653. *The Reactions of Carbenes and Diazoalkanes with Ketones. Part I. The Reaction of Carbene with Acetone.*
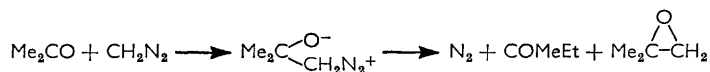
By J. N. BRADLEY and A. LEDWITH.

Singlet carbene reacts with one molecule of acetone, giving ethyl methyl ketone and 1,2-epoxy-2-methylpropane, and with two molecules of acetone gives 2,2,4,4-tetramethyl-1,3-dioxolan. A stable, and probably dipolar, intermediate is suggested to account for some of the products and it is significant that when conditions favour formation of triplet carbene only very small quantities of the dioxolan are obtained.

THE reactions of diazoalkanes with carbonyl compounds have been extensively studied, and mechanisms for these reactions, under certain conditions, have been described.[1,2] Diazomethane reacts readily with acetone in the presence of hydroxylic catalysts to give a mixture of ethyl methyl ketone and 1,2-epoxy-2-methylpropane, the reaction being usually represented [1] as illustrated. Although the total yield is usually very high, the ratio of 1,2-epoxy-2-methylpropane to ethyl methyl ketone depends critically upon the

[1] Gutsche, " Organic Reactions," Vol. III, Wiley and Sons, New York, 1954, p. 364.
[2] Huisgen, *Angew. Chem.*, 1955, **67**, 439; Zollinger, " Azo and Diazo Chemistry," Interscience Publ. Inc., New York, 1961; Hancox, *J. Proc. Roy. Austral. Chem. Inst.*, 1949, **16**, 282.

conditions.   Meerwein *et al.*[3] have shown that, in the absence of additives, acetone reacts with diazomethane if irradiated with ultraviolet light or kept in sunlight.   It seems likely that in these conditions some carbene [4] (methylene) would result from photodecomposition

$$Me_2CO + CH_2N_2 \longrightarrow Me_2C\underset{CH_2N_2{}^+}{\overset{O^-}{\diagup}} \longrightarrow N_2 + COMeEt + Me_2\overset{O}{\overset{\triangle}{C-CH_2}}$$

of diazomethane and, in agreement with this, Meerwein *et al.*[3] obtained significant amounts of methyl propyl ketone and other higher ketones as well as the above products.

Since carbene is now known to react with C–H,[5] C–Cl,[6] and C=C bonds,[7] it seemed worthwhile to examine the reaction of carbene with acetone under essentially anhydrous conditions, in order to determine whether there is any discrimination in the reaction of this highly reactive species with C–H and C=O bonds.

The reaction of diazomethane with acetone has been examined over a range of reaction conditions and it is shown that two distinct photochemical processes occur: (*a*) formation of singlet carbene by direct photolysis of diazomethane; this species then reacts with the C–H and C=O groups in acetone; and (*b*) a reaction induced by ultraviolet light which does not involve singlet carbene and almost certainly results from excitation of the acetone.
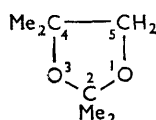
Throughout this work the products were separated and analysed by vapour-phase chromatography.   In this first paper it will be shown that reaction (*a*) leads to a new major product, 2,2,4,4-tetramethyl-1,3-dioxolan (I), in addition to the above products, and a mechanism for its formation is suggested.

$$\underset{Me_2}{\underset{|}{\overset{Me_2C\overset{4}{}\text{---}\overset{5}{}CH_2}{\underset{O}{\overset{|}{}}\,\,\,\underset{O}{\overset{|}{}}}}\quad (I)$$

EXPERIMENTAL

Materials.—" Analytical Reagent " grade acetone was pure according to vapour-phase chromatography (v.p.c.) and was used without further treatment.

Cyclohexane was of B.D.H. spectroscopic grade.   V.p.c. analysis showed the presence of traces of other hydrocarbons but these did not affect the product analyses.

" AnalaR " diethyl ether was used without purification.

N-Nitrosomethylurethane was obtained from L. Light and Co. and used without purification.

Preparation of Diazomethane.—*N*-Nitrosomethylurethane (20 ml.) was added during ~1 hr. to a 6% solution (100 ml.) of sodium in ethylene glycol.   The resultant diazomethane was blown by a stream of dry nitrogen, through a cooling coil at −25°, into decalin (200 ml.) at ~−40°, giving ~0·5M-diazomethane.   The diazomethane was then blown by a stream of dry nitrogen into a collecting vessel containing appropriate volumes of acetone.   Diazomethane concentrations were estimated by running aliquot parts into a measured excess of benzoic acid and back-titrating the excess of acid with sodium hydroxide (phenolphthalein).   Neutralised methanol was added to the mixture to prevent phase separation near the end-point.

1,2-Epoxy-2-methylpropane.—Isobutene in diethyl ether was epoxidised by an excess of perphthalic acid.[8]   The resulting mixture was extracted three times with aqueous sodium hydroxide, then three times with water.   The ethereal solution was then dried (Na$_2$SO$_4$).   Analysis (v.p.c.) showed the presence of one major component besides the solvent.   This had the same retention time as the product thought to be 1,2-epoxy-2 methylpropane obtained during photolysis of diazomethane in acetone.

Photolysis Experiments.—Acetone solutions of diazomethane were photolysed in quartz

[3] Meerwein, Disselnkötter, Rappen, Rintelen, and Van de Vloed, *Annalen*, 1957, **604**, 151.

[4] Kirmse, *Angew. Chem.*, 1960, **72**, 716; Trotman-Dickenson, *Ann. Reports*, 1958, **55**, 47.

[5] Knox, Trotman-Dickenson, and Wells, *J.*, 1958, 2897; Frey, *J. Amer. Chem. Soc.*, 1958, **80**, 5005; Doering and Knox, *ibid.*, 1956, **78**, 4947; Butler and Kistiakowsky, *ibid.*, 1960, **82**, 764; Bell and Kistiakowsky, *ibid.*, 1962, **84**, 3417; Doering and Prinzbach, *Tetrahedron*, 1959, **6**, 24; Frey, *Trans. Faraday Soc.*, 1961, **57**, 951; *Proc. Chem. Soc.*, 1959, 318.

[6] Bradley and Ledwith, *J.*, 1961, 1495; Frantzen, *Annalen*, 1959, **627**, 22.

[7] (*a*) Doering, Buttery, Laughlin, and Chaudri, *J. Amer. Chem. Soc.*, 1956, **78**, 3224; (*b*) Skell and Woodworth, *ibid.*, 1956, **78**, 4496.

[8] Vogel, " Text Book of Practical Organic Chemistry," Longmans, Green and Co., London, 1948, p. 768.

vessels by means of a Hanovia U.V.S. 500/A mercury-arc lamp. For reactions carried out near room temperature, the reaction vessel was cooled with a stream of cold water. Reactions at $-78°$ were carried out by immersing the quartz reaction vessel in a bath of carbon dioxide–methanol contained in a quartz Dewar vessel. Preliminary experiments showed that the products were identical irrespective of whether the mercury lamp or diffuse sunlight was employed. A series of experiments with ultraviolet radiation alone was conducted by interposing a 10 cm. Pyrex tube, with quartz end-windows, between the lamp and the reaction vessels. Great care was taken to ensure that stray light could not enter the reaction vessel. The filter solution was made up [9] from nickel sulphate hexahydrate (145 g.) and cobalt sulphate heptahydrate (41·5 g.) in water (1 l.).

No attempt was made to use monochromatic radiation, mainly because the decomposition was already inconveniently slow, and the filter merely eliminated radiation within the long-wavelength absorption region of diazomethane. Decompositions in sunlight were carried out in Pyrex vessels.

Spectra.—Infrared spectra were recorded in a Grubb-Parsons double-beam instrument fitted with sodium chloride optics. Nuclear magnetic resonance spectra were recorded on a Varian 4300B spectrometer operating at 56·4 Mc./sec. Chemical shifts were measured with respect to tetramethylsilane as internal standard.

Vapour-phase Chromatography.—The products were analysed with a Perkin-Elmer model 451 " Fractometer " fitted with a flame ionisation detector. The products were examined on several different columns. The most satisfactory stationary phase was polyethylene glycol. The major problem was that the individual products constituted only $\sim$0·1 mole % of the acetone solution and it was necessary to use a material which gave minimum " tailing " of the acetone peak. The conditions for optimum resolution were critical: columns, 2 m. long., and 4 mm. in diameter, were operated at 57° with a nitrogen-carrier flow velocity of 5 cm./sec. and gave a height equivalent to a theoretical plate of 0·1 cm. These conditions are almost identical with those found by Bohemen and Purnell [10] for similar separations. It is difficult to obtain absolute yields of products for the following reasons: (1) The sample is divided after injection by a stream splitter and the split ratio of this device shows long-term drift, requiring frequent calibration. (2) Pure samples of certain of the products are difficult to obtain. This applies particularly to the 2,2,4,4-tetramethyl-1,3-dioxolan which constituted the major product. (3) Some loss of diazomethane from the solution tended to occur. This was largely avoided by keeping the concentration at $\not> 0·1$M. (4) Small amounts of polymethylene were observed in some experiments. (5) Reproducible injection was difficult when the sample contained dissolved gas, *i.e.*, after photolysis of diazomethane. Because of this, relative yields only were determined for most experiments. The absolute yield was estimated in certain experiments. This was achieved by comparing the sensitivity of ethyl methyl ketone with that of 1,3-dioxolan and assuming that the sensitivity of the higher dioxolans would increase in the ratio of their molecular weights. On this basis, the apparent yield of ethyl methyl ketone, the epoxide, and the dioxalan accounted for 80—110% of the original diazomethane, the discrepancy presumably being due to underestimation of the sensitivity of the tetramethyldioxolan.

Results.—Diazomethane was photolysed in dry acetone and in all cases the main products were ethyl methyl ketone, 1,2,-epoxy-2-methylpropane, and a non-ketonic compound with a longer retention time. In addition, small amounts of more volatile compounds appeared on the v.p.c. traces at lower retention times; although these peaks were not identified unequivocally the largest is probably due to 2-methoxypropene. Ethyl methyl ketone and the epoxide were identified by comparison of their retention times with those of authentic samples. In order to identify the non-ketonic product, pure samples were separated by preparative v.p.c. and characterised by means of infrared and nuclear magnetic resonance spectroscopy. The infrared spectrum in carbon tetrachloride solution showed strong absorption at 1178, 1136, 1060, and 995 cm.$^{-1}$, consistent with the presence of a ketal (both linear and cyclic ketals give rise to characteristic absorption in this region [11]). In addition the strong

[9] Farkas and Melville, " Experimental Methods in Gas Reactions," Macmillan and Co., London, 1939, p. 233.
[10] Bohemen and Purnell, " Gas Chromatography," Butterworths Scientific Publns., London, 1958, p. 6.
[11] Jones and Sandorfy, " Technique of Organic Chemistry," ed. Weissberger, Vol. IX, Interscience Publ. Inc., New York, 1956, p. 441.

absorption at 1375 and 2970 cm.$^{-1}$ indicated the presence of CH_3–C groups. The nuclear magnetic resonance spectrum of a 20% solution in carbon tetrachloride showed only three signals, A, B, and C, having relative areas A : B : C = 3 : 3 : 1 with τ values of 8·77, 8·71, and 6·41, respectively. The dioxolan (I) was the only plausible compound which fitted the data and on this basis the high-field signals A and B were assigned to the 4,4-dimethyl protons and the 2,2-dimethyl protons, respectively (for the 2-ethyl-2-methyl analogue τ = 8·80 [12]), and the low-field signal C to the methylene protons in position 5 (for 2-H of tetrahydrofuran τ = 6·37 [12]). This product was therefore identified as 2,2,4,4-tetramethyl-1,3-dioxolan; although this compound has not been obtained previously, related 1,3-dioxolans have been obtained by reaction of diazomethane with alkoxy-ketones and carboxylic esters.[3,13]

The ratios of the various products estimated from the peak heights and areas of the chromatographic traces are shown in the Table (both peak heights and areas are included where

Photolysis of diazomethane in acetone.

Reaction	Temp.	Average reaction time (hr.)	(I)/COMeEt Peak heights	(I)/COMeEt Peak areas	Epoxide/COMeEt Peak heights	Epoxide/COMeEt Peak areas
Photolysis (mean of 12 expts.)	17°	0·5	2·34 (0·28 *)	3·08 (0·27 *)	0·95 (0·28 *)	0·39 (0·06 *)
Photolysis (mean of 2 expts.)	−78	2	2·4	3·0	1·1	0·6
Decomp. in sunlight (mean of 2 expts.)	24	12	3·0	4·0	1·1	0·5
Photolysis in u.v. only (mean of 2 expts.)	25	5	0·1	—	1·6	0·7
Photolysis in u.v. only (mean of 2 expts.)	−78	6	1·2	—	7·5	—
Photolysis in Et$_2$O †	17	0·5	2·1	2·24	Epoxide peak obscured by solvent	
Photolysis in the presence of 50% (v/v) of cyclohexane	17	0·5	2·0 (17·0 ‡)	2·5 (1·53 ‡)	1·2	0·6
Decomp. in sunlight in the presence of 50% of cyclohexane	24	12	2·7 (14·7 ‡)	3·7 (1·2 ‡)	1·1	0·4
Photolysis in u.v. only in presence of 50% of cyclohexane	17	5	0·03 (0·3 ‡)	—	1·7	0·7

* Standard deviation.   † [CH$_2$N$_2$] = 0·34M.   ‡ Ratio, methylcyclohexane/COMeEt.

possible because the absolute sensitivity of the instrument towards the various products could not be unequivocally determined). Absence of certain entries in the Table indicates that the measurements could not be made with sufficient accuracy, usually because of " tailing " from previous peaks. The Table shows that, except when ultraviolet light was used, the results vary little over a wide range of conditions. On photolysis of solutions of acetone and diazo-methane in diethyl ether, the resultant carbene reacted with the solvent as well as with the acetone. Similarly, photolysis in the presence of cyclohexane afforded methylcyclohexane. This reaction was used to provide an indication of the extent of carbene formation during photolysis, and hence the ratio, methylcyclohexane/COMeEt, was measured in the appropriate experiments. In addition, it was found that varying the concentration of diazomethane from 0·12M to 0·025M had no appreciable effect on the product ratios, nor did the use of glass vessels or addition of glass beads to the acetone solution. There was no reaction between diazo-methane and dry acetone in the dark. Experiments in which diazomethane was photolysed on admission to the reaction system gave irreproducible product ratios, probably owing to loss of products caused by the flow of nitrogen. It seemed possible that the dioxolan could have been formed by direct reaction [14] between acetone and the epoxide; however, neither five-fold variation in diazomethane concentration nor extended photolysis of the reaction mixtures after all the diazomethane had reacted altered the product ratios, so that the direct reaction appears not to occur.

[12] Jackman, " Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, London, 1959.
[13] Ref. 1, p. 397.
[14] Elderfield, " Heterocyclic Compounds," Wiley and Sons, New York, 1957, Vol. V, p. 11.

DISCUSSION

Photolysis of diazomethane in dry acetone, in light of wavelength greater than 3200 Å, leads to ethyl methyl ketone, 1,2-epoxy-2-methylpropane, and 2,2,4,4-tetramethyl-1,3-dioxolan, with much smaller amounts of 2-methoxypropene. These products are formed under the same conditions and at approximately the same rate as methylcyclohexane is formed from cyclohexane. The reaction does not occur in the dark and the product ratios are independent of temperature. Acetone [15] does not absorb appreciably above 3200 Å whereas diazomethane [16] absorbs continuously from 3200 Å up to 5000 Å and in accord with this the product ratios are substantially the same for reactions in quartz vessels with an ultraviolet lamp as for reactions in glass vessels with sunlight. In the latter case light of wavelength below 3200 Å is unlikely to be involved, so it is believed that diazomethane is the primary absorbing species.

The reaction is believed to be simply a photodecomposition of diazomethane to singlet carbene which attacks the C=O and C–H bonds of acetone. Although it is probable that the ground state of carbene is a triplet species,[17] the essentially indiscriminate [4-6] and stereospecific [7] reactions of the intermediate formed by direct photolysis of diazomethane suggest that singlet carbene is involved. On the other hand, decomposition of diazomethane with mercury [18] or benzophenone [19] as photosensitiser leads to an intermediate which is much more discriminating in its reactions and is probably a triplet state of carbene. Singlet carbene undergoes insertion reactions at a C–H bond whereas the triplet species does not.[18-20] Consequently, in the present work, the formation of methylcyclohexane during photolysis of diazomethane in the presence of cyclohexane has been used as a test for the production of singlet carbene.

Ethyl methyl ketone and 1,2-epoxy-2-methylpropane can then be formed by direct attack of carbene on acetone:
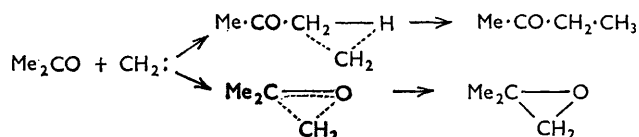
However, the most striking result is the formation of major amounts of 2,2,4,4-tetramethyl-1,3-dioxolan (I) by attack of singlet carbene on acetone. This compound cannot be formed by direct attack of carbene on either C–H or C=O bonds and must be formed by a reaction between a second molecule of acetone and a reactive intermediate formed in the initial attack. Since carbene is thought to be an electrophilic reagent, it is reasonable to assume that the oxygen end of the carbonyl group would be preferentially attacked and a possible mechanism for the formation of (I) is as follows:
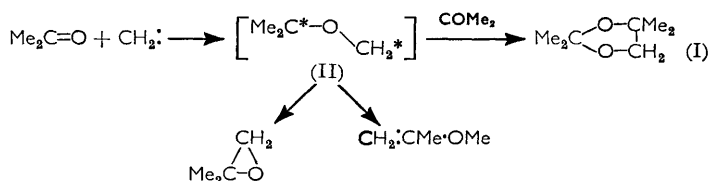
[15] Matsen, " Technique of Organic Chemistry," ed. Weissberger, Interscience Publ. Inc., New York, 1956, Vol. IX, p. 660; Masson, Boekelheide, and Noyes, jun., *ibid.*, Vol. II, p. 310.

[16] Adamson and Kenner, *J.*, 1937, 1551; Brinton and Vollman, *J. Chem. Phys.*, 1951, 1394; Kirkbride and Norrish, *J.*, 1933, 119.

[17] Hertzberg, *Proc. Roy. Soc.*, 1960, *A*, **262**, 291.

[18] Duncan and Cvetanovic, *J. Amer. Chem. Soc.*, 1962, **84**, 3593.

[19] Kopecky, Hammond, and Leermakers, *J. Amer. Chem. Soc.*, 1962, **84**, 1015.

[20] Setser and Rabinovitch, *Canad. J. Chem.*, 1962, **40**, 1425.

The exact nature of the intermediate (II) is not known but, in view of its subsequent reaction with acetone, some dipolar character seems likely (*e.g.*, $Me_2C^+-O-CH_2^-$). Furthermore, if the intermediate has dipolar character then the minor product, 2-methoxypropene, can be readily formed by an intramolecular proton shift. From the values of the product ratios it is clear that the preferred reaction of the intermediate is formation of the dioxolan and, whilst this is not surprising for reactions carried out in pure acetone, it is significant that this dioxolan is also a major product of reaction in dilute solution in ether. This suggests either that the intermediate has a significant lifetime or that there is some association between acetone molecules. If we assume, therefore, that all the products except ethyl methyl ketone arise initially from attack of carbene on the C=O bond, then the reactivity of this bond is at least 15 times greater than that of the C–H bonds. This value is comparable with corresponding values for relative reactivities in cyclohexene [7a] (C=C/C–H $\approx$ 6) and t-butyl chloride [6] (C–Cl/C–H $\approx$ 10). There has, however, been no previous evidence for the formation of a stable intermediate in reactions involving singlet carbene.

Photolysis of acetone solutions of diazomethane in ultraviolet light leads to a drastic change in the product ratios, and in particular the dioxolan is formed only in very small amounts. Since acetone and diazomethane both absorb below 3000 Å, and in view of their relative concentrations, the former is believed here to be the primary absorbing species. The reaction between diazomethane and acetone at 25° will then result from attack by an excited acetone molecule on ground-state diazomethane. Further, the products are unlikely to arise from attack by singlet carbene, since only insignificant amounts of methylcyclohexane are formed from cyclohexane under similar conditions.

The photochemistry of ketones [15] involves primary excitation of the ketone to a singlet state which is then quenched to a triplet state of lower energy, and it is the latter which takes part in any subsequent reaction. However, in this case it is not clear whether the reaction between diazomethane and acetone involves an excited singlet or triplet state of the ketone, although it seems more reasonable to consider reactions involving the lower state. The reaction would then be analogous to the photolysis of diazomethane in the presence of benzophenone [19] or mercury vapour.[18]

When the photolysis is carried out at −78° the product ratios again become comparable with those obtained when using light of longer wavelengths; this suggests that singlet carbene is again involved, but in view of the uncertainty about the nature of the reacting species in these photolyses no further explanation can be given. It should be noted, however, that photolysis with light of this wavelength invariably produces significantly higher amounts of the epoxide, especially at low temperatures.