygen should also be taken into account. Moreover, if only carbene-oxygen repulsion is a crucial factor, population of the conformer C should decrease as the electron density on oxygen is reduced. The reverse was found; the E/Z ratio was decreased as the ring substituents were successively changed from electron-donating to withdrawing groups, although such a change should result in the reduction of the electron density on aryloxy oxygen.

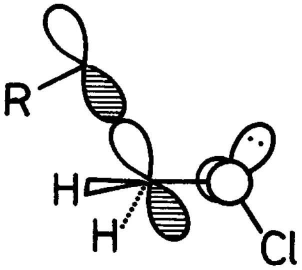
We would like to propose here that hyperconjugation plays an important role in determining the relative population of the carbene conformers. It is well documented in ionic species (i.e., carbenium ion and carbanion) that hyperconjugation comes to the fore. It has been shown[8] that the cation (e.g., $^+CH_2CH_2F$) will interact with the orbital of the least electronegative substituent (e.g., H) on the vicinal carbon while the anion (e.g., $^-CH_2CH_2F$) favors the interaction with most electronegative one (e.g., F). Since carbene has both vacant p orbital and occupied lone pair orbital, either orbital can be stabilized by interacting with the orbitals of the vicinal bonds. In the carbene **2** (R=OAr), cationic hyperconjugation is attained when the vacant p orbital is paralel to the migrating hydrogen, which is the most positive substituent on the vicinal carbon. Anionic hyperconjugation[9] is, on the other hand, attained by internal charge transfer between the occupied carbenic σ orbital and the unoccupied C-O σ^* orbital of the vicinal bond. The magnitude of this interaction, and hence the degree of stabilization, is highest when aryloxy group is antiperiplanar to the carbenic lone pair since σ^* orbital has its greatest extension in the direction opposite to C-O bond. Obviously such interaction is attained only in the carbene conformer C, while the interaction is not effective in the conformer T, where aryloxy group is synperiplanar to the carbenic lone pair, as shown below.

Lone pair-polar bond hyperconjugation is described in valence bond terminology by the reasonance hybrids **4** and **5**. In this view, hybrid **5** should be more stabilized by ArO group carring more electronegative aryl substituents. Thus, conformer C is more stabilized by "negative" hyperconjugation as more electronegative groups are introduced on aryloxy phenyl ring.

$$\underset{\textbf{4}}{ArOCH_2\text{-}\ddot{C}\text{-}Cl} \longleftrightarrow \underset{\textbf{5}}{ArO^-CH_2\text{=}\overset{+}{C}\text{-}Cl}$$



Conformer C



Conformer T

Thus, the present results, revealing the importance of stereoelectronically-controlled hyperconjugation in carbene conformer stability, can be applied, at least qualitatively, to interpret the effect of β-substituents on the stereochemistry in 1,2 H migration of other carbene systems. Thus, a dominant Z migration stereoselectivity caused by β-methoxy group in alkylcarbene[5] and by siloxy group in chlorocarbene[6] can be explained similarly. Moreover, the finding that similar increase in Z alkene formation by electron-withdrawing aryl substituents was also observed in the carbene **2** (R=Ar) implies that such negative hyperconjugation with C-C bond is also possible. Further investigations concerning the effect of the hyperconjugation on carbene chemistry are actively in progress in this laboratory.

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