CCLII.—*The Oxime of Mesoxamide (isoNitrosomalona-
amide) and some Allied Compounds. Part IV. The
Ethers of isoNitrosomalonanilide, isoNitrosomalon-
dimethylamide, and isoNitrosomalondibenzylamide.*

By ARTHUR GEOFFREY RENDALL and MARTHA ANNIE WHITELEY.

It was shown by one of us (Whiteley, T., 1903, **83**, 24) that the aryl-substituted derivatives of *isonitrosomalona*amide, notably *isonitrosomalonanilide*, exist in two isomeric forms, differing in colour and solubility but mutually convertible by heating, by the action of solvents, and by the action of acids on solutions of the alkali salts. Similar isomerism has been observed in other *isonitroso*-compounds, a striking example being afforded by the *isonitroso*-derivatives of camphor and epicamphor, each of which has been shown by Forster (T., 1912, **103**, 664) to exist in two forms, one stable and the other labile; in these cases, the isomerism has been shown conclusively to be stereochemical, the stable forms being the *syn*- and the labile forms the *anti*-oximes. Since the molecule in *isonitrosomalonanilide* is symmetrical with respect to the carbon atom associated with the *isonitroso*- or oximino-group, the isomerism in this series cannot be geometrical, and must be due to structural differences in the molecules of the two isomerides. The simplest explanation, based on the fact that one isomeride is coloured and the other colourless, represents them as having the oxime and *isooxime* structure respectively, the coloured compound having the conjugated double linkage that is not present in the colourless isomeride (Whiteley, *loc. cit.*).

Yellow isonitrosomalonanilide. Colourless isonitrosomalonanilide.

If this is the correct explanation of the isomerism occurring in this series of *isonitroso*-compounds, the ethers might be expected to exhibit similar isomerism, the coloured isomeride yielding an oxygen and the colourless isomeride a nitrogen ether, and these on hydrolysis should yield the α - and β -alkylhydroxylamine, respectively, as was obtained by Beckmann (*Ber.*, 1889, **22**, 537, 1521) in the case of the isomeric benzyl ethers of benzald-oxime.

By the action of the alkyl iodide on *isonitrosomalonanilide* in benzene solution and in the presence of dry silver oxide, *colourless* ethers were the only products and the yield was about 85 per cent. of that theoretically possible. The ethers were precipitated from the benzene medium in association with the silver iodide as greenish-yellow to orange solids, insoluble and stable in benzene, ether, or petroleum, but decomposed by boiling alcohol, yielding a solution of the ether and a residue of silver iodide. The methyl, ethyl, *n*- and *iso*-propyl, and *n*-butyl ethers of *isonitrosomalonanilide* were prepared by this method; they are well-defined, crystalline, colourless compounds, the melting point becoming lower, but the stability of the double compound with silver iodide increasing, as the series is ascended (see table).

In the preparation of the ethers of *isonitrosomalondimethylamide* by the same method, it was found that the methyl, ethyl, and *isopropyl* ethers were insoluble in benzene, but did not form double compounds with the silver iodide, the precipitate being a grey, heterogeneous mixture of the silver iodide and oxide with the colourless crystalline ether. The *n*-propyl and *n*-butyl ethers, on the other hand, remained in solution in the benzene, from which they were extracted by water. With the exception of the ethyl compound, the melting points of the ethers of *isonitrosomalondimethylamide* become lower as the series is ascended (see table).

The methyl and ethyl ethers of *isonitrosomalondibenzylamide*, similarly prepared by the silver oxide and alkyl iodide method, did not form double compounds with the silver iodide, but remained in solution in the benzene, and were isolated by evaporation of the solvent and subsequent crystallisation. These ethers are also colourless and the ethyl ether has the lower melting point (see table).

Ether.	M. p. of ethers of <i>isonitrosomalonanilide</i> .	M. p. of ethers of <i>isonitrosomalondimethylamide</i> .	M. p. of ethers of <i>isonitrosomalondibenzylamide</i> .
Methyl	194°	131°	83·5°
Ethyl	166	133	73·5
<i>n</i> -Propyl	156	94	
<i>iso</i> Propyl	170	128	
<i>n</i> -Butyl	136·5	66	

As the ethers of these *isonitroso*-compounds prepared by the silver oxide method—that is potentially through the silver salt—showed no isomerism, attempts were made to prepare the methyl ethers by the action of diazomethane, and in the case of *isonitroso*-malonanilide the colourless ether, m. p. 194° , and also an isomeric yellow ether, m. p. 147° (decomp.), were obtained. The yellow ether is unstable and readily converted into the colourless isomeride by the action of solvents, whilst the converse change cannot be brought about. The relative amounts of the two forms of the ether are the same whether the yellow or colourless isomeride of *isonitrosomalonanilide* is thus methylated, but are influenced by the nature of the solvent in which the reaction takes place; in alcoholic solution, the product is a mixture of the yellow and colourless isomerides, whilst in ether solution the yellow ether is the sole product.

All attempts to prepare the methyl ether of *isonitrosomalondimethylamide* by the action of diazomethane were unsuccessful. On adding the ethereal solution of diazomethane to the *isonitroso*-compound suspended in ether, there was a vigorous evolution of nitrogen, indicating that methylation was taking place, but the product was a syrup with a green fluorescence from which no definite compound could be isolated. It gave the yellow alkali and purple ferrous salts characteristic of the *isonitroso*-compounds of this series, and may be possibly *isonitrosomalontetramethylamide*, $(\text{CO}\cdot\text{NMe}_2)_2\text{C}\cdot\text{NOH}$, as it resembles the crude product obtained by the action of nitrosyl chloride on the condensation product of malonyl chloride with dimethylamine.

The value of methyl sulphate as a methylating agent on compounds of the *isonitroso*-type was also studied; in the case of *isonitrosomalonanilide*, it was found that the potassium salt, in the presence of potassium carbonate, was readily converted into the methyl ether by the action of methyl sulphate at the ordinary temperature, the *colourless* ether, m. p. 194° , being the sole product.

The foregoing results indicate that only those *isonitroso*-derivatives of the substituted malonamides that exhibit isomerism yield isomeric forms of ethers, for in the three cases studied, *isonitrosomalonanilide*, that exists in a colourless and in a yellow form, yields a colourless and a yellow methyl ether; whilst *isonitrosomalondimethylamide* and *isonitrosomalondibenzylamide*, known only in the colourless forms, yield only colourless methyl ethers.

The extension of the investigation to the ethers of those *isonitroso*-derivatives of the substituted malonamides in which the yellow isomeride is more stable than the colourless form has led to such far-reaching results that these will form the subject of a separate communication.

Assuming that the difference in structure between the yellow and colourless ethers of *isonitrosomalonanilide* is similar to that suggested for the two forms of the *isonitroso*-compound itself, namely, that the yellow ether is the oxygen and the colourless ether the nitrogen ether, it might be regarded as anomalous that the colourless ether should be produced by the action of methyl iodide on the *isonitroso*-compound in the presence of silver oxide, for presumably the silver salt, $(\text{PhHN}\cdot\text{CO})_2\text{C}\cdot\text{NOAg}$, would be formed first, and this should interact by double decomposition with the methyl iodide to yield the coloured or oxygen ether :

In this connexion, it is important to remember that the colourless ether was not obtained directly; the first product of the reaction was a yellow double compound of the ether with silver iodide, which was decomposed by boiling with alcohol. It is probable, therefore, that this compound is an additive compound of the silver salt with methyl iodide, which is stable in benzene and other non-hydroxylic solvents, but decomposed by alcohol to yield silver iodide and the colourless nitrogen ether according to the equations

The yellow or oxygen ether is the sole product when diazomethane reacts with *isonitrosomalonanilide* in dry ether solution, in which solvent the yellow form of the *isonitroso*-compound is the more stable, whilst in alcoholic solution a mixture of the yellow *O*-ether and the colourless *N*-ether is obtained. Since, however, the *O*-ether is very unstable and readily converted by the action of alcoholic solvents into the *N*-ether, it is probable that the yellow or *O*-ether is the sole product of the reaction between *isonitrosomalonanilide* and diazomethane, the colourless or *N*-ether arising from subsequent isomerisation in the alcoholic solution (I). This is the more probable seeing that diazomethane appears to have no methylating action on the *isonitroso*-group of *isonitrosomalondimethylamide*, which exists only in the colourless or nitrogen form (II).

Hydrolysis of isoNitrosomalonanilide and its Ethers.

It was hoped that the hydrolysis of the ethers of *isonitrosomalonanilide* would throw some light on the structure of these compounds, the *O*- and *N*-ethers yielding the corresponding α - and β -alkyl-hydroxylamines, respectively, together with mesoxanilide :

Experiment showed, however, that *isonitrosomalonanilide* does not yield hydroxylamine, nor its ethers the alkyl derivatives of hydroxylamine, on hydrolysis. *isoNitrosomalonanilide* is remarkably stable towards hydrolysing agents, and prolonged heating with acids causes profound decomposition. The ethers behave like the esters of weak acids on hydrolysis, yielding the alcohol and *isonitrosomalonanilide*.

Reduction of isoNitrosomalonanilide and its Ethers.

It might be expected that the two forms of *isonitrosomalonanilide* would yield the same product, *aminomalonanilide*, on complete reduction, with the intermediate formation of the *hydroxylamino*-compound in the case of the coloured or *O*-form (I), and of the *imino*-compound in the case of the colourless or *N*-form (II) :

On the other hand, the *O*-form of the ether should yield *alkyloxyaminomalonanilide* on partial and *aminomalonanilide* on complete reduction (III); whilst the *N*-form of the ether should furnish *alkyliminomalonanilide* or *iminomalonanilide* as the intermediate compound, and *alkylaminomalonanilide* or *aminomalonanilide* as the final product, according as water (IV) or alcohol (V) were split off from the unstable intermediate hydroxy-compound :

The behaviour of *isonitrosomalonanilide* and its ethers towards a large number of reducing agents, acid, alkaline, and neutral, was examined; the compounds were reduced very smoothly, but the results obtained failed to throw any further light on the question of the constitution of the original compounds; in no case could any pure intermediate compound be isolated, and the final product was always *aminomalonanilide* (Whiteley, P., 1904, 20, 92).

EXPERIMENTAL.

I.—*Preparation of the Ethers of isoNitrosomalonanilide by the Action of the Alkyl Iodide in the Presence of Silver Oxide.*

Ten grams of *isonitrosomalonanilide* (1 mol.) were suspended in 200 c.c. of dry benzene containing the alkyl iodide (3 mols.) in solution, 12.5 grams (1.5 mols.) of dry silver oxide were then added in many small portions, the mixture being well shaken after each addition. There was a slight rise in temperature and the formation of a copious yellowish-green precipitate. After remaining at the ordinary temperature during twelve hours, the mixture was filtered, the precipitated double compound of the ether with silver iodide drained on porous earthenware until free from benzene, boiled with absolute alcohol for about fifteen minutes, and filtered. The residue consisted of silver iodide with the slight excess of silver oxide, and the filtrate, on cooling, deposited the ether in a crystalline form, the portion remaining in solution being precipitated on dilution with water. The yield is about 85 per cent. of that theoretically possible. The solubility of the ethers in all the ordinary organic solvents increases with the complexity of the alkyl group, and they all crystallise well from formic acid.

Methyl ether of isonitrosomalonanilide (colourless form), $(\text{PhHN}\cdot\text{CO})_2\text{C} \begin{smallmatrix} \text{NMe} \\ \diagup \\ \text{O} \end{smallmatrix}$, is sparingly soluble in ethyl or methyl alcohol, ethyl acetate, benzene, petroleum (b. p. 100—120°), or chloroform; readily soluble in acetone, or formic or acetic acid, and insoluble in ether. It crystallises in stout, colourless prisms, m. p. 194° (Found: N = 14.18, 14.17. $\text{C}_{16}\text{H}_{15}\text{O}_3\text{N}_3$ requires N = 14.14 per cent.).

Ethyl ether of isonitrosomalonanilide (colourless form), $(\text{PhHN}\cdot\text{CO})_2\text{C} \begin{smallmatrix} \text{NEt} \\ \diagup \\ \text{O} \end{smallmatrix}$, is soluble in cold methyl alcohol, ethyl acetate, acetone, or chloroform; readily soluble in ethyl alcohol, formic or acetic acid, benzene, or petroleum (b. p. 100—120°), and very sparingly soluble in ether or petroleum (b. p. 60—80°). It crystallises in wheatsheaf clusters of thin prisms, m. p. 166° (Found: N = 13.58. $\text{C}_{17}\text{H}_{17}\text{O}_3\text{N}_3$ requires N = 13.5 per cent.).

isoPropyl ether of isonitrosomalonanilide (colourless form), $(\text{PhHN}\cdot\text{CO})_2\text{C} < \begin{smallmatrix} \text{NPr}^{\beta} \\ \text{O} \end{smallmatrix}$, closely resembles the ethyl ether in solubility. It crystallises in felted masses of very thin needles, m. p. 170° (Found : N = 13.00. $\text{C}_{18}\text{H}_{19}\text{O}_3\text{N}_3$ requires N = 12.92 per cent.).

n-Propyl ether of isonitrosomalonanilide (colourless form), $(\text{PhHN}\cdot\text{CO})_2\text{C} < \begin{smallmatrix} \text{NPr}^{\alpha} \\ \text{O} \end{smallmatrix}$, is soluble in cold ethyl or methyl alcohol, ethyl acetate, acetone, chloroform, or benzene, readily soluble in formic or acetic acid, and sparingly soluble in ether, or the petroleum (b. p. $60\text{--}80^{\circ}$ or $100\text{--}120^{\circ}$). It crystallises from formic acid in felted masses of thin, prismatic needles, or from petroleum in minute, stout prisms, m. p. 156° (Found : N = 12.96. $\text{C}_{18}\text{H}_{19}\text{O}_3\text{N}_3$ requires N = 12.92 per cent.).

n-Butyl ether of isonitrosomalonanilide (colourless form), $(\text{PhHN}\cdot\text{CO})_2\text{C} < \begin{smallmatrix} \text{N}\cdot\text{C}_4\text{H}_9 \\ \text{O} \end{smallmatrix}$, is soluble in cold ethyl or methyl alcohol, ethyl acetate, acetone, acetic acid, chloroform, or benzene; readily soluble in formic acid or petroleum (b. p. $100\text{--}120^{\circ}$); and sparingly soluble in ether or petroleum (b. p. $60\text{--}80^{\circ}$). It crystallises in well-formed, thin prisms, m. p. 136.5° (Found : N = 12.60. $\text{C}_{19}\text{H}_{21}\text{O}_3\text{N}_3$ requires N = 12.4 per cent.).

II.—Preparation of the Ethers of isoNitrosomalondimethylamide by the Action of the Alkyl Iodide in the Presence of Silver Oxide.

Five grams of isonitrosomalondimethylamide (1 mol.), suspended in 100 c.c. of dry benzene containing the alkyl iodide (3 mols.) in solution, were treated gradually and with constant shaking with 11.5 grams (1.5 mols.) of dry powdered silver oxide. The mixture became warm, and after remaining for twelve hours at the ordinary temperature it was filtered. In the cases of the methyl, ethyl, and isopropyl compounds, the grey precipitate was a mixture of the colourless ether with the silver iodide and the excess of silver oxide, from which the ether was extracted by means of warm alcohol. The n-propyl and n-butyl ethers were not precipitated with the silver iodide, but remained in solution in the benzene, from which they were extracted by means of water. The yield of the ether is about 80 per cent. of that theoretically possible.

The ethers obtained by this method are colourless, crystalline compounds and are probably the isooxime ethers, $(\text{MeHN}\cdot\text{CO})_2\text{C} < \begin{smallmatrix} \text{NR} \\ \text{O} \end{smallmatrix}$.

Methyl ether of isonitrosomalondimethylamide (colourless form), $(\text{MeHN}\cdot\text{CO})_2\text{C}(\text{NOMe})$, dissolves readily in cold ethyl or methyl

alcohol, acetone, ethyl acetate, formic or acetic acid, chloroform, or water, and is sparingly soluble in ether, benzene, or petroleum (b. p. 100—120°). It crystallises in stout prisms, m. p. 131° (Found: N = 24·36. $C_6H_{11}O_3N_3$ requires N = 24·28 per cent.).

Ethyl ether of isonitrosomalondimethylamide (colourless form), $(MeHN \cdot CO)_2C(NOEt)$, dissolves readily in cold ethyl or methyl alcohol, ethyl acetate, acetone, formic or acetic acid, chloroform, benzene or water, and is sparingly soluble in petroleum (b. p. 100—120°), and insoluble in ether or petroleum (b. p. 60—80°). It crystallises in well-formed, rhombic prisms having a fibrous fracture and melting at 133° (Found: N = 22·33. $C_7H_{13}O_3N_3$ requires N = 22·4 per cent.).

isoPropyl ether of isonitrosomalondimethylamide (colourless form), $(MeHN \cdot CO)_2C(NOPr^a)$, is readily soluble in the cold in all the ordinary organic solvents, with the exception of benzene and petroleum (b. p. 100—120°), in which it is sparingly soluble, and ether, in which it is insoluble. It crystallises in stellate clusters of flattened prisms melting at 128° (Found: N = 21·30. $C_8H_{15}O_3N_3$ requires N = 21·02 per cent.).

n-Propyl ether of isonitrosomalondimethylamide (colourless form), $(MeHN \cdot CO)_2C(NOPr^a)$, dissolves readily in the cold in water and in all the ordinary organic solvents with the exception of ether, in which it is insoluble. It can be crystallised from a mixture of amyl alcohol and light petroleum, and forms thin, prismatic needles melting at 94° (Found: N = 21·14. $C_8H_{15}O_3N_3$ requires N = 21·02 per cent.).

n-Butyl ether of isonitrosomalondimethylamide (colourless form), $(MeHN \cdot CO)_2C(NOC_4H_9)$, is readily soluble in the cold in water and in all the ordinary organic solvents except ether in which it is only sparingly soluble, and separates in well-formed, rhombic prisms melting at 66° (Found: N = 20·09. $C_9H_{17}O_3N_3$ requires N = 19·80 per cent.).

III.—*Preparation of the Ethers of isoNitrosomalondibenzylamide by the Action of the Alkyl Iodide in the Presence of Silver Oxide.*

Only the methyl and ethyl ethers in this series were prepared, and the method was the same as that adopted in the case of the isonitrosomalondimethylamide series. The ethers, being soluble in benzene, were obtained by evaporation of the benzene solution after filtering from the silver iodide and excess of oxide.* The

* The silver residues were found to contain an appreciable amount of silver cyanide. Complete analysis of the residues gave the following results. $Ag_2O = 47·5$; $AgI = 45$; $AgCN = 7·5$ per cent.

ethers are colourless, crystalline compounds, and therefore probably derivatives of the isooxime series, $(C_6H_5 \cdot CH_2 \cdot NH \cdot CO)_2C \begin{smallmatrix} \nearrow NR \\ \searrow O \end{smallmatrix}$.

Methyl ether of isonitrosomalondibenzylamide,

is readily soluble in alcohol or benzene, sparingly soluble in amyl alcohol, and insoluble in water or light petroleum. It crystallises from a mixture of amyl alcohol and petroleum (b. p. 40—60°) in slender, acicular prisms melting at 83·5° (Found: N = 12·9. $C_{18}H_{19}O_3N_3$ requires N = 12·92 per cent.).

Ethyl ether of isonitrosomalondibenzylamide,

is readily soluble in alcohol, ether, or benzene, less readily soluble in amyl alcohol, and insoluble in water. It crystallises in very small, colourless prisms from petroleum (b. p. 100—120°), and melts at 73·5° (Found: N = 12·36. $C_{19}H_{21}O_3N_3$ requires N = 12·4 per cent.).

IV.—*Methylation of isoNitrosomalonanilide by Means of Diazo-methane.*

Methyl Ether of isoNitrosomalonanilide (yellow form), $(PhHN \cdot CO)_2C \cdot N \cdot OMe$.—1. *isoNitrosomalonanilide* (1·4 grams), suspended in 15 c.c. of dry ether, was treated with a solution of diazo-methane in ether prepared from 3 grams of nitrosomethylurethane. There was a vigorous action, and a bulky, yellow solid separated; this was filtered after twelve hours and dried on porous earthenware. It was found to be the pure yellow *methyl ether of isonitrosomalonanilide*; it melts at 144° and decomposes at 150° (Found: N = 14·2. $C_{16}H_{15}O_3N_3$ requires N = 14·14 per cent.). It is readily soluble in all the ordinary organic solvents, with partial conversion into the colourless isomeride. Repeated crystallisation from ethyl alcohol converts it completely into this isomeride, m. p. 194°.

2. Two grams of *isonitrosomalonanilide* (either the yellow or the colourless form) and 1 gram of nitrosomethylurethane were dissolved in 15 c.c. of absolute alcohol that had been dried with diazo-methane; 10 c.c. of a 2·3 per cent. solution of sodium ethoxide in absolute alcohol were then added gradually. There was a vigorous reaction, which was moderated by external cooling, nitrogen was evolved, and a solid separated. This was filtered after twelve hours, washed with water to remove the sodium cyanate, and found to consist of a mixture of the yellow and colourless methyl ethers of *isonitrosomalonanilide*. A further quantity was obtained from the alcoholic filtrate on addition of water. The two ethers could not be separated by crystallisation, and repeated crystallisation from alcohol yielded the pure colourless ether, m. p. 194°.

V.—*Methylation of isoNitrosomalonanilide by Means of Methyl Sulphate.*

Excess of methyl sulphate was added to an alcoholic solution of the pure potassium salt of *isonitrosomalonanilide* containing an aqueous solution of potassium carbonate. Methylation occurred at the ordinary temperature and was complete in a few hours. The product was the colourless methyl ether of *isonitrosomalonanilide*, m. p. 194° .

VI.—*Reduction of isoNitrosomalonanilide and its Ethers.*

isoNitrosomalonanilide or its methyl or ethyl ether is readily and quantitatively reduced to *aminomalonanilide*, $(\text{PhHN}\cdot\text{CO})_2\text{CH}\cdot\text{NH}_2$, by the action of (a) zinc dust and glacial acetic acid, (b) aluminium-mercury couple in moist ether or moist alcohol, (c) ammonium sulphide in alcoholic solution; the reduction being effected at the ordinary temperature. *Aminomalonanilide* crystallises from alcohol in brilliant, flattened prisms melting at 146° (Found : N = 15.68. $\text{C}_{15}\text{H}_{15}\text{O}_2\text{N}_3$ requires N = 15.6 per cent.).

In conclusion, we tender our thanks to the Department of Scientific and Industrial Research for a grant to one of us (A. G. R.) which has enabled this investigation to be carried out.

IMPERIAL COLLEGE OF SCIENCE AND TECHNOLOGY,
SOUTH KENSINGTON, S.W.7.

[Received, July 27th, 1922.]