TRANSFORMATION OF PHENYLCHLORODIAZIRINES TO 1,3-DIOXOLANES AND A 1,3-DITHIOLANE

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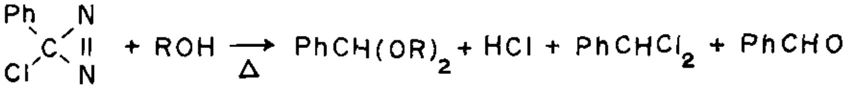
Abstract - Chlorophenylcarbene reacts with bifunctional or polyfunctional alcohols and ethanedithiol to form 2-phenyl-1,3-dioxolanes and 2-phenyl-1,3-dithiolane.

Considerable attention has been given to the interaction of carbenes and oxygen containing compounds.[1] The electron-deficient carbenes react with alcohols[2] and carboxylic acids[3] via O-H insertion reactions whereas the reaction with protected aldehydes (1,3-dioxolanes and 1,3-dioxanes) has been shown to proceed via a C-H insertion reaction.[4] Recently, carbene attack on the oxygen of an oxetane followed by an elimination or rearrangement process was described by Kirmse and co-workers.[5]

The kinetic behaviour for the reaction of singlet benzylchlorocarbene with methanol has been shown to be second-order in methanol.[6] In this respect the chlorocarbene should exhibit similar behaviour towards a molecule containing two O-H groups. Our experimental results confirm these predictions.

3-chloro-3-aryldiazirines were prepared according to Graham's method.[7] Thermal decomposition of 0.1 M 3-chloro-3-phenyldiazirine, **1**, at 80°C for 6 h in excess alcohol gave the following products as in equation (1) where R=Me, Et and ^{n}Bu.



(1)

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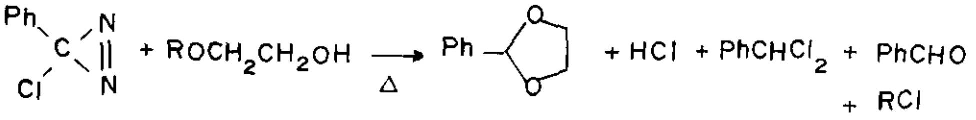
However, reaction with bifunctional or polyfunctional alcohols such as ethylene glycol (EG)/cyclohexane, ethylene glycol monoethyl ether (EGME) or diethylene glycol monoethyl ether (DEGME) under the same conditions produced[8] the cyclic acetal, 2-phenyl-1,3-dioxolane[9], and three other products as given in equation (2) where R=H, Et or $EtOCH_2CH_2$.



(2)

In order to understand the relationship between carbene reactivity and the conjugate effect of the phenyl ring, the reactions for substituted phenylchlorodiazirines and DEGME were carried out (Table 1). Despite numerous studies of carbenes with alcohols,[2,6,10,11] the mechanism for the reaction of chlorocarbene-alcohol remains obscure. Kirmse suggested that electrophilic or nucleophilic character of the carbene plays an important role in the mechanism of the O-H insertion reaction.[10]

Table 1: Experimental Data for the Reaction of Carbenes with Alcohols

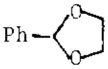
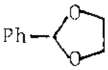
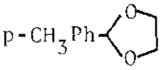
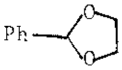
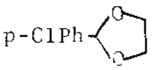
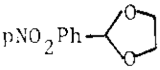
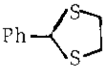
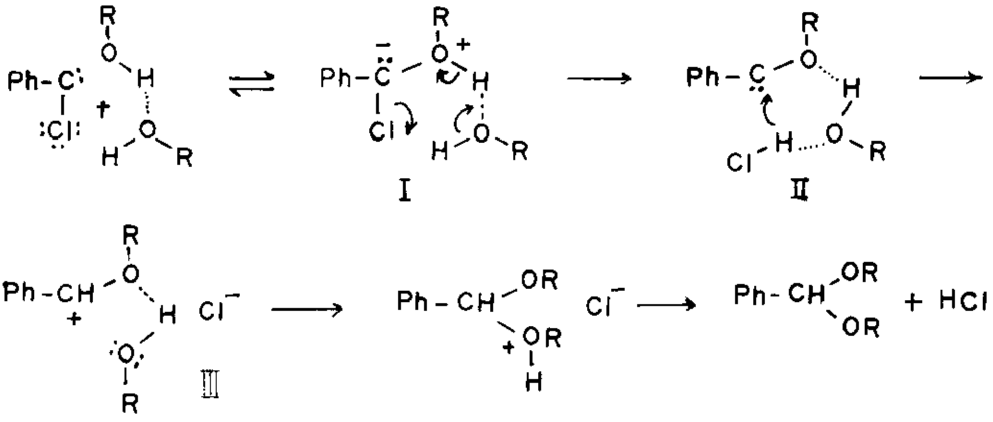
$X\text{-}Ph\text{-}\ddot{C}Cl$			NMR Chemical Shift Data, ppm				Yield %	
X	Substrate	Product	-CHO	Benzylic H	CH_2	Ar-H	acetal	aldehyde
H	MeOH	$PhCH(OMe)_2$		5.53	3.35	7.32	95	<1
H	EtOH	$PhCH(OEt)_2$		5.51	3.50	"	91	2
H		$PhCH(OBu)_2$		5.50	3.50	"	90	2
H	EG			5.67	3.97	"	65	30
H	EGME			5.67	3.97	"	10	70
p-CH_3O	DEGME	---	9.87	--	--	--	--	90
p-CH_3	DEGME		9.95	5.67	3.93	7.18	(trace)	71
H	"		10.0	5.67	3.97	7.32	17	70
p-Cl	"		9.97	5.67	3.98	7.32	71	22

Table 1 (continued)

X	Substrate	Product	-CHO	Benzylic H	CH_2	Ar-H	acetal	aldehyde
p-NO_2	"	 pNO_2Ph	--	5.88	4.06	7.90	93	--
H	$HSCH_2CH_2SH$	 Ph	--	5.58	3.22	7.33	65	--

In searching for a mechanism for the acetal formation, several facts must be borne in mind: (1) The O-H insertion by chlorocarbene involves associated alcohol.[2] (2) The reaction of benzylchlorocarbene with methanol is second-order in alcohol.[6] (3) Similar photolysis experiments (20°C) using benzylchlorodiazirine (0.01 M) and ethylene glycol (0.1-0.6 M) in nitromethane indicated that the reaction of benzylchlorocarbene with ethylene glycol is first-order in the glycol.[12] This confirms that, in the reaction of methanol, two alcohol molecules may be involved in the rate-determining step. (4) The ether bond is immune to the attack of phenylchlorocarbene.[13]



A possible mechanism as given above shows that the carbene inserts into the O-H bond of the alcohol by an electrophilic attack of the electron-deficient carbene to the oxygen lone pair which produces a reversibly-formed ylide intermediate (I).[11] It must be emphasized that $(ROH)_2$ in the scheme is in dimeric form and R=Me, Et, ^nBu, CH_2CH_2OEt or $CH_2CH_2OCH_2CH_2OEt$. In the case of ethylene glycol, R is connected to R and the dimeric form is not required, but the hydrogen bonding in the glycol may still exist. The hydrogen transfer process in the six-membered intermediate, I, is aided by the associated alcohol as well as by the loss of Cl^- from the electron rich carbanion. This is followed by a fast protonation from the HCl moiety on the alkoxy carbene (II) giving rise to a resonance stabilized carbocation (III) which then reacts with a second molecule of nucleophile (ROH) to give the required acetal. In the case of EGME or DEGME, the mechanism is similar to that already described, except that the intermediate III gives rise to the dioxolane by an intramolecular nucleophilic attack of the ether-oxygen on the carbocation. The product ratio for acetal/aldehyde in Table 1 is very sensitive to the substituents in the phenyl ring. Electron withdrawing groups increase the formation of 1,3-dioxolane which is consistent with the formation of a ylide as an intermediate in the reaction of chlorocarbene and alcohol.

The reaction of the chlorophenylcarbene with 1,2-ethanedithiol was also examined since little is known about the reactivity of the carbene towards the SH functionality. The products obtained on thermolysis of 1 with excess dithiol at 80°C were 2-phenyl-1,3-dithiolane, benzal chloride and HCl. The formation of 2-phenyl-1,3-dithiolane indicates that the behaviour of thiol is similar to that of alcohols. The intramolecular cyclization product probably results from an analogous reaction pathway involving a sulfur ylide and thioalkyl carbene. Such intramolecular cyclizations have been recently observed in the reaction of aminophenylcarbene with some secondary amines.[14]

ACKNOWLEDGEMENTS

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8. After all the diazirines were consumed the reaction mixture was washed with 1M sodium hydroxide, and the products were extracted with pentane.

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12. The experimental conditions were identical to those described in ref. 6.

13. When **1** was decomposed in Et-O-Et, no insertion product was found.

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