322. *Improved Preparations of Aliphatic Diazo-Compounds, and Certain of Their Properties.*

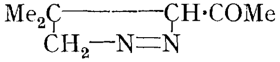
By Donald W. Adamson and J. Kenner.

The several factors determining the most advantageous mode of preparation of individual diazo-compounds are considered, and suitable conditions (which vary from case to case) are elaborated for relatively large-scale operations.

Free diazo-ethane, -propane, -*n*- and -*iso*-butanes have been isolated, their boiling points determined, and their absorption spectra in the visible and the near ultra-violet region examined.

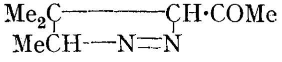
It was mentioned in a previous paper (J., 1935, 286) that an ethereal solution of diazo-octane, obtained by our method, did not survive an attempt to concentrate it by fractional distillation. We have since isolated from similar solutions of diazo-methane and -ethane the *pyrazoline* derivatives (I) and (II), and also prepared them from mesityl oxide.

(I.)



$$\begin{array}{l}\mathrm{Me_2C{-}{-}{-}{-}CH{\cdot}COMe}\\ \quad\mathrm{CH_2{-}N{=}N}\end{array}$$

(II.)



$$\begin{array}{l}\mathrm{Me_2C{-}{-}{-}{-}CH{\cdot}COMe}\\ \mathrm{MeCH{-}N{=}N}\end{array}$$

The formulæ (I) and (II) are based on the rule established by v. Auwers (*Ber.*, 1933, **66**, 1198), *viz.*, that diazo-methane and -ethane combine with αβ-unsaturated esters so that nitrogen becomes attached to the α-carbon atom; this rule, in turn, being an obvious consequence of the anionoid condition of the carbon atom of the diazomethane molecule. The products now in question exhibit the general characteristic of such pyrazolines that, although stable in presence of nitrogen, they are changed into brown oils on exposure to air. Apart from this we have, as detailed later, been able to obtain little positive evidence of their constitution. They show, however, a certain analogy with the product prepared by Kohler and Steele from diazoacetic ester and benzylideneacetophenone (*J. Amer. Chem. Soc.*, 1919, **41**, 1105), in a tendency to resinify in presence of acid.

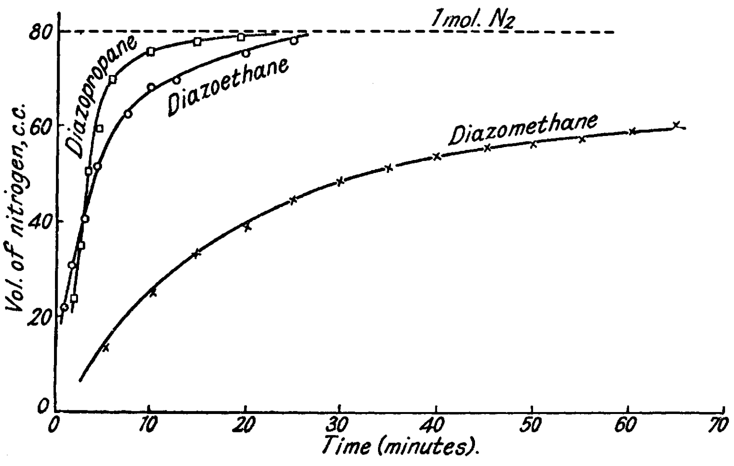
The formation of such products must be expected, not merely in the ethereal distillates, owing to volatilisation of some mesityl oxide, but also during the actual preparation of diazo-compounds by our procedure. This factor is additional to that discussed in the previous paper as contributing to a diminution in yield with increase in the scale of experiment, and may be to some extent counteracted by lowering the temperature employed from 80° to 50°. The following results show that very satisfactory results are thus achieved with moderately large quantities :

Nitroso-compound.	Yield of diazo-compound,	
	g.	%.
Methyl ($\frac{1}{3}$ mol.)	10·5	75
,, ($\frac{1}{2}$ mol.)	14·6	69·5
Ethyl ($\frac{1}{3}$ mol.)	12·9	69·2
n-Propyl ($\frac{1}{6}$ mol.)	7·5	65

In spite, therefore, of the difficulties indicated, the yields of diazomethane compare favourably with those claimed by Arndt (" Organic Syntheses," Vol. **15**, 3), and when account is taken of the instability of nitrosomethylurea and the stability of our nitroso-compounds, together with the improvement in their preparation described later (p. 1554), there can be little doubt that the new procedure is the best yet available for the preparation of ethereal solutions of diazomethane. A simple bulb fractionating column serves to obviate any considerable contamination with mesityl oxide, and the solutions may then be redistilled with very little loss.

FIG. 1.

Reactivity of diazo-compound towards phenol.



The homologues are more reactive than diazomethane itself, as is evident from Fig. 1, in reference to the etherification of phenol. This fact, together with a diminution in volatility with rise in molecular weight, explains, in the light of the foregoing, the corresponding diminution in the yields of diazo-compounds prepared by the general method.

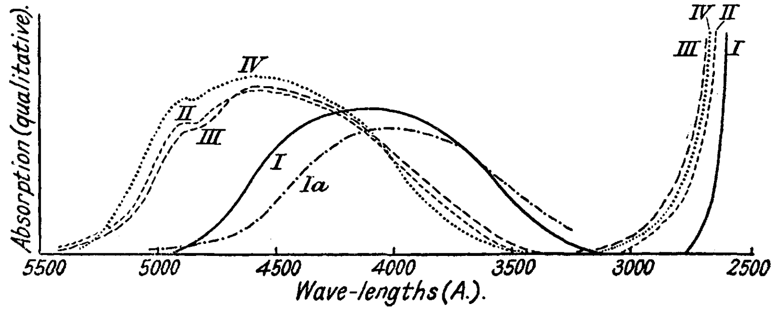
Nevertheless, the data already quoted show that very satisfactory preparations of diazo-ethane and -propane accrue from it.

A method more satisfactory for higher homologues, and in many circumstances also for those just discussed, resulted from the following considerations. Meerwein and Burneleit (*Ber.*, 1928, **61**, 1840), having shown that ether restrains the reactivity of diazomethane, prepared the gaseous compound in unspecified yield by the action of sodium glycollate on nitrosomethylurethane in a stream of nitrogen, and Arndt (*Z. angew. Chem.*, 1930, **43**, 444) obtained a 50% yield for the action of alcoholic potash on nitrosomethylurea. Excellent results (see *Nature*, 1935, **135**, 833) follow from gradual addition of our nitroso-compounds with anisole to a solution of sodium in benzyl alcohol or *cyclo*hexanol at 75—80° under reduced pressure. The appended results show the method to be also applicable to fairly large quantities.

Nitroso-compound.	Yield of diazo-compound,	
	g.	%.
Methyl ($\frac{1}{3}$ mol.)	8·8	63
Ethyl ($\frac{1}{5}$ mol.)	5·6	50
n-Propyl ($\frac{1}{6}$ mol.)	5·5	47
n-Butyl ($\frac{1}{6}$ mol.)	6·3	45

Highly concentrated solutions may be prepared by absorbing the diazo-ethane, -propane, or -butane thus obtained in any desired solvent or reactant at —50°, *e.g.*, 25 c.c. of ether for the quantities mentioned in the table, but the volatility of diazomethane under reduced pressure is too great for this purpose unless an acid or other reactant is also present. In such circumstances, however, the process is more expeditious for the generation of diazomethane than the ether distillation method.

FIG. 2.



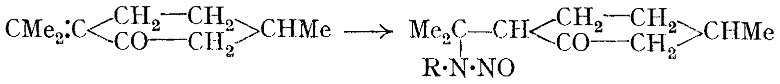
I *Diazomethane.* I*a Diazomethane vapour* (*Kirkbride and Norrish*). II *Diazoethane.* III *Diazopropane.* IV *Diazobutane.*

Small-scale experiments along these lines permitted the isolation of the free diazo-compounds and determination of their boiling points, *viz.*, diazoethane, — 19° to — 17°/89·5 mm.; diazo-*n*-propane, — 8° to — 7·5°/41·5 mm.; diazo-*n*-butane, — 3·5° to — 5·5°/26 mm.; diazo*iso*butane, — 1° to + 1°/32 mm.

The methane analogue has b. p. — 24° to — 23°/760 mm. (Staudinger and Kupper, *Ber.*, 1912, **45**, 507), and the *iso*propane compound b. p. — 31°/14 mm. (Staudinger and Gaule, *ibid.*, 1916, **49**, 1905). It may be emphasised that, neither in these nor in any other of our experiments, has there been any difficulty from the explosive character of the diazo-compounds.

By redistillation and collection of diazo-methane, -ethane, -*n*-propane, -*n*- and -*iso*-butane severally in *cyclo*hexane, solutions were prepared of which the absorption spectra in the visible and ultra-violet region down to 2100 A. were studied. As Fig. 2 shows, our results with diazomethane agree satisfactorily with those of Kirkbride and Norrish (J., 1933, 119), and in the homologues the main absorption band of diazomethane acquires a frequency lower by approximately 650 A., corresponding to the greater reactivity, and hence readiness of excitation, already mentioned. There is also a subsidiary band at 4900 A., which is not shown by diazomethane. The colours of diazo-*iso*propane and -*sec.*-butane suggest that they might exhibit this band still more intensely.

The rise in boiling point renders the separation of mesityl oxide from gaseous homologues higher than diazobutane in the procedure described unsatisfactory, but this difficulty is overcome by using the less volatile pulegone. The well-crystallised *nitroso*-derivatives (III) prepared from this ketone afford the same yields of diazo-compounds as those previously employed, but are formed with less facility than those from mesityl oxide and hence are considerably more costly. For these reasons, our experiments in this direction have hitherto been confined to the small scale.



$$\mathrm{CMe_2{:}C}<\begin{matrix}\mathrm{CH_2-CH_2}\\ \mathrm{CO-CH_2}\end{matrix}>\mathrm{CHMe} \longrightarrow \underset{\mathrm{R\cdot N\cdot NO}}{\mathrm{Me_2C}}-\mathrm{CH}<\begin{matrix}\mathrm{CH_2-CH_2}\\ \mathrm{CO-CH_2}\end{matrix}>\mathrm{CHMe}$$

(III.)

EXPERIMENTAL.

Preparation of Nitroso-derivatives.—(a) *From mesityl oxide.* The following procedure is generally applicable, gives better yields than that previously described, and affords products which can be used without distillation for the preparation of diazo-compounds. An ice-cooled solution of methylamine hydrochloride (97%; 139 g.) in water (200 c.c.) was treated with a solution of sodium hydroxide (95%; 84 g.) in water (200 c.c.), and to the stirred mixture, maintained below 20°, mesityl oxide (196 g.) was gradually added during 1 hour. After a further hour, the mixture was slowly neutralised below 7° with glacial acetic acid (120 g.), and, without special cooling, treated successively with a solution of sodium nitrite (90%; 360 g.) in water (450 c.c.), and glacial acetic acid (180 g.). The mixture was stirred for 4 hours, and its temperature allowed to rise to, but not to exceed, 35°. The nitroso-compound was removed by two extractions with ether, followed by another after saturation of the aqueous liquor with salt. The combined extracts were washed twice with dilute acetic acid, once with calcium chloride solution (10%), and dried over calcium chloride. Finally, ether and impurities of low b. p. were removed at 100°/30 mm. Yield, 75—80%. The derivative from methylamine has now been obtained as a solid, m. p. 21—22°. (b) *From pulegone.* Ethylamine (9 g.), water (30 c.c.), and pulegone (30—40 g.) were stirred for 3 hours, and neutralised at 0° with hydrochloric acid (20%). By extraction with ether, pulegone (13·1 g.) was recovered, and the aqueous liquor was then treated with sodium nitrite (95%; 36 g.) in water (50 c.c.) and glacial acetic acid (18 g.). The mixture was occasionally cooled to keep its temperature below 35°, and stirred for 24 hours. The solid product was purified by crystallisation from light petroleum. The following table summarises the data in regard to the *nitroso*-derivatives (III) in question.

Alkyl group.	M. p.	N found, %.	N required, %.	Yield, %.
Me	116·5°	13·6	13·2	35
Et	108·5	12·7	12·4	41
n-Pr	125·5	11·9	11·7	36
n-Bu	89	11·3	11·0	38
n-C_5H_{11}	88·5	10·8	10·5	52
n-C_7H_{15}	70	9·8	9·4	38
Allyl	108	12·0	11·8	43

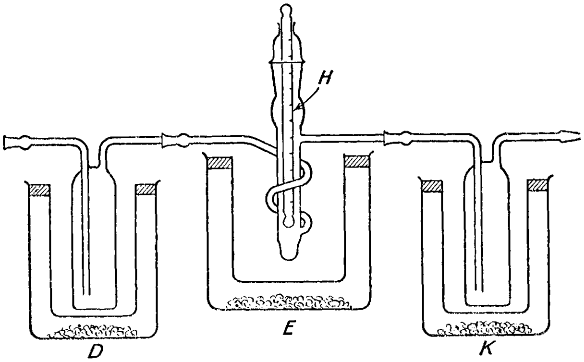
Preparation of Diazo-compounds. (a) *Ether distillation process.* The waxy mass prepared by dissolving sodium (2 g.) in *cyclo*hexanol (66 c.c.) was roughly broken up and added to dry ether (300 c.c.) in a 2-l. flask. After addition of nitroso-β-methylamino*iso*butyl methyl ketone ($\frac{1}{3}$ mol.) in dry ether (600 c.c.) at 10°, the mixture was slowly warmed by a bath at 50°. The vapour was passed through a bulb fractionating column to deposit mesityl oxide (this is unnecessary if the diazo-compound is to be employed for a rapid reaction, *e.g.*, esterification of an acid), and then through a condenser and an adapter into ether, until the condensate was colourless. Yield 10·3—10·8 g. in 730—750 c.c. of ether, and, from a similar experiment with $\frac{1}{2}$ mol. of nitroso-compound, 14·6 g. in 1160 c.c. of ether. The yields of diazo-ethane and -propane from similar experiments have been already quoted. The use of benzyl alcohol in place of *cyclo*hexanol causes a slight reduction in yield, but a more rapid evolution, and hence about 30% greater concentration in the ethereal solution obtained. Final purification was, if desired, achieved by allowing the ethereal solutions to stand for one hour over solid caustic potash, and redistilling all but *ca.* 100 c.c. through a Widmer column. The loss thus occasioned is slight, except in the case of diazopropane.

(b) *Gaseous phase process.* A mixture of nitrosoethylamino*iso*butyl methyl ketone ($\frac{1}{5}$ mol.) with anisole (60 c.c.) was added during 15—20 minutes from a tap-funnel to the product from sodium (0·6 g.) and *cyclo*hexanol (20 c.c.) at 300—400 mm. pressure, in a 150 c.c. flask, heated by a bath at 75—80°, and fitted with an inlet tube for a stream of dry nitrogen, as well as a worm reflux condenser. The resulting diazoethane passed from the condenser successively through a cooling coil at 0° and a **U**-tube charged with solid potassium hydroxide into the selected solvent. Yield, 50%. Similarly for diazo-*n*-propane (yield, 47%), and at 30—50 mm. for diazo-*n*-butane (yield, 45%).

The process is also much more expeditious for diazomethane (yield, 65%), but in this case the gas must be absorbed in a reactant. Otherwise, a 2-l. flask containing dry ether (300 c.c.) was employed for the interaction of the nitrosomethylamino-ketone ($\frac{1}{6}$ mol.), delivered from a tap-funnel, with the product from sodium (1 g.) and *cyclo*hexanol (33 c.c.). The mixture was gradually warmed to 50°, and the diazomethane conveyed in a slow stream of nitrogen through an inverted Allihn condenser, and solid potassium hydroxide into ether (650 c.c.), cooled by a freezing mixture. Yield, after 35 minutes, 5·1 g. (72·9%) in 670 c.c. of ether. With $\frac{1}{3}$ molar quantities, 9·7 g. in 1250 c.c. of ether are obtained.

Isolation of Diazo-compounds, and their Boiling Points.—The gaseous diazo-compounds were prepared as just described in a 25 c.c. flask from the nitroso-ketone (0·3 mol.) in anisole (4 c.c.) and 3% sodium benzyloxide (3 c.c.) at 70° in an atmosphere of dry nitrogen at 50—100 mm. pressure. From the **U**-tube containing solid caustic potash, the gas passed to a receiver (*D*, Fig. 3) cooled by solid carbon dioxide and ether in a beaker, luted by asbestos–water glass into a larger one, containing also some calcium chloride. Obscurity by frost being thus prevented, the pressure was increased to atmospheric, and the receiver removed; 1—1·5 c.c. of liquid were seen to have been collected. The inlet being quickly stoppered, connection was made to the receiver *E*, cooled by solid carbon dioxide and ether. By reducing the pressure, and allowing the temperature of *D* to rise, distillation of the diazo-compound was accomplished. A small quantity of a colourless solid remained in *D*. It melted to a clear liquid with a characteristic odour, contained nitrogen, decolorised bromine or alkaline potassium permanganate, and was resinified by a trace of acid. Similar products were gradually produced from the diazo-compounds themselves at the ordinary temperature, but have not yet been further examined.

FIG. 3.



By causing the liquid diazo-compounds to distil from *E* to *K*, their b. p.'s (see p. 1553) were determined with the aid of the thermometer *H*.

Absorption Spectra.—Solutions in pure *cyclo*hexane of diazo-compounds, purified as already described, were analysed by titration with benzoic acid, and examined in the visible region by means of a Hilger–Nutting industrial spectrophotometer, and in the ultra-violet down to 2100 A. by a Bellingham and Stanley quartz spectrograph (No. 2.) in conjunction with a polarisation photometer. The molecular extinction coefficients, calculated from the Bunsen coefficients, varied slightly with the concentration of the solution, and small discrepancies appeared between results obtained by the two instruments in the same part of the visible region. The wave-lengths of the absorption bands were, however, identical under all conditions. The results are exhibited in Fig. 2, together with those of Kirkbride and Norrish.

Reactivity of Diazo-compounds towards Phenol.—A solution of pure diazo-methane, -ethane, or -propane in toluene (0·066 g.-mol./litre); 50 c.c.) was allowed to react at 0° in a flask, from which light was excluded, with a solution of pure phenol (0·0033 g.-mol.) in toluene (10 c.c.). The rate of evolution of nitrogen, measured at constant pressure, is shown in Fig. 1.

Reaction of Diazo-methane and -ethane with Mesityl Oxide.—(a) A solution of diazomethane (4·2 g.) in dry ether (600 c.c.) was evaporated in an atmosphere of nitrogen with a solution of mesityl oxide (9·8 g.) in dry ether (1000 c.c.) after the mixture had become colourless ($3\frac{1}{2}$ days). The residue, on distillation in nitrogen, yielded 6·2 g., b. p. 110°/18 mm., m. p. 50—53·5°. After crystallisation from light petroleum (b. p. 40°), the product melted at 51·5—52·5° (Found :

N, 19·9. $C_7H_{12}ON_2$ requires N, 20·0%). 5-*Acetyl*-4 : 4-*dimethylpyrazoline* was also formed when a solution of nitrosomethylamino*iso*butyl methyl ketone (0·1 mol.) in alcohol (20 c.c.) was stirred with anhydrous potassium carbonate (4 g.) and dry ether (50 c.c.) below 20°. After 3 days, 0·044 mol. of nitrogen had been evolved, and the filtered liquor was distilled in an atmosphere of nitrogen. The main fraction (9·0 g.), b. p. 110—115°/18 mm., consisted of the pyrazoline. Although stable in nitrogen, it changed within 24 hours in a loosely stoppered bottle into a brown liquid, with a disagreeable odour. The pyrazoline was stable towards copper powder at 200°, and towards polished platinum at 230°; with semicarbazide in an atmosphere of nitrogen it yielded a product, m. p. 234—236° after four crystallisations from water, which was evidently not the desired semicarbazone (Found : N, 29·5, 29·7%), and was not further investigated. The presence of an acetyl group was indicated by an odour of bromoform observed when the pyrazoline was shaken with sodium hypobromite solution, but only a tarry product could be obtained on subsequent acidification with sulphurous acid.

(b) From diazoethane (5·6 g.) in ether (1000 c.c.) and mesityl oxide (9·8 g.) in ether (100 c.c.), 5-*acetyl*-3 : 4 : 4-*trimethylpyrazoline* (Found : N, 18·3. $C_8H_{14}ON_2$ requires N, 18·2%), m. p. 76·3°, was similarly obtained. It was also prepared by decomposition of the nitrosoethylaminoketone by potassium carbonate, and was isolated in small amounts from ethereal solutions of diazoethane, prepared without precaution in respect of mesityl oxide. The pyrazoline, although stable in presence of nitrogen, rapidly liquefied in presence of air. When 3·1 g. were heated with 0·3 g. of copper powder at 185—200° in an atmosphere of nitrogen for 7 hours, they remained unchanged except for a few drops of distillate, from which a *semicarbazone*, m. p. 139—140° after crystallisation from benzene, was prepared. Its composition was that of the semicarbazone of 2 : 2 : 3-trimethyl*cyclo*propyl methyl ketone (Found : N, 23·1. $C_9H_{17}ON_3$ requires N, 23·0%).

We are pleased to express our thanks to Drs. O. R. Howell and H. Lowery for guidance in the measurements of absorption spectra.

THE COLLEGE OF TECHNOLOGY, MANCHESTER.

[*Received, July* 31*st*, 1937.]