102. *The Ehrlich–Sachs Reaction.*

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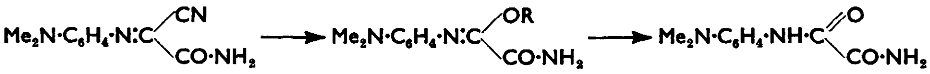
The course of the reaction between *NN*-dimethyl-*p*-nitrosoaniline and cyanoacetamide in alcohol has been established as (I) ⟶ (II) ⟶ (III). Nitrosobenzene with cyanoacetamide, methyl cyanoacetate, or ethyl cyanoacetate does not yield normal Sachs compounds, but gives $NPh{:}C(CN)\cdot NPh\cdot OH$.

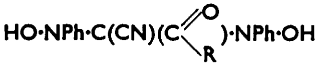
By the addition of aqueous sodium carbonate to a mixture of cyanoacetamide and *NN*-dimethyl-*p*-nitrosoaniline in ethanol Sachs[1] obtained a compound (I), m. p. 220—221°, which formed red needles with a blue reflex. McGookin,[2] using the same components in methanol and with solid potassium carbonate as condensing agent, obtained an isomeride which formed brown plates, m. p. 172°. This appeared to constitute an interesting example of isomerism of the oxime type and merit further examination.

It was soon found that Sachs's compound is produced from the two components under a variety of conditions and is, indeed, obtained in almost quantitative yield when methanol is used as solvent and potassium carbonate as condensing agent. When heated in methanol it loses hydrogen cyanide and passes into McGookin's compound, which is of different empirical formula and is now regarded as having formula (II*a*). A similar compound (II*b*) is obtained by use of ethanol as solvent. All of the compounds (I), (II*a*), and (II*b*) are converted into the oxamide (III) by passage of steam into suspensions in dilute aqueous potassium carbonate solution. Compound (III), which is analogous to 4-dimethylamino-benzanilide prepared by Barrow and Thorneycroft[3] by interaction of benzyl cyanide with *NN*-dimethyl-*p*-nitrosoaniline, is obtained most readily by the addition of 10% aqueous sodium hydroxide to a boiling ethanolic solution of molecular proportions of cyanoacetamide and *NN*-dimethyl-*p*-nitrosoaniline. Analogous compounds were prepared by the same method from nitrosobenzene, *N*-methyl-*p*-nitrosoaniline, and *NN*-diethyl-*p*-nitrosoaniline.



$$Me_2N\cdot C_6H_4\cdot N{:}C\begin{matrix}\diagup CN\\ \diagdown CO\cdot NH_2\end{matrix} \longrightarrow Me_2N\cdot C_6H_4\cdot N{:}C\begin{matrix}\diagup OR\\ \diagdown CO\cdot NH_2\end{matrix} \longrightarrow Me_2N\cdot C_6H_4\cdot NH\cdot C\begin{matrix}\diagup\!\!\diagup O\\ \diagdown CO\cdot NH_2\end{matrix}$$

(I) (IIa) R = Me. (IIb) R = Et. (III)



$$HO\cdot NPh\cdot C(CN)(C\begin{matrix}\diagup\!\!\diagup O\\ \diagdown R\end{matrix})\cdot NPh\cdot OH$$

(IV) R = NH_2 or OEt

All the condensations described by Sachs[4] and later workers have involved the interaction of the nitroso-compound with one molecular proportion of the reactive methylene compound, irrespective of the initial proportions of the reactants. Further examples are provided in the present paper by the condensations of *NN*-dimethyl-*p*-nitrosoaniline with methyl and ethyl cyanoacetate, of *N*-methyl-*p*-nitrosoaniline with cyanoacetamide, of *p*-nitroso-*NN*-di-*n*-propylaniline with methyl cyanoacetate and of 3 : *N* : *N*-trimethyl-4-nitrosoaniline with methyl cyanoacetate. It is now found that two other types of behaviour are possible.

Nitrosobenzene with cyanoacetamide or ethyl or methyl cyanoacetate in methanol or ethanol and with potassium carbonate as condensing agent gave a bright yellow compound regarded as α-cyano-*N*-hydroxy-*NN'*-diphenylformamidine, $NPh{:}C(CN)\cdot NPh\cdot OH$, probably produced *via* (IV). It is readily soluble in cold sodium hydroxide solution to yield a bright orange solution, which becomes cloudy when warmed, with liberation of aniline. The compound yields acetyl, propionyl, benzoyl, and methyl derivatives and the hydroxyl

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[1] Sachs, *Ber.*, 1900, **33**, 959.
[2] McGookin, *J. Appl. Chem.*, 1955, **5**, 65.
[3] Barrow and Thorneycroft, *J.*, 1939, 769.
[4] Sachs *et al.*, *Ber.*, 1901, **34**, 120, 494; 1902, **35**, 1224, 3319; 1903, **36**, 3234.

group may be replaced by chlorine by use of thionyl chloride. It undergoes complete decomposition with *p*-nitrophenyl *iso*cyanate or with toluene-*p*-sulphonyl chloride in pyridine.

EXPERIMENTAL

Sachs's Compound (I).—(*a*) Anhydrous potassium carbonate (5 g.) was stirred into a suspension of cyanoacetamide (1 g.) and *NN*-dimethyl-*p*-nitrosoaniline (1·8 g.) in methanol (10 c.c.). After the brisk reaction the mixture was immediately diluted with water, and the bright red precipitate filtered off. It had m. p. 220—226° (decomp.), raised to 230° by recrystallisation from 2-ethoxyethanol (Sachs gives m. p. 220—221°). Use of *NN*-diethyl-*p*-nitrosoaniline gave the much more soluble diethylamino-analogue, which readily recrystallised from ethanol as red prisms with a blue reflex, m. p. 165° (Sachs gives m. p. 165—166°). (*b*) The same products were obtained, but in inferior yield, by addition of a few drops of piperidine to warm solutions of the mixed components in ethanol or pyridine.

McGookin's Compound (IIa).—Sachs's compound (1 g.; m. p. 230°) and potassium carbonate (4 g.) in methanol (20 c.c.) were heated on a steam-bath for 1 hr. The brown solution, on dilution, gave plates which recrystallised from ethyl acetate to form straw-coloured needles, m. p. 182° (decomp.) (McGookin gives m. p. 172°) (Found: C, 59·8; H, 6·6; N, 18·6. Calc. for $C_{11}H_{15}O_2N_3$: C, 59·7; H, 6·8; N, 19·0%). Boiling this with sodium hydroxide solution afforded ammonia and, on cooling, the solution set to a starch-like paste.

This experiment was repeated with ethanol as solvent but only tar was obtained. Sachs's compound (I) (1 g.) was added to ethanol (15 c.c.) containing a little dissolved sodium and the mixture heated on a steam-bath for 20 min. The solution was treated with water and the precipitate crystallised from ethyl acetate, to give N-(*α-carbamoyl-α-ethoxymethylene*)-N′N′-*dimethyl*-p-*phenylenediamine* (IIb) as pale brown needles, m. p. 176° (decomp.) (Found: C, 61·4; H, 7·1. $C_{12}H_{17}O_2N_3$ requires C, 61·3; H, 7·2%).

On passage of steam into Sachs's compound (I) suspended in water containing a small amount of potassium carbonate the red colour was rapidly discharged and hydrogen cyanide evolved. The pale yellow product, after recrystallisation from water, ethanol, *o*-dichlorobenzene, or *cyclo*hexanone, gave p-*dimethylaminophenyloxamide* (III) as fine needles, m. p. 257—260° (Found: C, 58·7; H, 6·1; N, 20·1. $C_{10}H_{13}O_2N_3$ requires C, 58·0; H, 6·3; N, 20·3%). It was also obtained when compound (IIa) or (IIb) was submitted to the same treatment, but was most readily prepared in the following way. Sodium hydroxide (1 g.) in water (10 c.c.) was added to a boiling solution of *NN*-dimethyl-*p*-nitrosoaniline (3 g.) and cyanoacetamide (1·7 g.) in ethanol (125 c.c.). After ½ hr. the red solution was diluted with water, and the gelatinous precipitate filtered off and dried (1·1 g.; m. p. 257—260°). This method, applied to nitrosobenzene, gave N-*phenyloxamide*, which crystallised from ethanol in a cotton-wool like mass of almost colourless needles, m. p. 227—230° (Found: C, 58·3; H, 4·7; N, 16·9. $C_8H_8O_2N_2$ requires C, 58·5; H, 4·9; N, 17·1%), sublimable without decomposition.

Similarly p-*diethylaminophenyloxamide* was obtained from *NN*-diethyl-*p*-nitrosoaniline. It crystallised from ethanol in pale yellow needles, m. p. 224° (Found: C, 60·8; H, 7·2; N, 17·5. $C_{12}H_{17}O_2N_3$ requires C, 61·3; H, 7·2; N, 17·9%).

Condensation of *N*-methyl-*p*-nitrosoaniline with cyanoacetamide in methanol by use of potassium carbonate gave N-(*α-carbamoyl-α-cyanomethylene*)-N′-*methyl*-p-*phenylenediamine*, which crystallised from ethanol in red needles, m. p. 243° (Found: N, 27·2. $C_{10}H_{10}ON_4$ requires N, 27·7%), and was obtained also by the interaction of the α-cyano-α-ethoxycarbonyl analogue[4] with ammonia solution (*d* 0·88). By treatment with steam in the presence of a small amount of potassium carbonate it gave p-*methylaminophenyloxamide*, which crystallised from ethanol as needles, m. p. 206° (Found: C, 56·3; H, 5·7. $C_9H_{11}O_2N_3$ requires C, 56·0; H, 5·7%).

N-(*α-Cyano-α-methoxycarbonylmethylene*)-N′N′-*dimethyl*-p-*phenylenediamine*, from *NN*-dimethyl-*p*-nitrosoaniline and methyl cyanoacetate in methanol (K_2CO_3), formed orange-red needles, m. p. 161—163°, from ethyl acetate (Found: C, 62·5; H, 5·7; N, 18·3. $C_{12}H_{13}O_2N_3$ requires C, 62·4; H, 5·6; N, 18·3%). It was also obtained by use of ethyl cyanoacetate in the above experiment owing to ester interchange. When ethyl cyanoacetate was used with ethanol as solvent there was obtained N-(*α-cyano-α-ethoxycarbonylmethylene*)-N′N′-*dimethyl*-p-*phenylenediamine*, red prisms, m. p. 93° (from ethanol) (Found: C, 63·9; H, 5·8. $C_{13}H_{15}O_2N_3$

requires C, 63·7; H, 6·1%). Either of these esters passed into the corresponding amide, m. p. 230°, when kept in aqueous ammonia (*d* 0·88); on passage of steam into suspensions of these compounds in dilute potassium carbonate solution hydrogen cyanide was evolved but no other recognisable decomposition product was isolated.

NN-*Diethyl-3-methyl-4-nitrosoaniline*, obtained in the usual way from *NN*-diethyl-3-methylaniline, crystallised from aqueous methanol in green plates, m. p. 59° (Found: N, 14·0. $C_{11}H_{16}ON_2$ requires N, 13·5%). It reacted with methyl cyanoacetate (K_2CO_3) to give N-(*α-cyano-α-methoxycarbonylmethylene*)-N′N′-*diethyl-2-methyl*-1 : 4-*phenylenediamine*, which formed red plates with a blue reflex (from ethanol), m. p. 83° (Found: C, 65·2; H, 6·6. $C_{15}H_{19}O_2N_3$ requires C, 65·9; H, 7·0%), and with ethyl cyanoacetate in ethanol to give the *ethoxycarbonyl-analogue*, which crystallised from ethanol in reddish-blue needles, m. p. 79° (Found: N, 14·3. $C_{16}H_{21}O_2N_3$ requires N, 14·6%).

NN-Diethyl-3-methyl-4-nitrosoaniline with cyanoacetamide in methanol (K_2CO_3) gave N-(*α-carbamoyl-α-cyanomethylene*)-N′N′-*diethyl-2-methyl*-1 : 4-*phenylenediamine*, which formed small red prisms (from ethanol), m. p. 206° (Found: C, 64·6; H, 6·7. $C_{14}H_{18}ON_4$ requires C, 65·1; H, 7·0%).

N-(*α-Cyano-α-methoxycarbonylmethylene*)-2 : N′ : N′-*trimethyl*-1 : 4-*phenylenediamine*, produced by the interaction of 3 : *N* : *N*-tri-methyl-4-nitrosoaniline [5] with methyl cyanoacetate (K_2CO_3), crystallised from ethanol in red needles with a blue reflex, m. p. 150° (Found: C, 63·7; H, 5·5. $C_{13}H_{15}O_2N_3$ requires C, 63·7; H, 6·1%).

N-(*α-Carbamoyl-α-cyanomethylene*)-2 : N′ : N′-*trimethyl*-1 : 4-*phenylenediamine*, produced from 3 : *N* : *N*-trimethyl-4-nitrosoaniline and cyanoacetamide (K_2CO_3), crystallised from 2-ethoxyethanol in red needles, m. p. 252—254° (decomp.) (Found: N, 23·6. $C_{12}H_{18}ON_4$ requires N, 24·3%).

N-(*α-Cyano-α-methoxycarbonylmethylene*)-N′N′-*di*-n-*propyl*-p-*phenylenediamine*, produced by the interaction of *p*-nitroso-*NN*-di-*n*-propylaniline [6] with methyl cyanoacetate, crystallised from ethanol in red prisms with a blue reflex, m. p. 104° (Found: N, 14·0. $C_{16}H_{21}O_2N_3$ requires N, 14·6%).

α-Cyano-N-*hydroxy*-NN′-*diphenylformamidine*, obtained by the addition of anhydrous potassium carbonate to nitrosobenzene mixed with ethyl or methyl cyanoacetate in ethanol or methanol, crystallised from ethyl acetate in golden-yellow needles, m. p. 141° (Found: C, 70·8; H, 4·5; N, 17·9. $C_{14}H_{11}ON_3$ requires C, 70·9; H, 4·6; N, 17·7%). The same compound was obtained, slightly contaminated by *N*-phenyloxamide, when cyanoacetamide was used in place of the esters. By dissolution in warm acetic anhydride, subsequent precipitation by water, and recrystallisation from ethanol it gave an *acetyl derivative* as cubic crystals, m. p. 85° (Found: C, 69·5; H, 4·8. $C_{16}H_{13}O_2N_3$ requires C, 68·8; H, 4·7%). With propionic anhydride it gave the *propionyl derivative*, which crystallised from methanol in almost colourless needles, m. p. 69° (Found: C, 69·1; H, 4·7; N, 13·7. $C_{17}H_{15}O_2N_3$ requires C, 69·7; H, 5·1; N, 14·3%). On dissolution in aqueous sodium hydroxide and shaking with (*a*) benzoyl chloride there was obtained the *benzoyl derivative*, needles (from ethanol), m. p. 98° (Found: C, 73·2; H, 4·1. $C_{21}H_{15}O_2N_3$ requires C, 73·9; H, 4·4%), (*b*) dimethyl sulphate there was obtained the *methyl derivative*, pale-yellow prisms (from methanol), m. p. 58° (Found: C, 71·8; H, 5·1. $C_{15}H_{13}ON_3$ requires C, 71·7; H, 5·2%). On addition of thionyl chloride to the compound in benzene there was brisk reaction with immediate separation of N-*chloro-α-cyano*-NN′-*diphenylformamidine* NPh:C(CN)·NPh·Cl, in almost colourless needles, which had m. p. 124° (decomp.) after recrystallisation from ethyl acetate (Found: C, 65·8; H, 4·4. $C_{14}H_{10}N_3Cl$ requires C, 65·7; H, 3·9%). This chloro-compound on storage, even in the dark, underwent slow transformation to a dark plastic mass; it was instantly hydrolysed by cold dilute sodium hydroxide solution and dissolved rapidly in cold methanol or aniline to give solutions from which the original hydroxy-compound could be isolated.

The author is indebted to Dr. J. W. Minnis for the microanalyses, and to the Carnegie Trust for the Universities of Scotland for a grant.

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[*Received, August* 10*th*, 1956.]

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[5] Wurster and Riedel, *Ber.*, 1879, **12**, 1797.
[6] Mandl, *Monatsh.*, 1886, **7**, 99.