292. *The Reactions of Carbene with Alkyl Halides.*

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Carbene (methylene) has been allowed to react with mixtures of simple alkyl halides. The major products were formed by attack at the C–Cl and the α-C–H bonds, the order of reactivity for the C–Cl bond being primary > secondary > tertiary. The nature of the various products has been interpreted on the basis of the formation of a bicyclic intermediate.

The reactions of carbenes with a wide range of organic compounds have now been investigated[1] and it has been established that carbene and its derivatives behave as electrophilic reagents.[2] Carbene (methylene) itself shows very little discrimination between the various types of C–H and C=C bonds[3] although recent evidence[4] shows a small but definite trend of the form, tertiary > secondary > primary, in its reactions with simple C–H bonds.

Franzen[5] has shown that carbene reacts with both C–Cl and C–H bonds in simple alkyl halides, the reactivity towards the former being, on the average, about ten times greater. The present investigation was conducted in order to determine whether the C–Cl bonds in a series of halides show the same order of reactivity as the C–H bonds in the simple paraffins.

Experimental

Diazomethane was prepared from *N*-nitrosomethylurethane by Bawn and Rhodes's method,[6] and the vapour was passed, in a stream of dry nitrogen, into the alkyl halide mixture at −20°. The carbene was generated by photolysing this mixture with a Hanovia 500-w mercury-vapour lamp in a quartz vessel at 15°, no attempt being made to select a precise wavelength. The products were analysed by vapour-chromatography through an 11 ft. squalane column at 68° or at 90°. The alkyl halides were supplied by B.D.H. Ltd. and were fractionated before use. The purity of each halide was checked by vapour-phase chromatography.

The amount of each product formed was determined by measuring the area under the respective peak on the chromatogram. As only low conversions were obtained, it was necessary to operate the instrument at maximum sensitivity. This caused the reactant peaks to run off the scale so that only the relative peak areas corresponding to the various products could be obtained with any degree of accuracy. The results of the critical experiments are shown in Table 1, where, of the many experiments performed, only those with the largest peak areas, and hence the greatest accuracy, are included. To obtain the average ratios of the final column, the results have been weighted to favour the most accurate experiments.

The possible errors quoted here are based on the deviation between different experiments and on the accuracy with which peaks could be measured on the chromatograph traces. The n-propyl chloride was found to be contaminated with small amounts of isopropyl chloride and either s-butyl or isobutyl chloride. As further purification proved to be impracticable, allowance was made for these halides in the analysis. By virtue of the nature of the products formed, such impurities will only be important in the experiments on n-propyl–isopropyl chloride mixtures, in which the latter halide yields products similar to the contaminants. For this reason, the result of only one significant experiment is reported for this mixture and, as it is difficult to assess the error likely to be introduced, no reliance has been placed on the ratio obtained when determining the sequence of reactivities. The only other consideration used in weighting the data has been to assume that ratios given directly in a single experiment are

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[1] Trotman-Dickenson, *Ann. Reports*, 1958, **55**, 47; Hine and van der Veen, *J. Amer. Chem. Soc.*, 1959, **81**, 6446.

[2] Skell and Garner, *J. Amer. Chem. Soc.*, 1956, **78**, 5430; Doering and Henderson, *ibid.*, 1958, **80**, 5274; Ledwith and Bell, *Chem. and Ind.*, 1959, 459.

[3] Knox, Trotman-Dickenson, and Wells, *J.*, 1958, 2897; Doering, Buttery, Laughlin, and Chaudhuri, *J. Amer. Chem. Soc.*, 1956, **78**, 3224; Butler and Kistiakowsky, *ibid.*, 1960, **82**, 764.

[4] Frey, *J. Amer. Chem. Soc.*, 1958, **80**, 5005; Doering and Knox, *ibid.*, 1956, **78**, 4947.

[5] Franzen, *Annalen*, 1959, **627**, 22.

[6] Bawn and Rhodes, *Trans. Faraday Soc.*, 1954, **50**, 934.

TABLE 1. *Experimental results: reactions of* $\mathrm{CH_2}$ *radicals with alkyl halides.*

		Areas from chromatograph records (cm.^{2})				
Reactants	Products	I	II	III	IV	Mean ratio (*a*)/(*b*)
$\mathrm{Pr^{n}Cl}$	$\mathrm{Bu^{n}Cl}$ (*a*)	0·54	0·12			2·0 ± 0·2
$\mathrm{Bu^{t}Cl}$	$\mathrm{Bu^{t}{\cdot}CH_2Cl}$, $\mathrm{Bu^{s}{\cdot}CH_2Cl}$ (*b*)	0·27	0·06			
$\mathrm{Pr^{n}Cl}$	$\mathrm{Bu^{n}Cl}$ (*a*)	0·33				2·1 ± 0·1
$\mathrm{Pr^{i}Cl}$	$\mathrm{Bu^{i}Cl}$, $\mathrm{Bu^{s}Cl}$ (*b*)	0·15				
$\mathrm{Pr^{i}Cl}$	$\mathrm{Bu^{i}Cl}$, $\mathrm{Bu^{s}Cl}$ (*a*)	0·50	0·39			1·5 ± 0·1
$\mathrm{Bu^{t}Cl}$	$\mathrm{Bu^{t}{\cdot}CH_2Cl}$, $\mathrm{Bu^{s}{\cdot}CH_2Cl}$ (*b*)	0·37	0·25			
$\mathrm{Pr^{i}Cl}$	$\mathrm{Bu^{i}Cl}$, $\mathrm{Bu^{s}Cl}$ (*a*)	0·24	0·20	0·16	0·16	$1{\cdot}0\left\{\begin{matrix}-0{\cdot}1\\+0{\cdot}05\end{matrix}\right.$
$\mathrm{Bu^{n}Cl}$	$\mathrm{Bu^{n}{\cdot}CH_2Cl}$ (*b*)	0·23	0·21	0·19	0·17	
$\mathrm{Bu^{i}Cl}$	$\mathrm{Bu^{i}{\cdot}CH_2Cl}$ (*a*)	0·38	0·27			1·4 ± 0·2
	$\mathrm{Pr^{i}{\cdot}CHMeCl}$	0·33	0·24			
$\mathrm{Bu^{t}Cl}$	$\mathrm{Bu^{t}{\cdot}CH_2Cl}$, $\mathrm{Pr^{i}CMe_2Cl}$ (*b*)	0·24	0·22			
$\mathrm{Bu^{i}Cl}$	$\mathrm{Bu^{i}{\cdot}CH_2Cl}$ (*a*)	0·18	0·09			0·45 ± 0·05
	$\mathrm{Pr^{i}{\cdot}CHMeCl}$	0·17	0·09			
$\mathrm{(CH_2Cl)_2}$	$\mathrm{CH_2(CH_2Cl)_2}$ (*b*)	0·41	0·19			
$\mathrm{Bu^{s}Cl}$	$\mathrm{Bu^{s}{\cdot}CH_2Cl}$ (*a*)	0·07	0·05			0·45 ± 0·10
$\mathrm{Bu^{t}Cl}$	$\mathrm{Bu^{t}{\cdot}CH_2Cl}$, $\mathrm{CEtMe_2Cl}$	0·15	0·14			
$\mathrm{Bu^{s}Cl}$	$\mathrm{Bu^{s}{\cdot}CH_2Cl}$ (*a*)	0·79	0·36			1·45 ± 0·05
	$\mathrm{CEtMe_2Cl}$ (*b*)	0·57	0·24			

more reliable than those obtained indirectly by comparing the results from two different mixtures containing a common component.

The ratio of reactivities of t-butyl chloride and s-butyl chloride assumes some importance in the subsequent discussion. The experiments conducted with this mixture were repeated with halides from different sources and, in each case, the t-butyl chloride was found to be significantly the more reactive.

RESULTS AND DISCUSSION

The first series of experiments was carried out to characterise the products from the individual halides. In all cases, the major product was due to the insertion of $\mathrm{CH_2}$ at the C–Cl bond. Some reaction also occurred at the C–H bonds, the extent depending critically on the nature of the halide; with each halide, the α-hydrogen position was predominantly attacked. The results are summarised in Table 2. Small quantities of degraded products were also observed; some of these appeared to be halides of lower molecular weight, others contained olefinic bonds and were probably unsaturated halides or simple olefins.

In order to determine the relative rates of attack of $\mathrm{CH_2}$ radicals at the C–Cl bonds in different alkyl halides, a second series of experiments employed pairs of alkyl halides in equimolecular amounts. Because of the low conversions (2—5%), the products were frequently swamped in the chromatograms by the unchanged halides. This prevented many of the more interesting combinations from being studied and considerably reduced the accuracy of analysis. As pure samples of several of the higher halides were not available, it was also necessary to assume that the detector unit possessed a similar sensitivity to all species. This approximation was found to be satisfactory in all examples in which it could be checked. By combining data from different pairs of reactants and correcting them for the formation of inseparable products from isopropyl chloride and t-butyl chloride by means of Franzen's data,[5] the following sequence for the order of reactivity at the C–Cl bond was compiled: $\mathrm{Pr^{n}Cl}$ 3·5; $\mathrm{(CH_2Cl)_2}$ * 3·2; $\mathrm{Bu^{i}Cl}$ 2·3; $\mathrm{Bu^{n}Cl}$ 2·2; $\mathrm{Pr^{i}Cl}$ 1·5; $\mathrm{Bu^{t}Cl}$ 1·0; $\mathrm{Bu^{s}Cl}$ 0·8.

A mechanism for the reaction must take into account the following observations: The reactivity towards a series of isomers decreases in the order, primary > secondary > tertiary. s-Butyl chloride is anomalous, being less reactive than t-butyl chloride. Attack at the C–H bonds takes place preferentially at the α-position. The extent of C–H attack

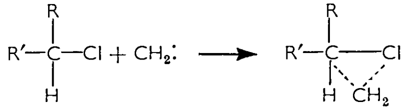
TABLE 2. *Major products from the reaction of* CH_2 *radicals with alkyl halides.*

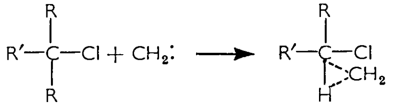
Reactant	Products: C–Cl attack	Products: α-C–H attack
$CH_3\cdot CH_2\cdot CH_2Cl$ *	$CH_3\cdot CH_2\cdot CH_2\cdot CH_2Cl$	$CH_3\cdot CH_2\cdot \underset{CH_3}{\underset{\vert}{C}}HCl$
$\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>CHCl$ *	$\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>CH\cdot CH_2Cl$	$\begin{matrix}CH_3 & & CH_3\\ & C & \\ CH_3 & & Cl\end{matrix}$
$CH_3\cdot CH_2\cdot CH_2\cdot CH_2Cl$	$CH_3\cdot[CH_2]_4\cdot Cl$ ($>90\%$)	$CH_3\cdot CH_2\cdot CH_2\cdot \underset{CH_3}{\underset{\vert}{C}}HCl$ ($<10\%$)
$CH_3\cdot CH_2\cdot \underset{CH_3}{\underset{\vert}{C}}HCl$	$CH_3\cdot CH_2\cdot \underset{CH_3}{\underset{\vert}{C}}H\cdot CH_2Cl$ (59%)	$CH_3\cdot CH_2\cdot \overset{CH_3}{\overset{\vert}{\underset{CH_3}{\underset{\vert}{C}}}}\cdot Cl$ (41%)
$\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>CH\cdot CH_2Cl$	$\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>CH\cdot CH_2\cdot CH_2Cl$ (53%)	$\begin{matrix}CH_3\\CH_3\end{matrix}\!\!>CH\cdot CH\!\!<\!\begin{matrix}CH_3\\Cl\end{matrix}$ (47%)
$\begin{matrix}CH_3\\CH_3\\CH_3\end{matrix}\!\!>CCl$	$\begin{matrix}CH_3\\CH_3\\CH_3\end{matrix}\!\!>C\cdot CH_2Cl$	—

* The amounts of α-C–H attack on n- and iso-propyl chloride could not be measured with sufficient accuracy. However, there was no doubt that the quantities of such products were lower than from C–Cl attack.

varies markedly over the range of isomers, independently of the reactivity of the C–Cl bond.

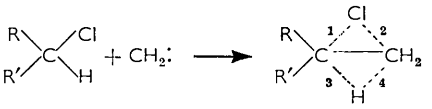
The sequence of reactivity of the C–Cl bond demonstrates that an ionic intermediate, such as might involve intermediate carbonium-ion formation, can be eliminated. As CH_2 undergoes many reactions which are most satisfactorily explained by a two-pronged attack leading to a cyclic intermediate, *e.g.*, addition to a C=C double bond to give a cyclopropane, it appears likely that simple three-membered rings may be the initial products, *e.g.*:





Whilst these two types of intermediate account satisfactorily for the nature of the products, they provide no direct explanation of the four characteristic properties listed above, or of the appearance of small quantities of unsaturated products, and it is evident that, although these intermediates may appear at some stage during the process, the actual mechanism must be somewhat more complex. One way in which this difficulty can be resolved is suggested below.

In all the alkyl halides studied here, except for t-butyl chloride, a hydrogen atom is attached to the α-carbon atom and a bicyclic intermediate of the type:



may be postulated. Such an intermediate, which might also be considered as representing a form of neighbouring group-interaction,[7] can break down to form a stable molecule in

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* Corrected for the presence of two C–Cl bonds.

[7] Winstein, *Bull. Soc. chim. France*, 1951, **18**, 55; Winstein and Takahoshi, *Tetrahedron*, 1958, **2**, 316.

two ways: either by rupture of bonds 1 and 4, to give the same product as insertion at the C–Cl bond, or by rupture of bonds 2 and 3, which is equivalent to attack at the α-hydrogen position. The formation of a bicyclic intermediate would be enhanced by additional hydrogen at the first carbon atom, so that the reactivity order, primary > secondary > tertiary, would be expected. In computing reactivities of C–Cl bonds, it then becomes necessary to include the products of α-hydrogen attack. The effect of this on the order of reactivity above is to move s-butyl chloride from its anomalous position on the right of the t-butyl compound, without affecting the relative positions of the other halides. The bicyclic intermediate naturally explains why attack at the α-position is favoured, the relative amounts of C–Cl and α-C–H reaction presumably being related to the effect of α-carbon substituents.

Similar bicyclic intermediates have been proposed to explain the mutarotation solvolysis of cholest-5-ene dibromide in non-polar media.[8] Moreover, the formation of small amounts of unsaturated products, observed in the present experiments, can be readily explained by the elimination of hydrogen chloride from the bicyclic intermediate, bonds 1—4 all breaking during the process.

The reactivity sequence for the C–Cl bond could also be explained on the basis of increased nucleophilic character caused by isovalent hyperconjugation,[9] but this would not account for the preferred reaction at the α-C–H rather than at the β-C–H position, although such an explanation might be valid for the reactions of carbene at C–H bonds in simple paraffins.[4]

Attempts to obtain corresponding information for the alkyl bromides have so far been unsuccessful, though preliminary results indicate that isopropyl bromide has a reactivity about twice that of isopropyl chloride.

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[8] Grob and Winstein, *Helv. Chim. Acta*, 1952, **35**, 782; Winstein and Robinson, *J. Amer. Chem. Soc.*, 1958, **80**, 178.

[9] Mulliken, *Tetrahedron*, 1959, **5**, 253.