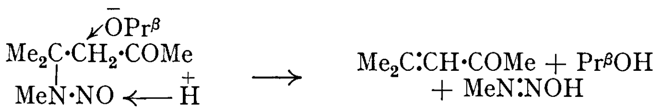
59. *The Preparation of Diazomethane and its Homologues.*

By DONALD W. ADAMSON and J. KENNER.

FURTHER experience of the method of preparing diazomethane previously described (Jones and Kenner, J., 1933, 363) revealed certain defects. These have now been remedied, and the applicability of the method to homologues and other derivatives of methylamine has been examined.

In one or two instances, large batches of freshly prepared nitroso-β-methylamino*iso*butyl methyl ketone suddenly underwent exothermic decomposition during the preliminary distillation. Since no such difficulty was encountered in redistillation of once distilled material, the decomposition was probably due to the presence of small amounts of basic substance, *e.g.*, either methylamine or its additive compound with mesityl oxide; it has been obviated by use of acetic in place of hydrochloric acid for preparation of the nitroso-derivative. As a further safeguard, the material is run continuously into the small distillation flask at a rate corresponding to that of evaporation. The product is quite stable when preserved in brown bottles.

A more subtle point was involved in a considerable reduction of the yield of diazomethane when large amounts of material were employed. This difficulty, which is also met in using the nitrosourethane method (compare Auwers and König, *Annalen*, 1932, **496**, 42, footnote), is due in our case to gradual volatilisation of *iso*propyl alcohol as the diazo-compound is removed by distillation in ether, and is therefore easily overcome. As the equation shows, proton as well as alkoxide anion is essential to the reaction :



$$\begin{array}{l} \quad\;\; \swarrow\overset{-}{\mathrm{O}}\mathrm{Pr}^{\beta} \\ \mathrm{Me_2C{\cdot}CH_2{\cdot}COMe} \\ \quad\;\;| \qquad\qquad\quad\; + \\ \mathrm{MeN{\cdot}NO} \longleftarrow \mathrm{H} \end{array} \longrightarrow \begin{array}{c} \mathrm{Me_2C{:}CH{\cdot}COMe + Pr^{\beta}OH} \\ \mathrm{+ MeN{:}NOH} \end{array}$$

The point is clearly illustrated by the stability of the nitroso-compound, in warm absolute ethereal solution, towards anhydrous potassium carbonate. Diazohydrocarbon is, however, at once evolved if alcohol is added to the mixture, though not in as satisfactory a yield as under our standard conditions.

Subject to these precautions the method would seem to be greatly superior in respect of yield and convenience to current procedure, and we have also successfully applied it to a considerable range of amines, as will be seen from the following table :

" Alkyl " group.	Yield of diazo-derivative, %.	*A*.	" Alkyl " group.	Yield of diazo-derivative, %.	*A*.	" Alkyl " group.	Yield of diazo-derivative, %.	*A*.
Me............	69·0	(7)	n-C_5H_{11}	33	(35)	$CHMe{:}CH{\cdot}CH_2$ ...	24	(20)
Et	50·4	(10)	n-C_6H_{13}	23	(50)	Furfuryl		
n-Pr	44	(10)	n-C_7H_{15}	17	(175)	$(C_4H_3O{\cdot}CH_2)$ ...	12	(175)
n-Bu	41	(20)	n-C_8H_{17}	16	(175)	$(CH_2)_3CH$	0	(–)
*iso*Bu	34	(20)	$CH_2{:}CH{\cdot}CH_2$	40·5	(10)	$(CH_2)_2CH{\cdot}CH_2$ ...	0	(–)

Nirdlinger and Acree (*Amer. Chem. J.*, 1910, **43**, 380) mention without any detail the use of solutions of diazopropane and diazobutane (compare also Werner, J., 1919, **115**, 1101), and Staudinger has described the preparation of diazo*iso*propane from acetone-hydrazone (*Ber.*, 1916, **49**, 1885). Apart from these, and diazo-methane and -ethane, the various diazo-compounds seem not to have been previously prepared. The general reaction is obviously applicable to still higher aliphatic amines than those shown, provided the corresponding nitroso-compounds can be distilled below about 180°, which appears to be the extreme temperature they will withstand without decomposition. The rapid rise in boiling point of the diazo-compounds with increase in molecular weight (compare Staudinger, *loc. cit.*) correspondingly hinders their volatilisation in ether, and so not only prolongs the operation but involves their preparation in comparatively dilute solution. The figures in parentheses in the above table (col. *A*) show the volumes of ether (c.c.) required for the complete distillation of the diazohydrocarbon generated in each case from

1 gram of nitroso-derivative. This difficulty can be met to some extent by use of *iso*propyl ether, but, on the other hand, it is not practicable to concentrate an ethereal solution by fractional distillation through, for example, a Widmer column. An experiment on these lines with a solution of diazo-octane resulted in decomposition of the diazohydrocarbon, and this instability is obviously partly responsible for the diminution in yield with increase in molecular weight. Staudinger has shown that diazo*iso*propane readily decomposes with formation of dimethylketazine (*loc. cit.*).

The diazohydrocarbons were estimated and characterised by conversion into the corresponding *p*-nitrobenzoates or 3 : 5-dinitrobenzoates, and the following table shows a comparison of melting points with those of specimens prepared by interaction of acid chloride and alcohol (compare Buchner and Meisenheimer, *Ber.*, 1905, **38**, 624), or as recorded by Henstock in connexion with his modification of the Schotten–Baumann method (J., 1933, 216).

p-*Nitrobenzoates.*

Ester.	From diazo-compound.	Buchner–Meisenheimer.	Henstock.
Me……………	95·5°	95·5°	96°
Et …………	56·0	56·0	57
n-Pr …………	35—35·5	35·0 (b. p. 114/0·05 mm.)	32
*iso*Pr ………	—	110·5 (b. p. 109/0·05 mm.)	55·5
n-Bu ………	35·5	35·2	35
*iso*Bu ………	68·5—69	68·5	67
n-C_5H_{11} ……	8½—10½	6½—8½ (b. p. 133/0·095 mm.)	54
CH_2:CH·CH_2	28	28	—

3 : 5-*Dinitrobenzoates.*

Ester.	From diazo-compound.	Buchner–Meisen-heimer.
n-C_5H_{11}…………	46·0°	45·5°
n-C_6H_{13} ………	58·2	58·5
n-C_7H_{15}…………	46	46·0
n-C_8H_{17}…………	58·5	60·5
CHMe:CH·CH_2…	50—51	—
Furfuryl (C_4H_3O·CH_2)	84—86	—

The agreement between the diazo- and the Buchner–Meisenheimer products is good, but there are striking discrepancies between the data for these and those of Henstock. A repetition of Henstock's work with *iso*propyl alcohol yielded a crude product, m. p. 54—78°, from which the pure product, m. p. 109—110·5°, was ultimately obtained by crystallisation from light petroleum. Henstock used alcohol as a solvent, and it seems significant that two of his discordant values agree with those of the ethyl ester. It is possible that a tendency to reduction of the nitro-group is an inherent difficulty in applying the Schotten–Baumann method to nitrobenzoyl chlorides and alcohols, because in our experience coloured impurities accompany the crude nitrobenzoates so obtained.

Since the use of the higher diazohydrocarbons for esterification or similar purposes involves in the first place reaction with proton, a complex kation should result which is closely comparable with that postulated as the cause of the Wagner–Meerwein change, *e.g.*, in the case of primary amines (compare Adamson and Kenner, J., 1934, 838),

$$R{\cdot}CH_2{\cdot}CH{:}N_2 \xrightarrow{\overset{+}{H}} R{\cdot}CH_2{\cdot}\overset{+}{C}H_2{\cdot}N_2$$

$$R{\cdot}CH_2{\cdot}CH_2{\cdot}NH_2 \longrightarrow R{\cdot}CH_2{\cdot}CH_2{\cdot}\overset{+}{N}_2$$

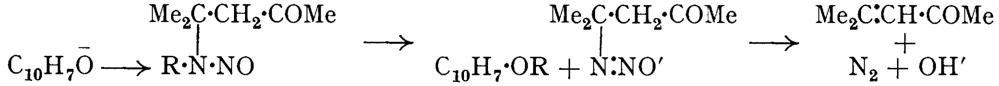
Since *iso*propyl alcohol is produced from *n*-propylamine, it was necessary to determine whether any *iso*propyl ester accompanied the *n*-propyl ester obtained from diazopropane. This was carefully investigated in the cases of the benzoate, the nitrobenzoate, and the iodide prepared from it, but in each instance no *iso*propyl derivative was detected. This is in agreement with the view that decomposition of the diazonium ion depends on attack by anion, *e.g.*, hydroxyl, in the α- or β-position to the diazonium group simultaneously with, and not subsequently to, the separation of nitrogen.

Reference was made in the previous paper to the use of our nitroso-compounds for the alkylation of phenols directly and without preliminary preparation of the corresponding diazohydrocarbon. Since then a process has been described which was devised by Meerwein for the preparation of methyl ethers by the use of nitrosomethylurethane in alcoholic solution in presence of weak bases, *e.g.*, solid potassium carbonate (Schering–Kahlbaum

A.-G., D.R.-P. 579,309). We have now applied this process to β-naphthol and some of the nitrosoalkylamino*iso*butyl methyl ketones with the results summarised :

" Alkyl."	Duration of experiment.	Yield, %.	M. p. of β-naphthyl ether obtained.
Methyl	20 hrs.	70	73°
Ethyl	20 ,,	35	35—36
n-Propyl	20 ,,	34	39—40
*cyclo*Propylmethyl	20 ,,	20	74
Furfuryl	4 days	38·5	oil

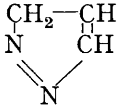
Again in the case of the propyl derivative, homogeneity of the product was confirmed, this time by identity of the picrates obtained from the recrystallised ether and from the mother-liquors. The yield of furfuryl ether is three times that of the diazo-compound already recorded, and the result in the case of the *cyclo*propylmethyl ether is even more striking. When account is also taken of the fact that alkylation occurs at the ordinary temperature, whereas diazohydrocarbon formation only takes place at 60—70°, the possibility has to be considered that alkylation may be alternative to diazohydrocarbon formation, just as dealkylation of a quaternary ammonium salt is alternative to olefin formation. The different result could be attributed to the fact that β-naphthoxy-ions enter into covalent combination with alkyl more readily than with hydrogen :



$$\mathrm{C_{10}H_7\bar{O}} \longrightarrow \mathrm{R{\cdot}}\overset{\mathrm{Me_2C{\cdot}CH_2{\cdot}COMe}}{\overset{|}{\mathrm{N}}}\mathrm{{\cdot}NO} \longrightarrow \mathrm{C_{10}H_7{\cdot}OR} + \overset{\mathrm{Me_2C{\cdot}CH_2{\cdot}COMe}}{\overset{|}{\mathrm{N}}}\mathrm{{:}NO'} \longrightarrow \overset{\mathrm{Me_2C{:}CH{\cdot}COMe}}{\overset{+}{\mathrm{N_2 + OH'}}}$$

As might be anticipated, vinyldiazomethane (I) is more highly coloured than its analogues derived from saturated amines, and moreover gradually loses its colour owing to formation of pyrazole :

(I.) $\mathrm{CH_2{:}CH{\cdot}CH{:}N_2} \longrightarrow$



This interesting reaction requires about 36 hours for completion in 0·5% ethereal solution at the ordinary temperature in daylight, but is sensitive to light. Our preliminary measurements under constant illumination have shown the reaction to be accurately unimolecular. The methyl homologue, derived from crotonylamine, is more intensely coloured, and also much more stable. In both instances, reaction with benzoic acid is very much slower than in the cases of the saturated derivatives.

EXPERIMENTAL.

Preparation of Nitroso-ketones.—A solution of sodium nitrite (2 mols.) in the minimum amount of water was added to the product of mixing mesityl oxide (1 mol.) with a primary amine (1 mol.) (compare Jones and Kenner, *loc. cit.*) after neutralisation with glacial acetic acid. Glacial acetic acid (1 mol.) was then added, and the mixture left for 2 hours, ice-cooling being applied if necessary to check too vigorous a reaction. An ethereal extract of the nitroso-compound was washed twice with dilute acetic acid and then with water, and dried over sodium sulphate. Ether having been removed at as low a temperature as possible, the residual nitroso-derivative was distilled under reduced pressure from a small Claisen flask, into the side of which a dropping-funnel had been fused to permit of continuous addition of the crude material. Further distillation of the higher homologues was necessary to remove the small quantities of olefin or alcohol which accompany the crude nitroso-derivative. The following table includes revised boiling points of the compounds previously described :

" Alkyl " group.	B. p./ mm.	N, found, %.	N, required, %.	Yield, %.
Me	111°/0·5	—	—	67
Et	124/0·7	—	—	72
n-Pr	121/0·5	—	—	73
*iso*Pr	120/0·7	15·2	15·0	20·4
n-Bu	127/0·6	—	—	70
*iso*Bu	133/0·7	14·0	14·0	50·4
n-C_5H_{11}	154/0·8	—	—	59
n-C_6H_{13}	160/0·6	12·0	12·3	60
n-C_7H_{15}	156°/0·8	11·6	11·6	60
n-C_8H_{17}	151/0·2	11·0	10·9	72
$(CH_2)_2CH{\cdot}CH_2$	136/0·7	14·1	14·1	56
$(CH_2)_3CH$	177/0·8	14·3	14·1	35
Furfuryl	158/0·8	12·4	12·5	40·2
$CH_2{:}CH{\cdot}CH_2$	117/0·4	15·3	15·2	64
$CHMe{:}CH{\cdot}CH_2$	123/0·14	14·2	14·1	65

Preparation of Diazohydrocarbons.—Experiments by E. C. S. Jones on the scale and lines of those previously described had shown that satisfactory yields of homologues of diazomethane could be obtained, but his results could not be reproduced on the larger scale, even in the case of diazomethane itself, until the general procedure below was evolved and employed in an apparatus consisting of a 20-c.c. Claisen flask carrying a tap funnel and connected to a condenser. The latter was fitted with an adapter dipping below ether (5 c.c.) in a receiver cooled by ice. A solution of the nitrosomethylamino-ketone (4 g.) in absolute ether (30 c.c.) and *iso*propyl alcohol (3 c.c.) was added drop by drop to a 1% solution of sodium in *iso*propyl alcohol (5 c.c.) at 76—80° at a rate equivalent to that of distillation. At an appropriate point in the operation a further quantity of sodium *iso*propoxide solution (4 c.c.) was added. Finally, absolute ether (*ca.* 5 c.c.) was added until the distillate was no longer coloured. In this way diazomethane (0·7 g.) was prepared in 20 minutes, and larger quantities were prepared as satisfactorily in separate batches as in one larger one. For the homologues, a longer period and a larger supplementary quantity of ether were required owing to the higher b. p.'s of the diazo-compounds. In such cases *iso*butyl alcohol was frequently used in place of *iso*propyl alcohol owing to its higher b. p. and the fact that it dissolves a quantity of its sodium derivative about five times greater than its lower homologue does. Very poor results were obtained by use of *sec.*-octyl alcohol or glycol. The yields were determined by titration as before and are recorded in the introduction.

Of the esters mentioned in the table, the following are new: *n-amyl p-nitrobenzoate*, b. p. 133°/0·1 mm. (Found: N, 6·2. $C_{12}H_{15}O_4N$ requires N, 5·9%); *crotonyl* 3 : 5-*dinitrobenzoate* (Found: N, 10·8. $C_{11}H_{10}O_6N_2$ requires N, 10·5%); *furfuryl* 3 : 5-*dinitrobenzoate* (Found: N, 9·6. $C_{12}H_8O_7N_2$ requires N, 9·6%).

Etherification of β-Naphthol.—Equimolecular proportions of β-naphthol and nitroso-ketone were stirred at the ordinary temperature in absolute alcoholic solution (1500 c.c. per g.-mol.) with anhydrous potassium carbonate until evolution of nitrogen had ceased. Alcohol and mesityl oxide having been removed from the filtered solution by evaporation under reduced pressure, the ethereal solution of the residue was washed with dilute alkali, dried, and evaporated. The table given in the introduction summarises the results obtained.

From a similar experiment in which the quantity of methylnitroso-ketone (1·33 mols.) corresponded to the yield of diazomethane already recorded, the yield of methyl ether was 85%.

Naphthyl *n*-propyl ether furnished a picrate, m. p. 80—81° (Found: N, 10·1. Calc. for $C_{19}H_{17}O_8N_3$: N, 10·1%), and no sign of any isomeride was detected, although Bodroux (*Compt. rend.*, 1898, **126**, 840) recorded 75° as the melting point of the picrate, and 92° as that of the picrate of β-naphthyl *iso*propyl ether.

Pyrazole from Vinyldiazomethane.—The deep red ethereal solution (75 c.c.) from the alkylnitroso-ketone (1·6 g.) became colourless after 36 hours at the ordinary temperature, and on evaporation furnished a crystalline residue (0·24 g.), m. p. 67°, which, recrystallised from light petroleum, gave needles, m. p. 69·5°. It did not depress the m. p. of pyrazole prepared by Balbiano's method (*Ber.*, 1890, **23**, 1105). A boiling *iso*propyl ethereal solution of the diazo-compound became colourless within a few minutes.

A quantitative study of the change was made by irradiating an ethereal solution (0·102%) with light from a 60 candle power Osram lamp from a distance of 10 cm., and measuring the Bunsen extinction coefficient at 5140 Å. (where least absorption occurred) in a Hilger Nutting spectrophotometer every ½ hour. The following readings were obtained, and conform closely to a linear relationship:

Time (hrs.)	0	0·5	1	1·5	2	2·5	3	3·5	4
Coefficient	19·4	17·2	15·0	12·6	10·6	8·6	6·4	4·2	2·4

An ethereal solution of propenyldiazomethane (0·05%) was deeper red than that of vinyldiazomethane and was only completely decolorised after 14 days at the ordinary temperature: a boiling ethereal solution lost its colour in 2 hours. The product was an oil and on account of the small quantity available was not definitely identified with 3-methylpyrazole, which is also an oil (Knorr and Macdonald, *Annalen*, 1894, **279**, 217).

The College of Technology, Manchester. [*Received, December, 8th,* 1934.]