material, but at 128°. By comparing the ester and the final N-benzoyl substance with known products Kanao was able to identify both as derivatives of nor-*dl*-ψ-ephedrine. In other words, in all this process phenylpropanolamine had undergone a shift in configuration and into the pseudo form. From his results Kanao was led to believe that the ester can exist only when the amino alcohol is in this configuration. While we have as yet made no studies with the possible stereoisomers of our compounds, it would appear that our ester is of the nor-ephedrine type, for not only has it a melting point different from that found by Kanao, but the amide resulting from the rearrangement of the ester (m. p. 142–143°) is the N-benzoyl derivative of nor-*dl*-ephedrine.

Summary

1. The synthesis of the benzoic ester of phenylpropanolamine hydrochloride has been described. This synthesis presumably does not result in isomerization into the pseudo configuration.

2. This ester is structurally related to pressors and anesthetics.

3. Benzoylation of the alcoholic hydroxyl conferred anesthetic properties but caused a decrease to a tenth or less of the pressor potency.

4. This is the first compound to possess a demonstrated pressor and anesthetic action.

PHILADELPHIA, PENNSYLVANIA

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

NITROSO COMPOUNDS. I. (PRELIMINARY PAPER.) THE PREPARATION AND REDUCTION OF CERTAIN NITROSO KETONES

BY JOHN G. ASTON, DAVID F. MENARD AND M. GLENN MAYBERRY

RECEIVED NOVEMBER 3, 1931 PUBLISHED APRIL 6, 1932

Introduction

The present paper deals with the preparation of α-nitroso ketones of the type, $(CH_3)_2C(NO)COCH_2R$, by the action of ethyl nitrite upon the corresponding ketones. The reduction of these α-nitroso ketones has also been studied with quite unexpected results.

The direct nitrosation of ketones upon an α-methylene group is a general reaction

$$RCH_2COR' + R''ONO \xrightarrow[C_2H_5ONa]{HCl} RC(=NOH)COR' + R''OH$$

The product of nitrosation in such cases is invariably the oxime.[1]

[1] Claisen and Manasse, *Ber.*, **22**, 526 (1889); Ponzio and DeGaspari, *J. prakt. Chem.*, [2] **58**, 392 (1896).

In order to obtain a stable true α-nitroso ketone, nitrosation must occur on a carbon atom with but one hydrogen atom; 4-nitrosomenthone has been prepared by the action of amyl nitrite and hydrochloric acid on menthone.[2] Simultaneously cleavage occurs between the nitroso substituted α-carbon and the ketone group, yielding 3,7-dimethyl-6-oximino-octanoic acid.[3]

Methyldesoxybenzoin is cleaved in a similar manner by the action of nitrous acid but in this case the intermediate nitroso compound is not obtained.[4]

$$C_6H_5COCH(C_6H_5)CH_3 + HNO_2 \longrightarrow C_6H_5COOH + C_6H_5C(=NOH)CH_3$$

Discussion of Results

When ketones of the type $(CH_3)_2CHCOCH_2R$ are treated with an equivalent quantity of ethyl nitrite in the presence of hydrochloric acid at about 50° it is possible to isolate the bimolecular true nitroso compounds. In the case of methyl isopropyl ketone a 24% yield of methyl α-nitroso-isopropyl ketone (I) was obtained.

$$2(CH_3)_2CHCOCH_3 + 2HNO_2 \longrightarrow 2H_2O + \underset{\text{(I)}}{[(CH_3)_2C(NO)COCH_3]_2}$$

No product corresponding to direct nitrosation on the methyl group was found. Evidence for a cleavage as in the case of methyldesoxybenzoin was obtained by the isolation of methylglyoxime which had apparently been formed by further nitrosation of the resulting acetoxime.

$$(CH_3)_2C(NO)COCH_3 + H_2O \longrightarrow (CH_3)_2C{=}NOH + CH_3COOH \xrightarrow{HNO_2} CH_3C(=NOH)CH{=}NOH$$

In the case of ethyl isopropyl ketone a yield of 6.8% of ethyl α-nitroso-isopropyl ketone (II) was obtained along with 27% of α-isonitrosoethyl isopropyl ketone (III)

$$2(CH_3)_2CHCOCH_2CH_3 + 2HNO_2 \longrightarrow 2H_2O + \underset{\text{(II)}}{[(CH_3)_2C(NO)COCH_2CH_3]_2}$$

$$(CH_3)_2CHCOCH_2CH_3 + HNO_2 \longrightarrow H_2O + \underset{\text{(III)}}{(CH_3)_2CHCOC(=NOH)CH_3}$$

Both α-nitrosoisopropyl ketones were bimolecular, and only upon heating their solutions in various solvents did the characteristic blue color of the monomolecular form slowly appear. The blue color disappeared again on cooling. The bimolecular form is thus quite stable and it is perhaps for this reason that these compounds withstand cleavage during their formation. That we are dealing with a true nitroso group is evident from the doubling up of the molecule and the appearance of the blue color, characteristic of monomolecular true nitroso compounds.

[2] Baeyer and Manasse, *Ber.*, **27**, 1912 (1894); Baeyer, *ibid.*, **28**, 652, 1586 (1895).

[3] See also Clarke, Lapworth and Wechsler, *J. Chem. Soc.*, **93**, 30 (1908).

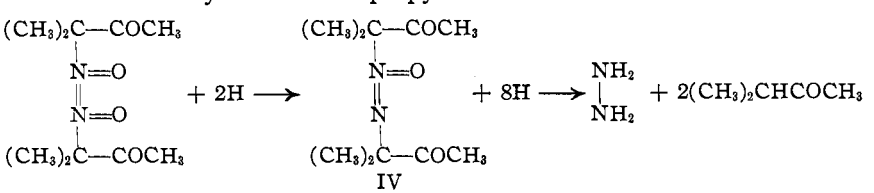
[4] Victor Meyer, *Ber.*, **21**, 1293 (1888).

The compounds were insoluble in alkali whereas isonitroso ketones (oximes) dissolve with a yellow color. It is extremely unlikely that this true nitroso group is elsewhere than on the only tertiary carbon atom, namely, the α-carbon atom of the isopropyl group.

Faworski has shown that when ketones of the type $(CH_3)_2CHCOCH_2R$ are treated with phosphorus pentabromide substitution of the first bromine atom takes place entirely on the α-carbon atom of the isopropyl group.[5] Oxidation of such ketones cleaves the ketone for the most part on the isopropyl side.[6]

It is perhaps surprising, therefore, that nitrosation occurs on the α-carbon of the ethyl group to such a large extent when ethyl isopropyl ketone is treated with an equivalent quantity of ethyl nitrite. Experiments now under way indicate that other ketones of the same type manifest a similar behavior with nitrous acid. Our results are in keeping with those of Fileti and Ponzio, who find that ethyl isopropyl ketone upon oxidation with nitric acid yields acetylisobutyryl.

The reduction of bimolecular methyl α-nitrosoisopropyl ketone by stannous chloride and hydrochloric acid yielded unexpected results. No detectable amount of methyl α-aminoisopropyl ketone was formed. The final products were hydrazine and methyl isopropyl ketone. If the reduction were stopped after twenty minutes even in the presence of excess reducing agent, a water-insoluble crystalline intermediate could be isolated. This intermediate had the chemical composition and molecular weight of 2-azoxy-2-methyl-3-butanone (IV) (methyl α-azoxyisopropyl ketone). Upon reduction with stannous chloride and hydrochloric acid it yielded hydrazine and methyl isopropyl ketone. We regard this as strong evidence that the compound contains the azoxy group, although this is not a characteristic reaction of aromatic azoxy compounds. The reduction of dimolecular methyl α-nitrosoisopropyl ketone is thus formulated as follows



IV

The only aliphatic azoxy compound we have found in the literature is *sym.*-tetramethyldinitroazoxymethane,[7] obtained by the action of hydroxylamine on propylpseudonitrol. Upon reduction with zinc dust and acetic acid it yields acetoxime.[8]

[5] Faworski, *J. prakt. Chem.*, [2] **88**, 641 (1913).
[6] Wagner, *ibid.*, **44**, 280 (1891).
[7] Scholl and Born, *Ber.*, **28**, 1367 (1895).
[8] Schäfer, *ibid.*, **34**, 1914 (1901).

The reduction of bimolecular ethyl α-nitrosoisopropyl ketone did not give ethyl α-aminoisopropyl ketone but as yet no products have been isolated.

The peculiar behavior of these nitroso ketones on reduction led us to examine the literature for cases in which aliphatic true nitroso compounds had been reduced. Perhaps on account of the difficulty of preparation very little work has been done. The yields of reduction products are, as a rule, poor and it is hard to draw any general conclusions. However, *up to the present it has not been demonstrated that the main product of reduction of true aliphatic nitroso compounds as a class is the corresponding amine.*[9] We have not been able to find any case in which either an azoxy compound or the denitrogenated compound and hydrazine are the final products.

Experiments were carried out upon the reduction of α-nitrosoisopropyl acetone using in one case stannous chloride and hydrochloric acid and in another sodium amalgam and water. Here also no appreciable amounts of the expected amino ketone were obtained, the chief products being ammonia and non-nitrogenous substances. In both cases, however, it is quite likely that the nitroso compound is decomposed before reduction as demonstrated in the experimental section, and for this reason the experiments upon the reduction of this compound have been temporarily abandoned.

The work on nitroso compounds is being continued from two points of view. The comparative ease of nitrosation on the α-carbon atom of various alkyl groups of ketones is being investigated. The reduction of various types of nitroso compounds is being studied in detail and possible intermediates investigated.

Experimental

Bimolecular Methyl α-Nitrosoisopropyl Ketone.—To 125 g. (1.45 moles) of methyl isopropyl ketone[10] in a flask fitted with a reflux condenser, was added 6.7 cc. of concentrated hydrochloric acid. The mixture was kept at 45–55° and the theoretical quantity of gaseous ethyl nitrite[11] was passed in over two hours. During the process the reaction

[9] In the following references are recorded cases in which true nitroso compounds of the aliphatic series have been reduced yielding the amine or hydroxyl amine in but small yields or only ammonia: Baeyer, *Ber.*, **28**, 2292 (1895); Cusmano, *Atti accad. Lincei*, **26**, II, 87 (1917) [*Chem. Abstracts*, **12**, 1183 (1918)]; Demjanow, *Chem. Zentr.*, I, 1064 (1899); *Ber.*, **40**, 245 (1907); Earl and Kenner, *J. Chem. Soc.*, 2142 (1927); Gomberg, *Ann.*, **300**, 79 (1898); Hantzsch, *Ber.*, **35**, 2979, 4120 (1902); Schmidt, *ibid.*, **35**, 2329, 3733, 3728 (1902); *ibid.*, **36**, 1766 (1903); Schmidt and Austin, *ibid.*, **36**, 1772 (1903); Schmidt and Leipprand, *ibid.*, **37**, 537, 546 (1904); Schmidt and Widmann, *ibid.*, **42**, 497, 1893 (1909); Schmidt and Dieterle, *Ann.*, **377**, 48 (1910); Tonnies, *Ber.*, **12**, 169 (1879).

[10] We wish to thank Dean F. C. Whitmore and his students for supplying us with large quantities of this ketone for which they have developed an excellent method of preparation soon to be published.

[11] "Organic Syntheses," John Wiley and Sons, Inc., New York, 1930, Vol. X, p. 22.

mixture turned green. At the end of the process the reaction mixture was placed in the ice box for three hours when crystalline plates with pyramid faces were deposited. The mixture was finally chilled with freezing mixture. The crystals were filtered off and washed with ether; yield, 40 g. (0.17 mole), of almost pure bis-nitroso ketone (m. p. 99–101°) (24% of the theoretical). The product, after crystallization from chloroform and petroleum ether, melted at 101.5–102° with decomposition.

Anal. Calcd. for $(C_5H_9O_2N)_2$: C, 52.2; H, 7.88; mol. wt., 230. Found: C, 52.2; H, 7.92; mol. wt. (cryoscopic in benzene), 231.

The compound is soluble in chloroform, less so in benzene, and very slightly soluble in ether, and petroleum ether. It is insoluble in water. Upon heating solutions of this compound in benzene or chloroform they slowly become bluish green; upon cooling this color disappears. It is insoluble in dilute sodium hydroxide. This compound has previously been obtained by Cusmano from the corresponding isonitro amine.[12] He records the melting point as 99° and that its solutions are not colored blue. Upon evaporating the filtrate from the bis-nitroso compound *in vacuo* at 40° a further 2.5 g. was obtained and 14 g. of liquid residue. The latter was dissolved in 100 cc. of 10% aqueous sodium hydroxide. The solution after extraction with chloroform and ether was acidified and extracted with ether. The ether extract upon evaporation yielded 0.5 g. residue, which after washing with benzene was almost pure methylglyoxime, m. p. 147–150°. The same material was obtained in somewhat larger quantities (1.5 g.) when 0.7 mole of ketone was treated with 100% excess of ethyl nitrite. The yield of bis-nitroso ketone was thereby considerably reduced, being only 0.043 mole or 6% of the theoretical. The methylglyoxime obtained in this case after crystallization from ether and benzene melted 150–152°. The identity of both samples was established by a mixed melting point (150–152°) with a known sample of methylglyoxime m. p. 156°, and by analysis.[13]

Anal. Calcd. for $C_3H_6O_2N_2$: C, 35.3; H, 5.93; N, 27.5. Found: C, 36.1, 36.2; H, 6.03, 5.95; N (Dumas), 28.0.

The sample was evidently not quite pure as also indicated by its melting point but there was insufficient material to purify further the analytical sample.

Bimolecular Ethyl α-Nitrosoisopropyl Ketone.—Into 92 g. (0.92 mole) of ethyl isopropyl ketone and 5.3 cc. of concentrated hydrochloric acid was passed 0.92 mole of ethyl nitrite, as previously, keeping the temperature 30–40°. During the reaction the mixture turned green and white crystals of the bis-nitroso compound were deposited. At the end of the reaction the mixture was cooled and the crystals were filtered off; yield 8.0 g. (0.031 mole), of almost pure compound (6.8% of the theoretical); m. p. after recrystallization from alcohol, 119.2–120°.

Anal. Calcd. for $(C_6H_{11}O_2N)_2$: C, 55.7; H, 8.59; mol. wt., 258.2. Found: C, 55.8; H, 8.58; mol. wt. (cryoscopic in benzene), 241.

The compound is practically insoluble in hot or cold water, ether, cold alcohol and dilute sodium hydroxide solution but soluble in chloroform and hot alcohol. Upon heating its solutions they became blue but they became colorless again on cooling.

α-Isonitrosoethyl Isopropyl Ketone.—The liquid after filtering off the bis-nitroso compound, was neutralized with solid potassium carbonate, filtered, and distilled under reduced pressure from a bath at 34–36°. The residue on cooling yielded crystals of α-isonitrosoethyl isopropyl ketone. By distilling almost to dryness 32 g. (0.25 mole) of isonitroso compound was obtained; m. p. 92–93°, after recrystallization from chloroform and petroleum ether; yield 27% of the theoretical.

Anal. Calcd. for $C_6H_{11}O_2N$: C, 55.7; H, 8.59. Found: C, 55.4; H, 8.11.

[12] Cusmano, *Atti accad. Lincei*, **22**, I, 225–231; *Chem. Abstracts*, **7**, 2550 (1913).

[13] Charrier, *Gazz. chim. ital.*, **37**, II, 147 (1907); *Chem. Zentr.*, II, 1232 (1907).

The compound is soluble in chloroform, ether and alcohol and cold dilute sodium hydroxide solution but insoluble in petroleum ether and cold water. Solutions of the compound in sodium hydroxide were bright yellow; upon acidification the compound was precipitated and the solution became colorless. This latter behavior, along with the analysis and melting point, identified the compound as that obtained by Ponzio (m. p. 93–94°)[14] by the action of amyl nitrate on ethyl isopropyl ketone. This he proved to be isonitroso ethyl isopropyl ketone by the action of N_2O_4. The liquid distilled from the above reaction mixture in isolating the isonitroso compound was redistilled. It all distilled over between 77.3 and 78° and left only a slight residue. It was shown to contain ethyl isopropyl ketone by the isolation of the semicarbazone. By measurement of refractive index, it was estimated that it contained 16 g. of unreacted ketone (17%) which therefore probably forms a minimum boiling mixture with ethyl alcohol. Fifty per cent. of the original ketone has thus been accounted for; the remainder probably escaped isolation in the form of cleavage products.

The Reduction of Bimolecular Methyl α-Nitrosoisopropyl Ketone.—To a vigorously stirred solution of 84.5 g. (0.375 mole) of stannous chloride ($SnCl_2 \cdot 2H_2O$) in 123 cc. of concentrated hydrochloric acid was added slowly 17.25 g. (0.15 mole) of finely ground bimolecular methyl α-nitrosoisopropyl ketone, keeping the temperature below 25° by running water. The mixture was then stirred at room temperature until all the insoluble material had gone into solution (five hours). The solution was then poured into 190 cc. of water and distilled until 150 cc. of distillate was collected, the first portion of which separated into two layers. This distillate after repeated fractionation and saturating the first fractions with potassium carbonate yielded a further quantity of the non-aqueous layer. In all, after drying with anhydrous potassium carbonate, 4.1 g. was obtained. This material upon fractional distillation yielded two fractions (1) 70–85°, 1.0 g., (2) 85–94°, 2.5 g. The last fraction was shown to be mostly methyl isopropyl ketone by converting into methyl isopropyl ketone semicarbazone which after recrystallization melted at 115–115.5°. A mixed melting point with a known sample established its identity.[15] The first fraction yielded a quantity of methyl isopropyl ketone semicarbazone which indicated that it also contained a considerable quantity of the ketone. The estimated yield of ketone is 0.036 mole, or 24% of the theoretical, assuming that 75% of the original 4.1 g. was methyl isopropyl ketone.

The acid residue from which the ketone was obtained was made strongly alkaline and distilled. The distillate was still coming over basic even after 1.5 liters had been distilled. The distillate was made acid with hydrochloric acid, evaporated to dryness on the steam-bath, and the resulting hydrochloride dried over calcium chloride and potassium hydroxide *in vacuo*. It weighed 1.7 g. and was shown to be hydrazine dihydrochloride by analysis and by treating with benzaldehyde to get dibenzal-azine whose identity was established by a mixed melting point with a known sample. There was no evidence that it contained appreciable quantities of any other base.

A better method of isolating the hydrazine dihydrochloride is to precipitate the tin from the residue with hydrogen sulfide after distilling out the ketone; evaporate almost to dryness, then add absolute alcohol, filter off the hydrochloride and wash with ether. In this way from 4.3 g. (0.037 mole) of the bis-nitroso compound, reduced as above, were obtained 0.79 g. (0.0075 mole) of almost pure hydrazine dihydrochloride; yield, 40% of the theoretical; 0.13 g. when treated with benzaldehyde gave 0.15 g. of dibenzal azine, m. p. 94–94.5° (after recrystallization).

2-Azoxy-2-methyl-3-butanone (Methyl α-Azoxy Isopropyl Ketone).—To a vigo-

[14] Ponzio, *Gazz. chim. ital.*, **27**, [1] 271–279 (1897).

[15] Faworski, *J. prakt. chem.*, [2] **88**, 684 (1913), gives m. p. 114° for methyl isopropyl ketone semicarbazone.

rously stirred solution of 84.5 g. (0.375 mole) of stannous chloride ($SnCl_2 \cdot 2H_2O$) in 123 cc. of concentrated hydrochloric acid, 17.25 g. (0.15 mole) of bimolecular methyl α-nitroso isopropyl ketone was added over ten minutes, keeping the temperature at 18–21°. The bis-nitroso compound went into solution until about one-third had been added, then an insoluble material was observed to separate. When all the bis-nitroso compound had been added the reaction mixture was stirred for ten minutes and then poured into 500 cc. of cold water. The solution was immediately filtered. After washing the insoluble material with water and drying, it melted at 58.5–60°; yield, 10.0 g. (0.047 mole), (62% of theoretical).

It was recrystallized from ether and then from water and alcohol; flat prisms m. p. 60–61°.

Successive crystallizations from various solvents did not raise this melting point.

Anal. Calcd. for $C_{10}H_{18}O_2N_2$: C, 56.0; H, 8.47; N, 13.1; mol. wt. 214.2. Found: C, 55.8, 55.7, 56.4; H, 8.27, 8.35, 8.51; N, 13.6, 13.6; mol. wt. (cryoscopic in benzene), 215. (Between the second and third carbon and hydrogen analyses the compound was again recrystallized.)

The compound is soluble in methyl and ethyl alcohols, benzene, ether, chloroform, and carbon tetrachloride, but insoluble in water.

Reduction of 2-Azoxy-2-methyl-3-butanone.—Ten grams (0.047 mole) of the azoxy compound were stirred vigorously with 43.5 g. (0.193 mole) of stannous chloride ($SnCl_2 \cdot 2H_2O$) in 63 cc. of concentrated hydrochloric acid until all had gone into solution (about fifteen hours). The reaction mixture was diluted with 100 cc. of water and the volatile non-basic substances distilled out. A second phase separated in the first fraction. By redistilling the distillate and saturating the first distillates with potassium carbonate, 4 g. of nonaqueous layer was obtained after drying with potassium carbonate. This liquid upon distillation gave two fractions: (1) 68–84°, 1.3 g.; (2) 84–94°, 1.1 g., the loss being due to manipulation. Fraction (2) was mostly methyl isopropyl ketone. This was shown by converting into methyl isopropyl ketone semicarbazone (m. p. 115–116.5°), which was identified by a mixed melting point. Fraction (1) upon treating with semicarbazide and sodium acetate yielded two semicarbazones. (A) That which first separated: 0.3 g., m. p. 115–116°, after recrystallization from alcohol and water; this was shown to be crude methyl isopropyl ketone semicarbazone by a mixed melting point with a known sample. (B) That which separated upon allowing the mother liquor from (A) to stand: 0.23 g. of solid m. p. 184–187° after recrystallization from hot water. This was shown to be acetone semicarbazone by a mixed melting point with a known sample (m. p. 188–189.5°).

On the assumption that 75% of the original 4 g. was methyl isopropyl ketone the yield is 0.035 mole or 37% of the theoretical.

One-half of the acid residue from the distillation was treated with hydrogen sulfide to precipitate the tin and evaporated. The residue was treated with absolute alcohol and the hydrochloride filtered off and dried. It was shown to be almost pure hydrazene dihydrochloride by analysis and conversion into dibenzalazine (m. p. 93–94°) which was identified by a mixed melting point. There was no evidence of an appreciable quantity of any other basic substances; yield, 0.9 g.; that is, 1.8 g. (0.017 mole) from 0.047 mole of azoxy (36.5% of the theoretical).

Reduction of Bimolecular Ethyl α-Nitrosoisopropyl Ketone.—The bis-nitroso compound was treated with stannous chloride and hydrochloric acid in the manner described for reducing bimolecular methyl α-nitrosoisopropyl ketone to the azoxy compound. From 4 g. was obtained 0.8 g. of an oil which upon combustion yielded an inorganic residue. No appreciable quantities of ethyl isopropyl ketone were found. The aqueous solution from the reduction was freed from tin by hydrogen sulfide and evapo-

rated. A negligible quantity of solid was left. Thus no basic substances were obtained although it was shown that all the nitroso compound had reacted. Further experiments upon the reduction of this nitroso compound will be carried out when larger quantities are available.

The Reduction of Bimolecular 2-Nitroso-2-methyl-4-pentanone.—The nitroso ketone was prepared by the oxidation of an aqueous solution of crude 2-hydroxylamino-2-methyl-4-pentanone oxalate with excess freshly precipitated mercuric oxide with mechanical stirring, keeping the temperature at 64–67°. The nitroso ketone was steam distilled from the reaction mixture under reduced pressure (150–210 mm.). The blue oil first coming over solidified to crystals of m. p. 72–74°. Recrystallization from chloroform did not raise the melting point; yield, 30%. Thus we could obtain this nitroso compound pure from the crude oxalate in one operation. Harries and Joblonski[16] prepared this compound by oxidation of the free hydroxylamine in boiling chloroform solution with yellow mercuric oxide. He reports a 60% yield of material, m. p. 75–76°. We believe that, in spite of the lesser yields, the fact that the starting product is the crude oxalate (obtained in 66% yields from mesityl oxide) makes our method more satisfactory because the preparation of the free hydroxylamine involves considerable trouble and loss.

The bis-nitroso compound, when reduced by stannous chloride and hydrochloric acid by the method already described in the case of bimolecular methyl α-nitrosoisopropyl ketone, yielded only mesityl oxide in 27% yield (identified by mixed melting point of its semicarbazone and refractive index), and ammonium chloride. The latter was isolated in 55% yield by first distilling out the mesityl oxide and precipitating the tin with hydrogen sulfide and then evaporating to dryness. It was identified by its chlorine analysis and behavior with alkali. It contained no appreciable quantities of hydrazine dihydrochloride as shown by its action with benzaldehyde.

The nitroso compound, however, upon stirring with concentrated hydrochloric acid at 10–11° went completely into solution with evolution of gas. Mesityl oxide was recovered from the solution in 55% yield by distillation. The fate of the nitroso group was not determined. The above results may thus have been due to preliminary cleavage by the hydrochloric acid.

Twenty grams nitroso compound were also reduced by shaking it with excess 2.5% sodium amalgam and water. The chief product was a non-nitrogen containing liquid of b. p. 217–219° (8.4 g. from 20 g. of nitroso compound). This substance was evidently a mixture as shown by analysis (C, 77.9, 78.0; H, 11.25, 11.03). On treating with sodium acetate and semicarbazide hydrochloride it gave a semicarbazone, m. p. 111–112°, in small yield. It was surprising to find that only a small quantity of basic material could be isolated. There were certainly none of the expected amines or hydrazine formed in the reduction.

Summary

1. Bimolecular methyl α-nitrosoisopropyl and bimolecular ethyl α-nitrosoisopropyl ketone have been prepared by the action of ethyl nitrite on the corresponding ketones.

2. Bimolecular methyl α-nitrosoisopropyl ketone yields 2-azoxy-2-methyl-3-butanone upon reduction with stannous chloride and hydrochloric acid and the latter compound in turn is further reduced to methyl isopropyl ketone and hydrazine.

3. The reduction of α-nitrosoisopropyl acetone by stannous chloride

[16] Harries and Joblonski, *Ber.*, **31**, 1379 (1898).

and hydrochloric acid or by sodium amalgam and water gave neither the corresponding amine or hydrazine.

4. It is pointed out that there is no evidence that, as a rule, the true nitroso group in aliphatic compounds is reduced to the corresponding amine or hydroxylamine except in small yields.

STATE COLLEGE, PENNSYLVANIA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF TEXAS]

THE NUMBER OF STEREOISOMERIC AND NON-STEREOISOMERIC PARAFFIN HYDROCARBONS

BY CHARLES M. BLAIR WITH HENRY R. HENZE

RECEIVED NOVEMBER 3, 1931 PUBLISHED APRIL 6, 1932

No detailed attempt to relate the number of stereoisomeric and non-stereoisomeric paraffin hydrocarbons to their respective carbon contents is recorded in the chemical literature. Having first developed a mathematical relationship between carbon content and the number of structural isomers, both among the paraffin hydrocarbons[1] and their mono-substitution products,[2] the authors were successful in developing a series of recursion (finite) type formulas permitting the calculation of the number of stereoisomeric and non-stereoisomeric mono-substitution products of the paraffins[3] from their carbon content. By utilizing a combination of the methods previously developed it is possible to derive analogous mathematical formulas by means of which the number of stereoisomeric and non-stereoisomeric paraffin hydrocarbons may be estimated accurately.

In this treatment we find it desirable to separate the paraffin hydrocarbons into classes according to whether their carbon content is even or odd. Those whose carbon content, N, is an even number are further divided into two groups: **A**, consisting of those isomeric hydrocarbons whose graphic formula may be divided into two parts of $N/2$ carbon atoms each; and **B**, the remaining hydrocarbons whose graphic formula cannot be so divided. Division of the graphic formula into two parts signifies breaking the single bond between two adjacent carbon atoms thus obtaining two alkyl radicals.

Likewise, the hydrocarbons whose carbon content, N, is an odd number are also divided into two groups: A, consisting of those isomers whose graphic formula can be divided into two parts, one of $(N + 1)/2$ carbon atoms and the other of $(N - 1)/2$ carbon atoms; and B, consisting of the remaining hydrocarbons whose graphic formula cannot be so divided.

Group A. Even Carbon Content.—If two alkyl radicals of $N/2$ carbon atoms each are combined, a hydrocarbon of N carbon atoms is obtained,

[1] H. R. Henze and C. M. Blair, THIS JOURNAL, **53**, 3077–3085 (1931).

[2] H. R. Henze and C. M. Blair, *ibid.*, **53**, 3042–3046 (1931).

[3] C. M. Blair with H. R. Henze, *ibid.*, **54**, 1098 (1932).