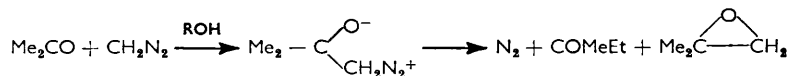


834. Reactions of Carbenes and Diazoalkanes with Ketones. Part III.¹ Kinetics of the Non-photolytic Reaction between Acetone and Diazoalkanes.

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The kinetics of the non-photolytic reaction between diazoalkanes and acetone have been investigated. Both rates and products depend critically on the concentration of added alcohols. For the reaction between diazomethane and acetone, two reactions occur simultaneously: one leading to formation of 1,2-epoxy-2-methylpropane and the other giving a mixture of ethyl methyl ketone and 1,2-epoxy-2-methylpropane. The relative rates of reaction decrease in the order diazoethane > 1-diazopropane \gg diazomethane.

DIAZOMETHANE reacts readily with acetone^{1,2} in the presence of hydroxylic promoters to give a mixture of ethyl methyl ketone and 1,2-epoxy-2-methylpropane, the reaction being usually represented thus:



Although the yield is usually high, the ratio Δ of 1,2-epoxy-2-methylpropane to ethyl methyl ketone depends critically upon the conditions. The reaction is normally carried out in an inert solvent such as diethyl ether and may take several days to reach completion.

¹ (a) Part I, Bradley and Ledwith, *J.*, 1963, 3840; (b) Part II, Bradley, Cowell, and Ledwith, *J.*, 1964, 353.

² Gutsche, "Organic Reactions," Vol. VIII, p. 364, Wiley and Sons, New York, 1954; Huisgen, *Angew. Chem.*, 1955, **67**, 439; Zollinger, "Azo and Diazo Chemistry," Interscience, London, 1961; Hancox, *Roy. Australian Chem. Inst. J. and Proc.*, 1949, **16**, 282.

Use of Lewis acids, *e.g.*, BF_3 or AlCl_3 , as catalysts,³ reduces reaction times considerably and yields predominantly the homologous ketone.

The reaction with and without alcohols was previously found to be photocatalysed¹ and the present investigation is concerned with the kinetics of the alcohol-promoted dark reaction.

EXPERIMENTAL

Materials.—AnalaR acetone was dried over Linde Molecular Sieves Type 4A and distilled to give a middle fraction, b. p. $56.0^\circ/760$ mm.

n-Butanol (b. p. 117.7°), n-propanol, (97.2°) propan-2-ol (82.3°) were AnalaR reagents distilled immediately before use. AnalaR methanol (64.5°) and ethanol (78.3°) were dried over Linde Molecular Sieves type 4A and distilled immediately before use. Purified samples of isobutanol (b. p. 108.0°), t-butyl alcohol (82.5°), and n-pentanol (137.9°) were kindly supplied by Professor C. E. H. Bawn.

Diazoalkanes. Diazomethane was prepared from methyl *N*-nitrosourethane as described previously.^{1a} Diazoethane and 1-diazopropane were obtained from the corresponding *N*-alkyl urethanes in identical manner except that a solution of potassium hydroxide in n-propanol was used for hydrolysis. The diazoalkane was collected finally in acetone, and concentrations were measured 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.

Stability of diazoalkane solutions. When stored in the dark diazomethane solutions in acetone are quite stable at room temperatures for several days. Diazoethane and 1-diazopropane undergo a significant non-catalysed reaction with acetone (see Table 6) giving the corresponding ketone. Consequently, solutions of these diazoalkanes were stored at -80° until required, and all the rate constants reported were corrected for the non-catalysed reaction.

Kinetic Measurements.—The reaction mixtures were prepared by adding the appropriate volume of alcohol, from a calibrated rapid delivery pipette, to the acetone-diazomethane solution. All reactants were previously equilibrated at the appropriate temperature in a water thermostat for 25.0° and in an ice-water bath for 0° . Volumes and molar concentration were calculated with neglect of any volume changes on mixing.

Aliquot parts of the reaction mixture were withdrawn by semi-automatic pipette at appropriate intervals and quenched by running into a measured excess of benzoic acid solution in toluene. The diazoalkane concentration was estimated as above. To obtain a better estimate of the initial diazoalkane concentration, an aliquot part of reaction mixture was removed for analysis immediately after mixing. This procedure was necessary because it was found that solutions of

TABLE 1.

Effect of dilution on stability of diazomethane in acetone.*

Initial $[\text{CH}_2\text{N}_2]$ in acetone (M)	Added solvent	$[\text{CH}_2\text{N}_2]$ in soln. immediately after mixing (M)	Loss in $[\text{CH}_2\text{N}_2]$ (%)
0.0861	Acetone	0.0384	10.8
0.0863	Diethyl ether	0.0386	10.6
0.0860	Ethylbenzene	0.0383	10.9
0.0826	n-Butanol	0.0315	23.7

* Determined by mixing equal volumes of solvent and acetone containing CH_2N_2 .

diazoalkanes in most organic solvents could not be diluted, mixed with other solvents, or shaken without significant loss of diazomethane. This behaviour^{4,5} may have led to wrong interpretations.⁵ Typical losses are in Table 1. Since no obvious product was found we concluded that the fall in concentration on mixing was purely physical.

¹ House, Grubbs, and Gannon, *J. Amer. Chem. Soc.*, 1960, **82**, 4099; Johnson, Neeman, Birkeland, and Fedoruk, *ibid.*, 1962, **84**, 989; Müller, Bauer, and Rundel, *Tetrahedron Letters*, 1960, No. 13, 30; 1961, No. 4, 136.

⁴ Hammond and Williams, *J. Org. Chem.*, 1962, **27**, 3775.

⁵ Bawn, Ledwith, and Matthies, *J. Polymer Sci.*, 1959, **34**, 93.

The reaction was uniformly of first order in CH_2N_2 and rate coefficients, k_1 , were estimated from the first order plots derived from the fall in $[\text{CH}_2\text{N}_2]$ with time by the method of least

TABLE 2.
Typical kinetic run for reaction of CH_2N_2 with acetone in the presence of 20 vol. % n-butanol at 25.0°.

Time (sec.)	Back titre of NaOH* (ml.)	$10^2[\text{CH}_2\text{N}_2]$ (M)	10^4k_1 (sec. ⁻¹)
0	3.13	6.67	—
340	3.31	6.44	1.029
663	3.47	6.24	1.003
1212	3.70	5.96	0.929
2106	4.18	5.37	1.026
3331	4.66	4.77	1.012
4850	5.20	4.10	1.003
6673	5.77	3.39	1.014

Ave. 1.01

* 5.0 ml. aliquot portions of reaction mixture added to 5.0 ml. of benzoic acid solution, the latter being equivalent to 8.51 ml. of 0.0620M-NaOH.

squares. Typical results are in Table 2. For diazomethane reactions the reproducibility of k_1 was always within 2%, and for diazoethane and 1-diazopropane better than 5%. Tables 3—6 give the average value for at least duplicate runs.

Products.—All products were determined by vapour phase chromatography.¹ For diazomethane the total yield of reaction products was never less than 80% and in most cases greater than 90%. The products were ethyl methyl ketone and 1,2-epoxy-2-methylpropane except for the few reactions carried out at 0°, in which a significant amount of n-butyl methyl ether was found. Below 0° diazoethane and 1-diazopropane gave 3-methyl-2-butanone and 3-methyl-2-pentanone gave >90% yield. At 25°, however, the yield of homologous ketone was 70—80% and, although no epoxide was detected by vapour-phase chromatography, it is possible that minor amounts of epoxides could have been obscured by the solvent acetone peak.

RESULTS

Although diazomethane decomposed slowly, no product was detected from any reaction with acetone in the dark even after up to 2 weeks. In the presence of hydroxylic compounds, the products are 1,2-epoxy-2-methylpropane and ethyl methyl ketone and (Table 3) both reaction rates and product ratios (epoxide/ketone = Δ) are strongly influenced by the nature and concentration of the promoter. At low alcohol concentrations and low temperatures, and hence long reaction times, some n-butyl methyl ether was also detected; subsequent discussion is concerned only with conditions under which this reaction is unimportant.

TABLE 3.
Catalysed reaction between CH_2N_2^a and acetone at 25.0°.

ROH	10^4k_1 (sec. ⁻¹)	Mole ratio of products, Δ	ROH	10^4k_1 (sec. ⁻¹)	Mol. ratio of products, Δ
Water ^b	69.0	0.80	Pentan-1-ol ^b	6.40	—
Methanol ^b	31.1	1.14	Butan-1-ol ^c	7.47	1.35
Ethanol ^b	7.65	1.39	2-Methylpropan-1-ol ^c	6.70	1.45
Propan-1-ol ^b	6.84	1.32	1-Methylpropan-1-ol ^c	2.13	3.30
Propan-2-ol ^b	2.03	3.07	t-Butyl alcohol ^c	0.85	4.10
Butan-1-ol ^b	6.40	1.50			

^a Initial $[\text{CH}_2\text{N}_2] \sim 0.05\text{M}$. ^b 39.6 moles % ROH. ^c 46.0 moles % ROH (50 vol. %).

The reaction in the presence of n-butanol was studied over a wider range of conditions (Table 4). At 25°, the product ratio Δ falls rapidly with increasing $[\text{Bu}^n\text{OH}]$ but approaches a limiting value at high alcohol concentrations. At 0°, the fall in Δ is less marked and, at -20°, Δ is reasonably constant over the entire range of alcohol concentrations although the limiting value

of Δ remains dependent on temperature. Also included in Table 4 are the partial rate constants k_0 and k_K for the production of oxide and ketone, respectively. Plots of $\log k_0$ versus $\log [\text{Bu}^\alpha\text{OH}]$ were curved indicating that no simple relation exists between k_0 and $[\text{Bu}^\alpha\text{OH}]$.

TABLE 4.
The reaction between CH_2N_2^a and acetone promoted by n-butanol.

Vol. % n-butanol	[Bu ^α OH] (M)	[Acetone] (M)	Temp.	Δ^b	First-order rate constant ^c (sec. ⁻¹)				
					$10^5 k_1$	$10^5 k_0$	$10^5 k_K$	$10^5 k_0^A$	$10^5 k_0^B$
5.0	0.55	12.85	25°	13.2	1.56	1.45	0.11	1.34	0.11
10	1.09	12.16	25	5.9	3.23	2.76	0.47	2.29	0.47
20	2.18	10.80	25	3.2	10.1	7.67	2.42	5.25	2.42
30	3.27	8.07	25	1.8	22.3	14.5	7.85	6.6	7.85
40	4.36	7.47	25	1.6	50.7	31.2	19.5	11.7	19.5
50	5.46	6.81	25	1.3	74.7	44.2	30.5	13.7	30.5
60	6.54	5.41	25	1.3	132	75.0	57.0	18.0	57.0
70	7.63	4.05	25	1.3	179	107	78.0	23.0	78.0
80	8.72	2.70	25	1.2	293	160	133	27.0	133
10	1.09	12.16	0	3.8	0.43	0.34	0.09	0.21	0.14
30	3.27	8.07	0	1.8	6.18	3.98	2.20	0.64	3.3
50	5.46	6.81	0	1.5	32.1	19.9	12.2	—	19.9
10	1.09	12.16	-20	2.5					
30	3.27	8.07	-20	3.7					
50	5.46	6.81	-20	2.7					
70	7.63	4.05	-20	2.6					
50	5.46	6.81	25	1.3					
50	"	"	0	1.5					
50	"	"	-25	2.6					
50	"	"	-50	3.4					
50	"	"	-80	5.8					

^a $[\text{CH}_2\text{N}_2] \approx 0.05\text{M}$. ^b Δ = mole ratio 1,2-epoxy-2-methylpropane/ethyl methyl ketone. ^c k_1 = overall rate constant (see experimental) = $(k_0 + k_K)$ where, k_0 = total rate constant for oxide formation and k_K = total rate constant for ketone formation, and $\Delta = k_0/k_K$.

TABLE 5.

The reaction between CH_2N_2^a and acetone promoted by methanol at 25° in solvents.

Solvent	[MeOH] (M)	[Acetone] (M)	$10^5 k_1$ (sec. ⁻¹)	Product ratio, Δ
Bis-(2-methoxyethyl) ether	0.49	0.51	3.5	12.5
" "	1.00	0.50	5.6	7.2
" "	1.46	0.49	10.7	6.0
Ethylbenzene	0.30	0.33	2.5	<i>b</i>
"	0.58	0.32	5.8	<i>b</i>
"	1.14	0.31	8.5	<i>b</i>
Acetone	0.46	13.3	2.5	10.0
"	0.94	13.0	4.1	7.5
"	1.39	12.75	5.3	5.1
"	2.27	12.3	17.8	2.2
"	2.92		product run only	1.4
"	5.46	10.55	189	1.1
"	6.47	9.93	311	1.1

^a Initial $[\text{CH}_2\text{N}_2] \approx 0.05\text{M}$. ^b The product ratio was difficult to measure accurately because of interference by an impurity peak in the solvent. However, $\Delta > 5$ in each case.

Table 5 shows kinetic results from the methanol-promoted reaction between diazomethane and acetone in various solvents. For ethylbenzene, bis-(2-methoxyethyl) ether, and acetone, values of $10^5 k_1$ in the presence of 0.49M-methanol can be extrapolated from data at other methanol concentrations, and are 4.7, 3.5, and 2.5 sec.⁻¹, respectively. The corresponding values of Δ for the last two solvents are also very similar indicating clearly that the reaction rates are kinetically independent of [acetone], depending primarily on the concentration of methanol, and less on the solvent.

The corresponding reactions with diazoethane and 1-diazopropane yield mainly the appropriate ketone and, although the data are insufficient for detailed analysis, it is clear from Table 6 that these reactions also show a high kinetic-order dependence on $[\text{Bu}^\alpha\text{OH}]$.

TABLE 6.

The reaction between diazoalkanes ^a and acetone promoted by n-butanol.

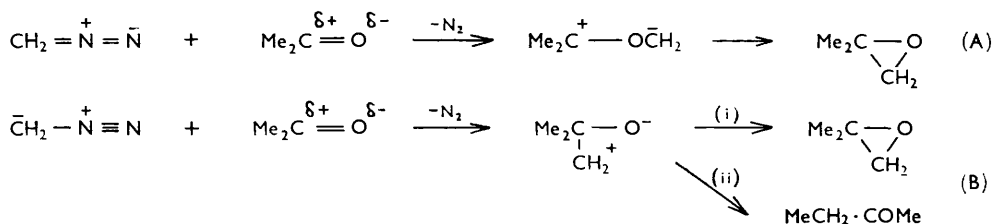
Diazoalkane	Bu ⁿ OH (vol. %)	Temp.	Overall first-order rate coefficient 10 ⁵ k (sec. ⁻¹)	Corrected rate coefficient for alcohol-promoted reaction 10 ⁵ k ₁ (sec. ⁻¹)
Diazomethane	0	25°	nil	
	10	25	3.23	3.23
	10	0	0.43	0.43
Diazoethane	5	25	1.56	1.56
	10	25	47.1	43.3
	0	25	3.84	
	10	0	11.2	10.8
	0	0	0.36	
	5	25	19.0	15.2
1-Diazopropane	5	0	3.94	3.58
	10	25	20.0	17.5
	0	25	2.45	
	10	0	6.01	5.11
	0	0	0.90	
	5	25	9.40	6.95
	5	0	2.90	2.0

^aInitial [RCHN₂] ≈ 0.05M.

DISCUSSION

Acetone and diazomethane do not react in the dark but in the presence of alcoholic promoters there is a significant reaction, the rate of which is critically dependent on the concentration of alcohol, and essentially independent of acetone and solvent (Tables 3—5). This implies that, at least for the lower alcohol concentrations, the effect of alcohol is not simply a solvent effect but involves direct catalysis of the reaction.

The two principal canonical structures for diazomethane ^{2,6} suggest immediately that for the reaction with acetone two paths are possible,* *i.e.*,



These reactions give products which correspond exactly with those found experimentally. Furthermore the relative extents of the two reactions would be expected to depend critically on the polar nature of the environment.

Hydrogen-bonding materials, *e.g.*, alcohols, would be expected to promote the reactions by increasing the polarization of diazomethane and the overall rates of reaction correspond roughly to the expected hydrogen-bonding efficiency ⁷ of the promoter (Table 3). In addition, hydrogen bonding to acetone would be expected to favour reaction *B* rather than reaction *A* so that the former would show a higher kinetic-order dependence on

* The original mechanism for this type of reaction² involved a 1,3-dipolar addition of diazomethane to acetone followed by rapid breakdown of the resulting heterocyclic derivatives. Although this mechanism has never been rigorously demonstrated or disproved, there would still be two reaction paths proceeding *via* the intermediates



on breakdown would give products as indicated by reactions *A* and *B*.

⁶ Ledwith and Friedrich, *J.*, 1964, 504.⁷ Brandt, *J. Amer. Chem. Soc.*, 1963, **85**, 2628.

[BuⁿOH]. Lewis acids promote the homologation of ketones by diazoalkanes,³ presumably by a path corresponding to reaction *B*, and the absence of oxide formation is then explained by the strength of the bond formed between the promoter and the carbonyl oxygen atom.

Complete mechanisms for the two reactions cannot be elucidated from the present data: however, the absence of any kinetic dependence on [acetone] shows that the reaction between diazomethane and alcohol is rate-determining. Very probably the initial rapid reaction involves complex formation between diazomethane and acetone.

Assuming that reactions *A* and *B* do in fact occur, we can analyse the kinetic data further. Table 4 shows that reaction *B* predominates at high alcohol concentrations and yields a value of Δ which is independent of [BuⁿOH] but which varies with temperature. The limiting Δ at 25° is assigned a value of unity which corresponds to the oxide-ketone ratio for reaction *B* alone. Denoting the rate constants for formation of oxide *via* reactions *A* and *B* by k_0^A and k_0^B , we find that plots of $\log k_0^A$ and $\log (k_0^B + k_K)$ *versus* $\log [\text{Bu}^n\text{OH}]$ are straight with slopes of 1.0 and 2.6, respectively. Thus, for reaction *A*

$$\frac{-d[\text{CH}_2\text{N}_2]}{dt} = k_A[\text{CH}_2\text{N}_2][\text{Bu}^n\text{OH}]$$

and for reaction *B*

$$\frac{-d[\text{CH}_2\text{N}_2]}{dt} = k_B[\text{CH}_2\text{N}_2][\text{Bu}^n\text{OH}]^{2.6}$$

A similar analysis for the results obtained at 0° using a limiting Δ of 1.5 again yields exponents for the alcohol dependence of 1.0 and 2.6 for reactions *A* and *B*. Comparison of the rate constants at 0 and 25° yields $\Delta H_A^\ddagger, 25^\circ = 17$ kcal./mole and $\Delta S_A^\ddagger, 25^\circ = -26$ e.u. for reaction *A*. With reaction *B*, the enthalpy of activation decreases with increasing alcohol concentration, thus ΔH_B^\ddagger in 50, 30, and 10 vol. % of n-butanol is 3.5, 6.0, and 8.5 kcal./mole, respectively.

For the higher diazoalkanes, reaction *B* is clearly dominant, the rates decreasing in the order diazoethane > 1-diazopropane \gg diazomethane. The major effect results from the enhanced nucleophilic reactivity of the higher diazoalkanes, supporting the mechanism proposed for reaction *B*. The disparity between diazoethane and 1-diazopropane can probably be attributed to steric factors. Significantly the enthalpies of activation of the corresponding reaction of CH_2N_2 , $\text{CH}_3\cdot\text{CHN}_2$, and $\text{CH}_3\cdot\text{CH}_2\cdot\text{CHN}_2$ with acetone in the presence of 10 vol. % BuⁿOH at 25° are 8.5, 9.0, and 8.1 kcal./mole, respectively.

From the limiting values of Δ , the difference in temperature coefficients for the formation of oxide and ketone by reaction *B* is about 2 kcal./mole.

Table 7 shows that the ratio of rates $\text{CH}_3\cdot\text{CHN}_2/\text{C}_2\text{H}_5\cdot\text{CHN}_2$ is independent of both temperature and [BuⁿOH] whilst the ratio $\text{CH}_2\text{N}_2/\text{RCHN}_2$ varies with [BuⁿOH], probably

TABLE 7.
Relative rates for reaction of R·CHN₂ with acetone by reaction B.

Diazo-compound	Relative rates		
	10 vol. % Bu ⁿ OH at 25° c	10 vol. % Bu ⁿ OH at 0°	5 vol. % Bu ⁿ OH at 25
Diazomethane	1	1	1
1-Diazopropane	19 [1]	22 [1]	32 [1]
Diazoethane	46 [2.4]	47 [2.1]	69 [2.2]

owing to different kinetic orders in [BuⁿOH] for diazomethane and the higher diazoalkanes.

The results in this and earlier Papers¹ demonstrate that there are several distinct mechanisms, not necessarily leading to different products, for the reaction between acetone and diazomethane. Stereochemical anomalies reported recently⁸ for similar systems might perhaps be explained by the participation of more than one reaction path.

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⁸ Gutsche and Chang, *J. Amer. Chem. Soc.*, 1962, **84**, 2263.