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Intramolecular Reactivity of Arylcarbenes: 2-(Alkoxymethyl)phenylcarbenes

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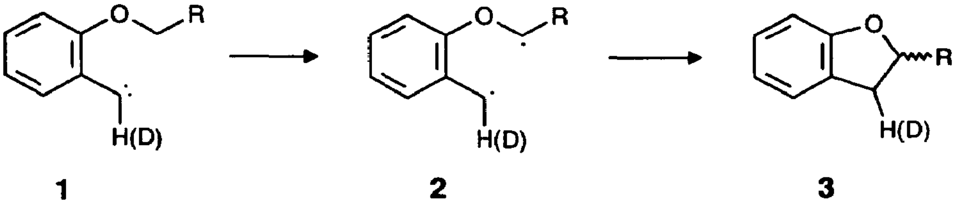
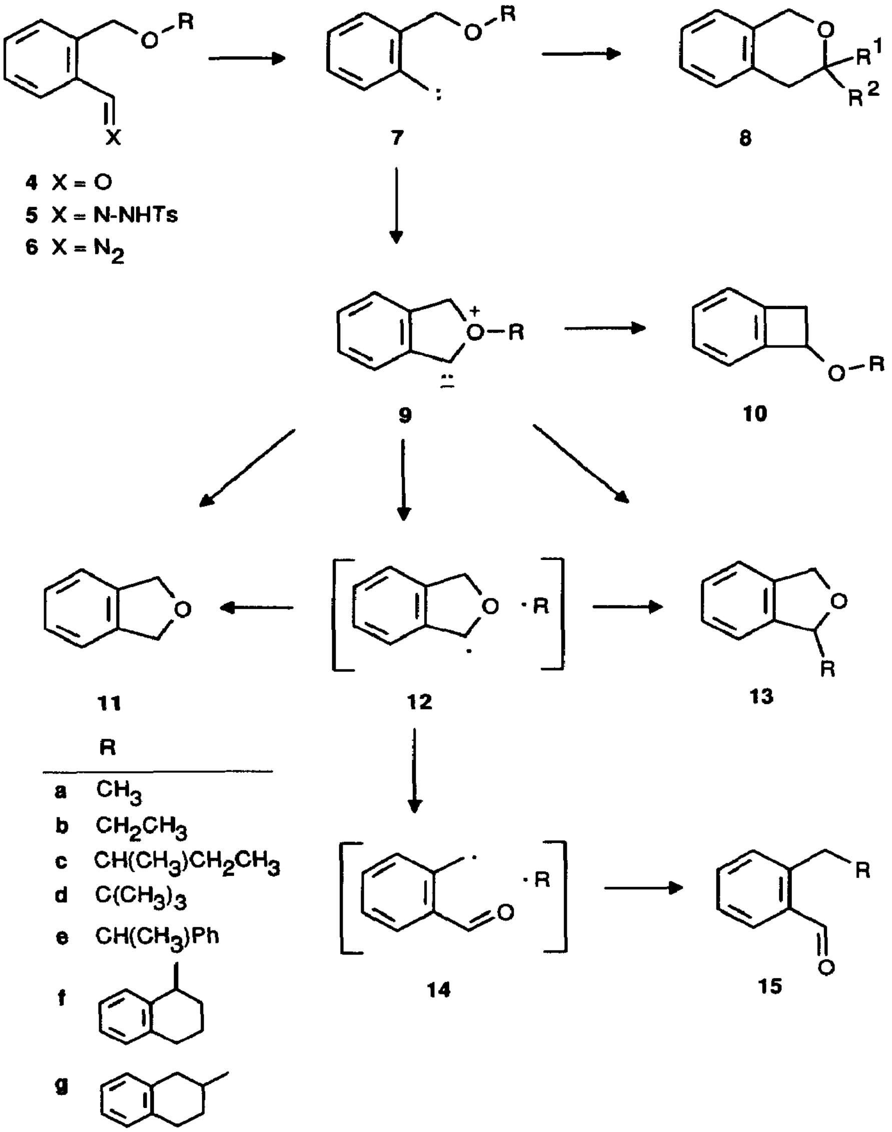
Abstract: Both singlet and triplet states contribute to the intramolecular C-H insertion reactions of 2-(alkoxymethyl)phenylcarbenes, leading to dihydro-1*H*-2-benzopyrans. Competitively, oxygen ylides are generated which eventually give rise to benzocyclobutenes and dihydroisobenzofurans. The radical pair mechanism of the Stevens rearrangement is confirmed by variation of the alkyl groups and by means of chiral substrates.

Many reactions of phenylcarbene, including *intermolecular* insertion into C-H bonds, proceed from the singlet state.[1,2] In contrast, we have found that 2-alkoxyphenylcarbenes produce five-membered rings by way of a triplet abstraction-recombination mechanism (**1** → **2** → **3**).[3,4]



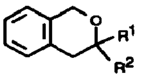
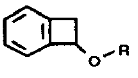
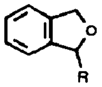
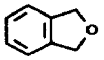
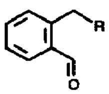
The low *intramolecular* reactivity of singlet **1** is attributed to steric constraints in the transition state of concerted C-H insertion. These adverse effects should be attenuated in the formation of six-membered rings **8** from the homologous 2-(alkoxymethyl)phenylcarbenes **7**. In a previous paper, carbenes **7** were shown to undergo C-H insertion (**7** → **8**) and ylide formation (**7** → **9**) competitively.[5] For mechanistic insight, we have studied additional alkyl groups and chiral substrates.

Ylide-derived products. The Stevens rearrangement of **9a** gives **10a** exclusively,[5] but the fraction of **13** increases with increasing stabilization of R· (Table). Migration of the *sec*-butyl group (**9c** → **13c**) proceeds with complete racemization, while **13e**, **13f**, and **13g** are formed with ca. 50% *ee*.[6] The stereoselectivity of the Stevens rearrangement appears to correlate with the bulk (or stacking ability) of the migrating group, rather than with radical stabilization. Analogous observations have been reported for the Wittig rearrangement.[7] In some pyrolytic reactions, ring cleavage of radical **12** leads eventually to aldehyde **15**. Dihydroisobenzofuran (**11**) can arise from ylide **9** by concerted α',β-elimination, via disproportionation of radical pair **12**, or by reaction with adventitious traces of moisture. The relative yield of **11** clearly depends on the number and reactivity of the β hydrogens available in R.



C-H Insertion. The relative yield of **8** in direct photolyses is but slightly affected by the nature of the ε-C-H bond (secondary, tertiary, benzylic). However, the stereoselectivity of the insertion reaction is higher for aliphatic (**7c**, **7g**) than for benzylic C-H bonds (**7f**). In all cases, the stereoselectivity exceeds that of analogous 2-alkoxyphenylcarbenes (**1c**, **1e**), indicating enhanced participation of singlet **7**. The kinetic and stereochemical deuterium isotope effects observed with D-**7b** (k_H/k_D = 1.75; *cis/trans* = 0.85) also differ substantially from those recorded for the isomer D-**1b** (k_H/k_D = 6.7; *cis/trans* = 4.0).[4] On sensitization, the fraction of **8** increases at the expense of ylide-derived products, with concomitant decrease in *ee* (**8f**, **8g**). Obviously, the hydrogen abstraction by triplet **7**

Table. Distribution (%) and Enantiomeric Excess (*ee*) of Products Derived from 2-(Alkoxymethyl)phenylcarbenes (7)

R	Δ a) hv,[Ph$_2$CO] b)								
		8		**10**	**13**		**11**	**15**	
		%	*ee* c)	%	%	*ee* c)	%	%	*ee*
Ethyl	Δ	40.5		40.5	4.7		4.3	-	
7b	hv	31.4		58.4	7.8		2.3	-	
sec-Butyl	Δ	55.7	*100*	14.8	7.4	*0; 0* d)	8.1	14.0	*0*
7c	hv	34.4	*81*	9.3	41.5	*0; 0*	14.8	-	
	hv, 0.03	74.5		5.0	14.9		5.6	-	
	hv, 0.06	79.6		2.5	12.6		5.3	-	
	hv, 0.12	81.0		2.3	11.7		5.0	-	
	hv, 0.35	84.6		2.1	9.9		3.4	-	
tert-Butyl	Δ	-		11.3	40.1		12.0	36.6	
7d	hv	-		8.4	81.4		10.2	-	
α-Phenylethyl	Δ	57.5		-	26.2		16.3	-	
7e	hv	33.6	*nr* e)	-	59.4	*44; nr*	7.0	-	
	hv, 0.003	78.1		-	17.2		4.7	-	
	hv, 0.006	83.6		-	13.1		3.3	-	
	hv, 0.06	87.8		-	9.4		2.8	-	
α-Tetralyl	hv	35.0	*26*	-	58.5	*nr; 51*	6.5	-	
7f	hv, 0.003	82.4	*8*	-	15.2		2.4	-	
	hv, 0.006	87.7		-	10.2		2.1	-	
	hv, 0.06	89.3	*6*	-	8.8		1.9	-	
β-Tetralyl	hv	31.8	*75*	-	45.3	*52; 36*	22.9	-	
7g	hv, 0.003	70.1	*61*	-	18.5		11.4	-	
	hv, 0.006	83.8	*56*	-	10.7		5.5	-	
	hv, 0.06	95.8	*52*	-	2.9		1.3	-	

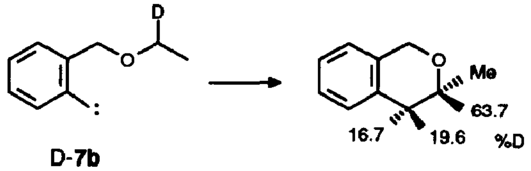
a) Pyrolysis of tosylhydrazone sodium salt (5-Na) at 280-300°C.

b) Photolysis of diazo compound (6) in pentane (medium pressure mercury arc; pyrex).

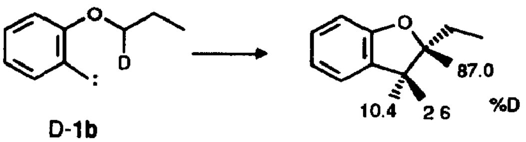
c) Estimated by GC on heptakis(3-*O*-acetyl-2,6-di-*O*-methyl)-β-cyclodextrin (**c**, **e**, and **f**) and heptakis(2,6-di-*O*-methyl-3-*O*-trifluoroacetyl)-β-cyclodextrin (**g**) in OV 1701, respectively.

d) "First" and "second" diastereomer, in the order of elution from GC.

e) Not resolved.



D-7b



D-1b

competes efficiently with intersystem crossing. Closer inspection reveals that the yield of **8g** increases much faster than the *ee* decreases. From these data, a retention to inversion ratio of ca. 3 is estimated for triplet **7g**, while that for triplet **7f** is close to unity. The divergence is explained by the nature of the intervening diradicals: the α-tetralyl radical derived from **7f** is thought to be planar whereas a substantial barrier is anticipated for conformational equilibration of the β-tetralyl radical derived from **7g**. In summary, 2-(alkoxymethyl)phenylcarbenes **7** provide a case of balanced singlet and triplet reactivity toward ε-C-H bonds.

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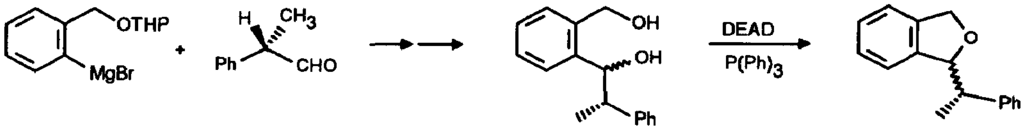
(5) Kirmse, W.; Kund, K. *J.Am.Chem.Soc.* **1989**, *111*, 1465.

(6) Predominant retention of configuration was confirmed by synthesis of **13e** from (*S*)-2-phenylpropanal (hydratropaldehyde):



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