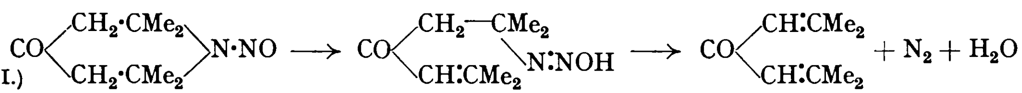
98. *The Catalytic Decomposition of Nitroso-β-alkylamino-ketones. Part I. A New Method of preparing Diazomethane, and Evidence of the Occurrence of Diazotisation in the Aliphatic Series.*

By E. C. S. Jones and J. Kenner.

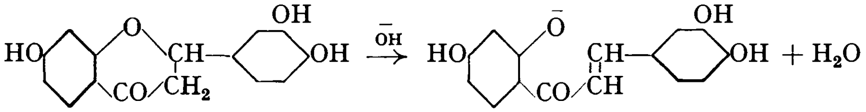
The importance of the tendency of nitroso-compounds to pass into oximino-derivatives having been illustrated in previous papers (J., 1928, 2697; 1930, 919), it appeared that the first stage of the catalytic decomposition of nitrosotriacetoneamine (I) by hydroxyl ions (Heintze, *Annalen*, 1877, **187**, 250; Francis and collaborators, J., 1912, **101**, 2356; 1913, **103**, 1722; 1915, **107**, 1651, 1673) might supply a further instance of this kind:

(I.)



The reaction would thus be formally analogous to the decomposition of chromanones by alkali, as exemplified by butin (II) (Perkin and Hummel, J., 1904, **85**, 1463) and rotenone (Butenandt, *Annalen*, 1932, **494**, 17):

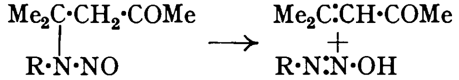
(II.)



In each case the determining factor is considered to be the tendency of the oxygen atom to acquire more complete control of its octet.

In order to test this hypothesis, we have in the first place examined the behaviour of open-chain nitroso-derivatives derived from the additive products of primary amines with mesityl oxide (cf. Hochstetter and Kohn, *Monatsh.*, 1903, **24**, 779; 1904, **25**, 841):

(III.)



(IV.)

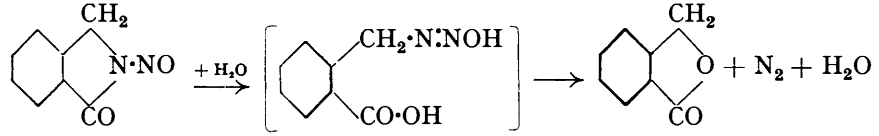
$$\underset{R\cdot N\cdot NO}{Me_2C\cdot CH_2\cdot COMe} \longrightarrow Me_2C{:}CH\cdot COMe + R\cdot N{:}N\cdot OH$$

As anticipated, each of the substances investigated underwent catalytic decomposition by alkali, and further, the *nitrosophenylamino*-derivatives (type III) yielded a diazo-solution (type IV) from which benzeneazo-β-naphthol was prepared by coupling. This corresponds to the similar behaviour of nitrosoacetanilide, described by Bamberger (*Ber.*, 1897, **30**, 366). Similarly, Hantzsch and Lehmann were able to isolate potassium methyl diazotate as the primary product of the action of concentrated potassium hydroxide solution on nitrosomethylurethane, and to show that diazomethane is only evolved when this salt undergoes hydrolytic dissociation (*Ber.*, 1902, **35**, 901):

$$EtO\cdot CO\cdot NMe\cdot NO \longrightarrow MeN{:}NOK \longrightarrow CH_2{:}\overset{+}{N}{:}\overset{-}{N} + KOH$$

In fact, it would appear that the preparation of the gas from the urethane or from nitrosomethylurea (cf. Arndt and Amende, *Z. angew. Chem.*, 1930, **43**, 444) involves a compromise in regard to the concentration of alkali between a speedy preliminary hydrolysis and restraint on the second reaction. This, together with the temperature at which the reaction is carried out, possibly accounts for the moderate yield (about 45%). These difficulties are avoided by the catalytic decomposition of our *nitrosomethylamino*-derivative (type III) at a low temperature and we have obtained upwards of an 80% yield in presence of sodium *iso*propoxide. The efficiency of an alkoxide for this purpose is obviously dependent on the relative acidities of the nitroso-ketone and of the alcohol in question, and the comparative experimental results illustrate very clearly the importance of this factor. Repression of decomposition by excess of alkali also occurs in this case as in those first discussed, and in that of nitrosotriacetonamine (Francis, *loc. cit.*).

It is thus clear that the nitrosoalkylamino*iso*butyl methyl ketones (III) afford a source from which aliphatic diazotates may be generated under the mildest conditions. It would be anticipated that their decomposition in aqueous solution would yield alcohols, and the catalytic formation of phthalide from nitrosophthalimidine in presence of alkali (Graebe, *Ber.*, 1884, **17**, 2598; *Annalen*, 1888, **247**, 288; Brück, *Ber.*, 1901, **34**, 2746) is an illustration of this:

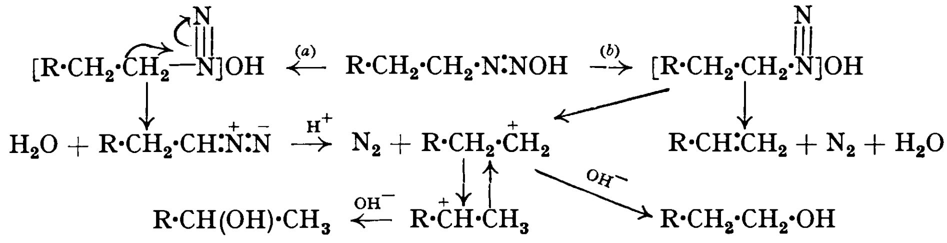


Similarly, *nitrosobenzylamino*iso*butyl methyl ketone*, a stable well-defined crystalline compound, can be conveniently used for the benzylation of phenols, in the same way as nitroso-acid and -sulphonic alkyl amides may be employed for alkylation (cf. D.R.-P. 89843, 95644, 224388). The matter is of some interest in view of the increasing use of benzyl ethers for synthetic purposes (cf. Robinson and collaborators, J., 1928, 1544; 1929, 68; 1930, 817; 1931, 3163; Douglas and Gulland, J., 1931, 2895). We have also used the corresponding methyl derivative directly in place of diazomethane for methylation (cf. D.R.-P. 95644; Karrer, *Ber.*, 1916, **49**, 2074); but our experience here is similar to that noted in the preparation of diazomethane in that, for these purposes also, the most suitable proportion of alkali varies with the acidity of the phenol, and must be determined in each case.

Within recent years the barriers between aromatic and aliphatic chemistry have been gradually demolished, until in 1929 Wieland, whose own researches in this direction have been prominent, declared that the only outstanding point was actual evidence of diazotisation in the case of primary aliphatic amines, apart from the isolated instances of the α-amino-acid esters (*Z. angew. Chem.*, 1929, **42**, 904). Nevertheless there has been a tendency to assume its occurrence. McKenzie, for instance, has incorporated the idea in his views on the course of semipinacolinic deamination (*Ber.*, 1929, **62**, 272, 284) and one of us has recently indicated its value in relation to the Walden inversion (*Nature*, 1932, **130**, 309). We have now supplied an experimental basis for the assumption by showing that propylene, propyl alcohol, and *iso*propyl alcohol all result from the catalytic decomposition of *nitroso*-n-*propylamino*iso*butyl methyl ketone*, as from that of *n*-propylamine nitrite (Linnemann, *Annalen*, 1872, **161**, 3; V. Meyer, *Ber.*, 1876, **9**, 535; 1877, **10**, 130). Similarly olefins are present in the gaseous products from the n-*butyl* and n-*amyl* homologues.

The various modes of decomposition of aliphatic diazo-compounds thus revealed correspond broadly to those of quaternary ammonium hydroxides (cf. *Ann. Reports*, 1930, 143), though it will be desirable to ascertain whether the Hofmann decomposition can also yield a mixture of alcohols. The results illustrate the point that the constitutive influences in the alkyl group which have been accorded such prominence in recent discussions of this reaction are really subsidiary to the tendency of the nitrogen atom to recover its tervalent condition in determining the reaction.

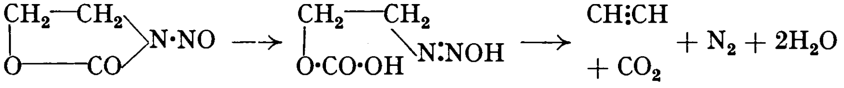
Assuming that avoidance of excess of hydroxyl ions permits formation of the diazonium hydroxide, as in the aromatic series, reaction may proceed according to one or other of the following schemes:



Clearly (a) alone is applicable to the nitrosomethylamino-ketone. Lengthening of the carbon chain in the homologues might be expected to favour (b) at the expense of (a), but the occurrence of the latter is indicated by the almost complete absence of ethylene from the products of decomposition of the ethyl derivative, and similarly the proportion of olefin from the propyl and butyl derivatives is much less than in the normal Hofmann decomposition. Further, there are already statements in the literature in regard to the formation of some of the homologues of diazomethane (v. Pechmann, *Ber.*, 1898, **31**, 2643; Arndt and Martius, *Annalen*, 1932, **499**, 278; Nirdlinger and Acree, *Amer. Chem. J.*, 1910, **43**, 380; cf. Werner, J., 1919, **115**, 1101). In a future paper we hope to contribute a study of the properties of these compounds, which our improved method of preparation renders more feasible. The behaviour of α-amino-acid esters towards nitrous acid accords with the above schemes, there being a greater tendency to formation of hydroxy- rather than of diazo-acid esters from the homologues of glycine ester (Curtius and Müller, *Ber.*, 1904, **37**, 1263).

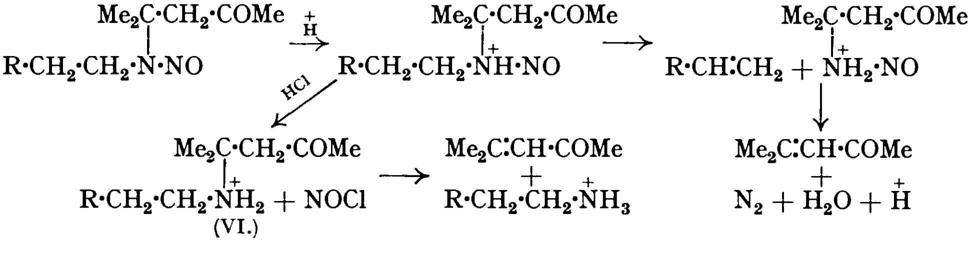
The formation of olefins in the above instances corresponds to the second stage in the decomposition of nitrosotriacetonamine: and to the formation of acetylene by the catalytic decomposition of nitroso-oxazolone (V) in presence of alkali (Gabriel, *Ber.*, 1905, **38**, 2410):

(V.)



The production of secondary alcohols from primary amines is presumably a result of the Meerwein rearrangement of cations. Striking instances of this kind are already on record (Tissier, *Compt. rend.*, 1891, **112**, 1065; Henry, *ibid.*, 1907, **145**, 899; Freund and Levene, *Ber.*, 1891, **24**, 2151; Noyes and Skinner, *J. Amer. Chem. Soc.*, 1917, **39**, 2692), and the familiar work of Demjanow on the enlargement of alicyclic ring structures also falls within this category (*J. Russ. Phys. Chem. Soc.*, 1903, **35**, 26; 1904, **36**, 166; *Ber.*, 1907, **40**, 2589). Similarly it does not appear previously to have been emphasised that the formation of secondary as well as normal products when *n*-alkyl halides are employed in the Friedel–Crafts reaction must be accepted as evidence that the course of the latter involves a cationic condition of the alkyl radical. The recent measurements of Wohl and Wertyporoch (*Ber.*, 1931, **64**, 1362) are in agreement with this suggestion.

Our nitroso-derivatives also suffer decomposition in presence of concentrated mineral acid, owing to salt formation at the aminic nitrogen atom, and the nitrogen evolved is accompanied by a considerable proportion of olefin. We were unable, however, to develop the reaction as a satisfactory alternative to the exhaustive methylation process for the degradation of amines, and the yields of ethylene obtained in a series of experiments under various conditions did not attain 40%. This is due to an alternative course of the reaction, which results in the formation of amine hydrochloride, and alone occurs in a non-dissociating solvent, *e.g.*, with ethereal hydrogen chloride:



Under the latter conditions, for example, the hydrochloride of the ethylamino-base (VI) was isolated and no gas evolution took place.

EXPERIMENTAL.

Nitroso-β-alkylaminoisobutyl Methyl Ketones.—When mesityl oxide (1 mol.) was added to a mixture of an aliphatic amine (1 mol.) with twice its wt. of H_2O, the whole rapidly became homogeneous and some heat was evolved. After 1 hr., the mixture was just acidified at 0°

with HCl aq. (*d* 1·16), extracted with Et_2O to remove any mesityl oxide, and treated at 0° with $NaNO_2$ (1 mol. in its own wt. of H_2O). When no further formation of oil seemed to occur, $NaNO_2$ (1 mol.) was again added, and the mixture gradually treated at 0° with 5*N*-HCl (1 mol.). Finally an ethereal extract of the *nitroso*-compound was washed twice with ice-water and dried over $CaCl_2$. In every case the yield after distillation at the press. indicated in the table was good.

Alkyl group.	B. p.	N found.	N required, %.
Me	111°/0·8 mm.	17·9	17·7
Et	114°/0·5 mm.	16·61	16·3
n-Pr	120°/1 mm.	15·05	15·05
n-Bu	127°/0·6 mm.	14·06	14·0
n-C_5H_{11}	127°/0·3 mm.	13·38	13·08

These compounds decompose with formation of olefins when heated, so that their analysis requires corresponding care.

β-Benzylamino*iso*butyl methyl ketone was isolated in the form of its hydrochloride, which crystallised from alcohol in silky needles (Found: N, 6·0. $C_{13}H_{19}ON,HCl$ requires N, 5·8%). The *nitroso*-derivative, well-defined transparent needles, m. p. 85—86° (Found: N, 12·0. $C_{13}H_{18}O_2N_2$ requires N, 12·0%), was moderately sol. in hot EtOH or Et_2O and sparingly in C_6H_6 or ligroin.

β-*Arylamino*iso*butyl Methyl Ketones*.—A mixture of mesityl oxide (0·1 mol.) with aromatic amine (0·1 mol.) was kept at 40—50° for 5 days, and then at 0° rendered just acid with conc. HCl. After extraction with Et_2O, and treatment with NaOH aq., the mixture of bases was extracted with Et_2O and dried. The yields of β-arylamino*iso*butyl methyl ketone finally isolated by distillation at low press. were about 25% of the theo. amount in each case. The corresponding nitrosoamines were prepared by treating the cooled bases successively with 5*N*-HCl and 50% $NaNO_2$ aq. Finally, to complete the reaction, a further quantity of $NaNO_2$ aq. was added, followed gradually by an equiv. of 5*N*-acid. The nitrosoamine was removed by Et_2O, dried, and isolated in good yield in the cryst. condition.

*Nitroso-β-phenylamino*iso*butyl methyl ketone*, from the crude secondary base, b. p. 108°/3 mm., separated from ligroin in thick sandy prisms, m. p. 59—61° (Found: N, 13·0. $C_{12}H_{16}O_2N_2$ requires N, 12·7%). *Nitroso-β-*m*-tolylamino*iso*butyl methyl ketone*, from the secondary base, b. p. 120—128°/35 mm., was obtained in somewhat reddish prisms, m. p. 78° (Found: N, 12·1. $C_{13}H_{18}O_2N_2$ requires N, 12·0%). Nitroso-β-*p*-tolylamino*iso*butyl methyl ketone, from the secondary base, b. p. 120—128°/35 mm., formed orange prisms, m. p. 105—108°. From each of these, azo-compounds were obtained when the nitroso-derivative and sodium β-naphthoxide (equal mols.) were treated in aq. alc. solution with NaOH (0·1 mol.). The products were identified by direct comparison with the authentic arylazo-β-naphthols.

*Decomposition of Nitroso-β-alkylamino*iso*butyl Methyl Ketones*.—*Formation of diazomethane*. A weighed quantity of nitroso-β-methylamino*iso*butyl methyl ketone was treated in ethereal solution with a definite amount of sodium alkoxide (0·1 mol.), and the mixture then warmed. The distillate, collected in Et_2O in a receiver cooled in a freezing mixture, was an ethereal solution of diazomethane, the concn. of which was determined by titration with ethereal benzoic acid solution. Diazomethane appeared to be generated only on warming, since the first drops of distillate were colourless.

Nitrosoamine, g.	Ether, c.c.	Na in alcohol.		Yield of diazomethane, %.
		Sodium.	Alcohol.	
0·160	10	0·0023 g.	1·0 c.c. EtOH	50
0·316	20	0·0046 g.	2·0 c.c. EtOH	55
0·316	40	0·005 g.	2·5 c.c. $Pr^{\alpha}OH$	70
0·316	40	0·058 g.	2·5 c.c. $Pr^{\beta}OH$	83·5
2·0	70	0·04 g.	4·0 c.c. $Pr^{\beta}OH$	70
0·316	40	2·0 c.c. *sec.*-butyl alcohol sat. with Na		70
0·316	40	2·0 c.c. methylpropylcarbinol sat. with Na		75
0·316	20	2·0 c.c. *tert.*-butyl alcohol sat. with Na		Almost nil

Decomposition of nitrosoamines. A weighed amount of nitroso-compound was placed in a 50-c.c. flask connected to a CO_2 generator and, through a small reflux condenser, to a nitrometer charged with KOH aq. (1 : 1). The apparatus was evacuated and filled with CO_2, and alkali or acid introduced from a small tap-funnel; heat was then applied until reaction commenced, and afterwards to complete it. The gaseous products were swept into the nitrometer in CO_2, and olefin was estimated in the gaseous product by absorption with Br after transference to a suitable burette. The gaseous products of acid decomp. also contained acetone, which, however, was easily removed by means of brine.

A. Alkaline decomposition.

Alkyl group.	Nitroso-derivative, g.	Alkali added.	Percentage of theo. yield.	
			Unsaturated gas.	Nitrogen.
Methyl	0·2	4·5 c.c. 5% NaOH	Nil	100
Ethyl	0·2	4·5 c.c. 5% NaOH	—	100
n-Propyl	0·35	20 c.c. H_2O + 3·5 c.c. 20% NaOH	24·3	100
n-Butyl	0·24	15 c.c. 3·3% NaOH	30·2	100
n-Amyl	0·27	5·0 c.c. $Pr^{\beta}OH$ + 5·0 c.c. 10% NaOH = 5% NaOH	26·6	100

*Examination of the products from the nitroso-*n*-propylamino-derivative.* When the nitroso-compound (14 g.) in H_2O (100 c.c.) and NaOH (0·3 g.) were mixed, reaction set in immediately. After some time the mixture was warmed and finally gently boiled. The gaseous products were collected in an aspirator, from which they were later slowly passed through Br and H_2O in a " Wöhler " tube cooled in ice-water. In this way 2·0 g. of pure propylene dibromide were obtained, b. p. 141° (Found : Br, 78·9. Calc. : Br, 79·1%).

The alkaline liquor was saturated with K_2CO_3 and extracted with Et_2O. The ethereal solution, dried with K_2CO_3 and fractionated, yielded 3·4 g. of liquid, b. p. 80—110°. From this, by refractionation, 1·1 g., b. p. 80—83°, and 1·3 g., b. p. 83—100°, were separated.

The former fraction was essentially *iso*propyl alcohol and furnished a *p*-nitrobenzoate, m. p. 108—110° alone or mixed with authentic *iso*propyl *p*-nitrobenzoate. Refractionation of the portion, b. p. 83—100°, provided 0·8 g., b. p. 92—98°, from which *n*-propyl *p*-nitrobenzoate, m. p. and mixed m. p. 35°, was prepared.

In a similar expt., *n*-propyl alcohol was also identified through its *p*-nitrobenzyl phthalate, m. p. 50—53° (Reid, *J. Amer. Chem. Soc.*, 1917, **39**, 1251), but this procedure did not prove satisfactory for identification of *iso*propyl alcohol.

B. Acid decomposition.

Alkyl. group.	Nitroso-derivative, g.	Acid.	Percentage of theo. yield.	
			Unsaturated gas.	Nitrogen.
Ethyl	0·295	4·5 c.c. HCl (*d* 1·16)	39	100
,,	0·3625	5 c.c. 66% H_2SO_4	38	100
,,	0·360	Ethereal HCl	No gas evolved. Crystals deposited, m. p. 135—140°, which did not depress the m. p. of authentic β-ethylamino*iso*butyl methyl ketone hydrochloride, m. p. 140°. Ether solution turned moistened starch-iodide paper blue. Crystals dissolved in H_2O, and when boiled with NaOH gave characteristic smell of ethylamine and of mesityl oxide.	
n-Propyl	0·745	5·5 c.c. HCl (*d* 1·16)	54	96·1
n-Butyl	0·315	2·5 c.c. HCl (*d* 1·16)	20	90
,,	0·317	5 c.c. HCl (1·3*N*)	36	82
,,	0·329	4·5 c.c. formic acid	28	91
n-Amyl	0·354	4·5 c.c. HCl (3·3*N*)	31	67
			No NO, but amine produced, identified as *n*-amylammonium chloride, m. p. 225° (mixed m. p. gave no depression).	

Identification of ethylene from the nitrosoethylamino-ketone. The gas obtained by decomposing the ketone (9·75 g.) with HCl aq. (20 c.c., *d* 1·16) was passed slowly through bromine water. The resultant ethylene dibromide (2·0 c.c.), b. p. 131°, m. p. 8°, was identified by condensation with phthalimide; the product had m. p. 232°, alone or mixed with authentic 1 : 2-diphthaliminoethane (Gabriel, *Ber.*, 1887, **20**, 2225).

Alkylation Experiments.—The following table of representative expts. is sufficiently explanatory. In each case the identity of the alkylation product was established by direct comparison with authentic material. All the expts. were performed at the ordinary temp. unless otherwise stated.

Methylation.

Nitroso-compound, g.	Phenol, g.	Alcohol.	Water.	Alkali.	Yield, %.
0·8	β-Naphthol, 0·72	—	10 c.c.	0·1 g. NaOH	90
0·8	*p*-Nitrophenol, 0·7	—	10 c.c.	0·2 g. NaOH	79
0·8	Morphine hydrochloride, 1·7	—	10 c.c.	0·3 g. NaOH	44
		Warmed—vigorous reaction.			
0·8	β-Naphthol, 0·7	Fused, added 2—3 drops 20% NaOH, removed mesityl oxide at pump.			63
		Ethylation.			
0·09	*p*-Nitrophenol, 0·7	5 c.c.	5 c.c.	0·3 g. NaOH	25
		Benzylation.			
1·0	β-Naphthol, 0·62	10 c.c.	0·5 c.c.	0·1 g. NaOH	50*
4·8	,, 2·8	25 c.c. *iso*propyl	(2·3 c.c. *iso*propyl Na)	0·023 g.	32*
1·17	,, 0·72	—	11 c.c.	0·2 g. NaOH	Nil †
1·17	,, 0·72	Fused, added 2 drops 20% NaOH; heated till reaction ceased. Removed mesityl oxide at pump.			70

Duration of expt.: * 2 days, † *ca.* 20 min.

Grateful acknowledgment is made of a research grant from Imperial Chemical Industries, Ltd.

THE COLLEGE OF TECHNOLOGY, MANCHESTER.

[*Received, February* 11*th*, 1933.]