



Kinetics of the Reaction of Phenylchlorocarbene with an Azabicyclobutane

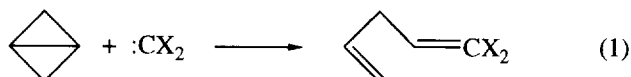
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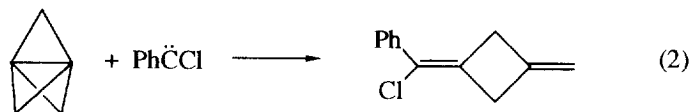
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Summary. The reaction of phenylchlorocarbene with 3-ethyl-1-azabicyclo[1.1.0]-butane (**3**) in pentane at 25 °C occurs with a rate constant of $3.2 \times 10^8 \text{ M}^{-1}\text{s}^{-1}$, most likely via ylide **4**. Copyright © 1996 Elsevier Science Ltd

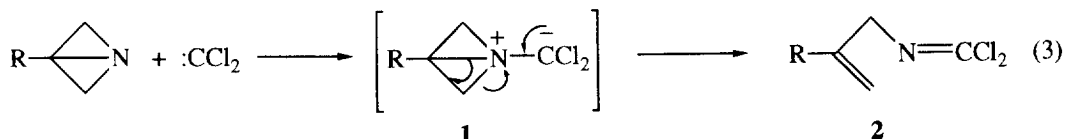
Reactions of carbenes with the strained single bonds of (alkyl)bicyclobutanes generally afford ring-opened pentadienes; eq. (1).¹ Several mechanisms have been offered to account for the bond reorganization



attending this family of reactions, including those proceeding via diradical,² or zwitterionic^{1b,3,4} intermediates. In contrast, Jones *et al.* proposed a concerted, 2-bond "pluck" mechanism in which the carbene reacts simultaneously with the central and a side bond of the bicyclobutane.^{1a} In the related reaction of phenylchlorocarbene (PhCCl) with [1.1.1]propellane, eq. (2), both a biradical and a concerted mechanism were considered.⁵



Recently, Mlostoń *et al.*⁶ reported that the reactions of dichlorocarbene with 3-substituted 1-azabicyclo[1.1.0]butanes gave ring-opened products analogous to those found in the bicyclobutane reactions. Carbenes are known to react very rapidly with amines via the formation of *N*-ylides⁷⁻⁹ so that, in addition to the mechanisms proffered above for the carbene/bicyclobutane reactions, the intervention of an azabicyclobutane ylide, **1**, seems most apposite in the dichlorocarbene/azabicyclobutane reaction,⁶ *cf.*, eq. (3).

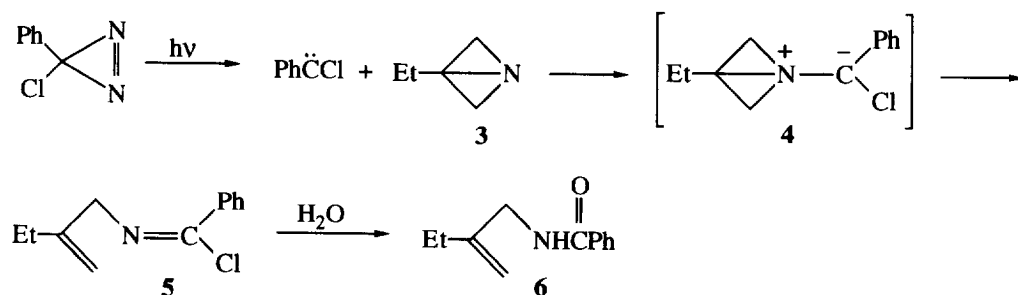


Here, we report on the reaction of PhCCl with 3-ethyl-1-azabicyclo[1.1.0]butane (**3**).¹⁰ In particular, the rate constant for this reaction, as determined by laser flash photolysis (LFP), exceeds even that found for the

reaction of PhCCl with the highly strained [1.1.1]propellane,⁵ eq. (2), and is consistent with an ylide-mediated ring opening.

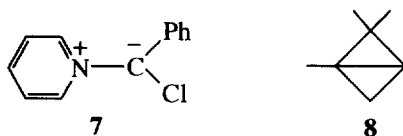
Photolysis of ~30 mM phenylchlorodiazirine¹¹ with 100 mg (1.2 mmol) of **3** in 10 ml of pentane using a Rayonet reactor ($\lambda = 350$ nm, 5 min, 25 °C), followed by an aqueous wash (2 x 10 ml of water), drying (MgSO₄) and flash chromatography on silica gel (eluent: pentane, then ether) afforded as the sole major product 120 mg (53%) of *N*-2-ethyl-3-propenylbenzamide, **6**; cf., Scheme 1.

Scheme 1



The formation of **6** from **3** and PhCCl is most readily rationalized by the addition of PhCCl to **3** at nitrogen, affording ylide **4**. Ring opening of the latter gives the phenylchloroimine, **5**, which readily hydrolyzes to benzamide **6**.¹² Control experiments indicated the absence of a dark reaction between **3** and phenylchlorodiazirine after 3 h at 25 °C.

The rate constant for the reaction of PhCCl and **3** was determined by LFP. To avoid potential interference from product or ylide absorbances in the 300-350 nm region we employed the pyridine ylide methodology,¹³ in which a varying concentration of substrate **3** competed with a fixed concentration (1 mM) of pyridine in pentane for a flux of PhCCl. A pentane solution of phenylchlorodiazirine [$A = 1$] was irradiated with a 14 ns, ~ 50 mJ pulse of 351 nm light from a xenon fluoride excimer laser, yielding PhCCl which reacted either with 1×10^{-3} M pyridine to produce ylide **7** ($\lambda_{\text{max}} 480$ nm¹³) or with azabicyclobutane **3** (3.19×10^{-3} - 2.18×10^{-2} M).



Apparent rate constants for the formation of ylide **7** as a function of [**3**] were measured by LFP, affording the results shown in Figure 1. The slope of this linear correlation ($r = 0.996$), $3.2 \times 10^8 \text{ M}^{-1}\text{s}^{-1}$, is taken as the rate constant for the reaction of PhCCl with **3**.¹⁴

The reaction of PhCCl and **3** is 5.2 times faster than the PhCCl-propellane reaction of eq. (2), for which $k = 6.1 \times 10^7 \text{ M}^{-1}\text{s}^{-1}$ in cyclohexane.⁵ We suggest that the former reaction occurs via the ylide mechanism of

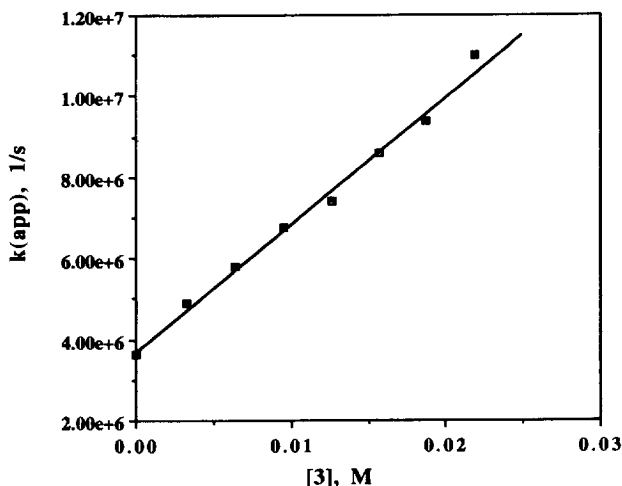


Figure 1. Apparent rate constants (s^{-1}) for the formation of ylide **7** (480 nm) as a function of **[3]** (M) in the reaction of PhCCl and **3** in pentane containing 1 mM pyridine at 25 °C.

Scheme 1. In comparison, ylide formation between *p*-Cl-PhCCl and triethylamine features a comparable rate constant, $k = 7.2 \times 10^8 \text{ M}^{-1}\text{s}^{-1}$, and the transient ylide can be spectroscopically detected.^{9a} We could not observe ylide **4** (expected at $\lambda \sim 340 \text{ nm}^{9a}$) during the LFP reaction of PhCCl and (up to 2.2 M **3**), but this ylide should open very rapidly to **5**. Indeed, the *N*-ylide derived from *p*-Cl-PhCCl and *N*-allylaniline was also not observed by LFP, presumably due to very fast 1,2-allylic or 2,3-sigmatropic rearrangements.^{9c}

Finally, we determined the rate constant for the reaction of PhCCl with the readily available^{1a} 1,2,2-trimethylbicyclo[1.1.0]butane (**8**) in pentane using the pyridine ylide LFP methodology. With **8** varied from 0.064 - 0.48 M, we obtained a linear correlation ($r = 0.999$, 6 points) of the apparent rate constants for the formation of ylide **7** as a function of **[8]** which afforded a slope of $4.3 \times 10^6 \text{ M}^{-1}\text{s}^{-1}$, equal to the rate constant for the reaction of PhCCl with **8**.¹⁵ The attack of PhCCl on **3** is thus 74 times faster than its reaction with **8**, which can be attributed both to the availability of the ylide pathway with **3** and to steric hindrance originating at the *gem*-dimethyl groups of **8**.¹⁶

In conclusion, PhCCl reacts with azabicylobutane **3** more rapidly than with either [1.1.1]propellane or with trimethylbicyclobutane **8**. Presumably, much of this kinetic advantage derives from the incursion of an ylide-mediated reaction in the case of **3**.

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- (14) See ref. 13b, pp. 97ff for a discussion of this kinetics method. We estimate the error in the rate constant at $\pm 10\%$. Direct LFP monitoring of the decay of PhCCl in pentane at 316 nm while varying [**3**] gave $k = 2.9 \times 10^8 \text{ M}^{-1} \text{ s}^{-1}$, in good agreement with the pyridine ylide-determined rate constant.
- (15) The "preparative" photolysis of phenylchlorodiazirine ($A_{370} \sim 3$) with 1.1 M **8** in pentane (Rayonet reactor, 350 nm) afforded a mixture of 6 "adducts" (GC/MS parent ions at m/e 220) which, by NMR spectroscopy, appeared to be regio- and stereoisomeric trimethyl-substituted 1-phenyl-1-chloro-1,4-pentadienes. This reaction is notably less specific than that of CCl₂ and **8**.^{1a}
- (16) The steric factor will be accentuated if the carbene must approach the bicyclobutane along an endo trajectory.^{1a,b}