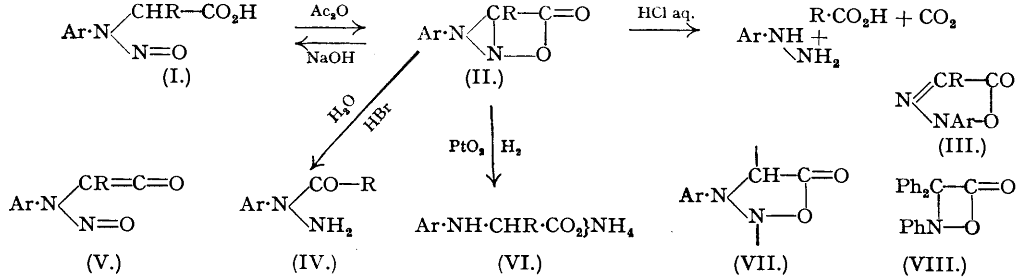
73. *Cyclic Meso-ionic Compounds. Part I. The Structure of the Sydnones and Related Compounds.*

By Wilson Baker, W. D. Ollis, and V. D. Poole.

The sydnones, obtained by dehydration of the *N*-nitroso-*N*-arylglycines (I) with acetic anhydride, have previously been given the improbable dicyclic structure (II). It is now shown in a detailed discussion that this formulation is inconsistent with the properties of these compounds. A modified hybrid structure of aromatic type is proposed, which is derived from a number of contributing ionic forms, some of which are shown in formulæ (IX—XXII). The term " meso-ionic " is suggested for compounds of this type. N-cyclo*Hexylsydnone* and N-*benzylsydnone* are typical sydnones, and the stability of the heterocyclic ring, therefore, does not depend upon union with an aromatic nucleus. A number of other new sydnones required for dipole moment investigation have been prepared. A brief review is given of some of the many molecules of this type which are known or may be capable of existence.

The work of J. C. Earl and his collaborators has shown that the *N*-nitroso-*N*-arylglycines (I; R = H) readily lose a molecule of water when treated with acetic anhydride at room temperature to give unimolecular anhydro-compounds (Earl and Mackney, *J.*, 1935, 899; Eade and Earl, *J.*, 1946, 591). The reaction also occurred in the case of *N*-nitroso-α-anilinopropionic acid (I; R = Me; Ar = Ph), but not with *N*-nitroso-α-anilino*iso*butyric acid, $Ph\cdot N(NO)\cdot CMe_2\cdot CO_2H$. As these anhydro-compounds had been prepared in the University of Sydney they were termed " sydnones ", the anhydro-derivative of *N*-nitroso-*N*-phenylglycine being referred to as *N*-phenylsydnone.

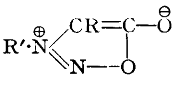
The sydnones were shown to be neutral, highly crystalline, stable compounds, fairly soluble (except *p*-nitrophenylsydnone) in most organic solvents including benzene. When hydrolysed with hot, dilute alkali they regenerated the *N*-nitroso-*N*-arylglycines, but hydrolysis with hot, concentrated hydrochloric acid gave one molecule each of an arylhydrazine and formic acid, carbon dioxide being also evolved. In the case of the sydnone derived from *N*-nitroso-α-anilinopropionic acid, acetic acid was produced in place of formic acid. The structure (II), the " lactone of 2-hydroxy-1-phenyldiaziridine-3-carboxylic acid ", was tentatively suggested for these compounds; it contains fused 3- and 4-membered rings, the latter being of the β-lactone type. This structure was regarded as incompletely satisfactory by two of us (Baker and Ollis, *Nature*, 1946, **158**, 703), and later by its proposers (Earl, *ibid.*, p. 909), but the evidence (*a*) in favour of a structure related to (II), and (*b*) against certain details of this formulation, have not previously been set out.

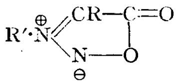


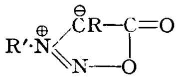
(*a*) The ready regeneration of the *N*-nitroso-*N*-arylglycines from the sydnones by alkaline hydrolysis shows that a very close relationship exists between the two compounds, and excludes the possibility that the sydnones might be represented by the simple five-membered ring formula (III), which would require a migration of the aryl group from nitrogen to nitrogen during the preparation of the sydnones, and the reverse migration during hydrolysis. Neither is likely to occur under the reaction conditions employed. No additional evidence of structure is provided by the production of an arylhydrazine by acid hydrolysis, but we have now established that this breakdown is a specific reaction of the sydnones and is not exhibited by the *N*-nitroso-*N*-arylglycines. Similarly, the interesting production of α-acylhydrazines (IV) by treatment of a sydnone in benzene solution with hydrogen bromide (Kenner and Mackay, *Nature*, 1947, **160**, 465) again gives no additional evidence of structure, nor does the observation now recorded in this paper that *N*-phenylsydnone can be reduced catalytically in presence of platinum oxide to give the ammonium salt of *N*-phenylglycine (VI; Ar = Ph, R = H). The sydnones do not show the Liebermann nitroso-reaction, and hence do not contain an *N*-nitroso-group, but the presence of a readily hydrolysable lactonic grouping is without doubt. The only conceivable alternative to a lactone is to regard the sydnones as *N*-nitroso-α-anilino-ketens (V), but this can be excluded because the sydnones do not possess a nitroso-group, and because they do not exhibit the properties characteristic of the ketens; they are, for example, stable towards boiling methyl and ethyl alcohols. Further, the nitroso-keten formula (V) cannot be a contributor to a hybrid structure containing the 5-membered ring (see below) shown in (II), as has been suggested by Earl, Leake, and Le Fèvre (*Nature*, 1947, **160**, 366), since the keten group $>C{=}C{=}O$ is linear (as is equally the polarised form $>\overset{\ominus}{C}{-}C{\equiv}\overset{\oplus}{O}$ also considered in this connection), whereas in any cyclic structure this grouping would of necessity be angular. The sydnones are soluble in hydrocarbons and cannot, therefore, possess a purely zwitterionic structure, and the evidence in favour of their possessing a heterocyclic 5-membered ring as in the formula (VII) is overwhelming.

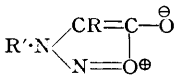
(*b*) The reasons which render structure (II) unacceptable (Baker and Ollis, *loc. cit.*) are as follows. (1) A system possessing fused three- and four-membered rings would be highly strained, and unlikely to be produced by dehydration with acetic anhydride in the cold. β-Lactones of the ordinary type are not formed under these reaction conditions. (2) Many β-lactones are unstable to heat and readily lose carbon dioxide, and compound (VIII), which contains a four-membered β-lactone ring closely analogous to that present in structure (II), loses carbon dioxide spontaneously (Staudinger and Jelagin, *Ber.*, 1911, **44**, 365; quoted by Earl, *loc. cit.*). The sydnones do not decompose readily on being heated (for example, *N*-phenylsydnone can be sublimed unchanged at 110°/1 mm.), and are, therefore, unlikely to be β-lactones. The fact that some carbon dioxide is evolved and resinous products formed when *N*-phenylsydnone is boiled with water and a small amount of sodium carbonate or acetate is used by Earl as an argument supporting a β-lactone structure, but this evidence is unacceptable. Since acidic products are formed by the hydrolysis of the sydnones, the evolution of carbon dioxide from sodium carbonate solution is without significance, but we now find that carbon dioxide is also evolved when *N*-phenylsydnone is boiled with water and a little sodium borate. However, as *N*-nitroso-*N*-phenylglycine must be produced in the early alkaline stage of the experiments, later, when the solution becomes acid, its known decomposition into carbon dioxide and *N*-nitrosomethylaniline will occur (O. Fischer, *Ber.*, 1899, **32**, 249). These experiments throw no light on the chemical behaviour of the sydnone molecule. (3) If the sydnones were correctly represented by structure (II) they should be capable of existing in optically active forms, even where R = H. Kenner and Mackay (*Nature*, 1946, **158**, 909) have prepared dextrorotatory *N*-nitroso-*N*-phenylalanine (I; R = Me; Ar = Ph) and find that it is converted by acetic anhydride into the optically inactive *N*-phenyl-*C*-methylsydnone (II; R = Me; Ar = Ph), and a similar loss of activity was recorded by Earl (*loc. cit.*) during the conversion of optically active *N*-nitroso-α-anilinophenylacetic acid (I; R = Ar = Ph) into *NC*-diphenylsydnone (II; R = Ar = Ph) (no m. p. or other details of this preparation are recorded). Whilst these experiments are of some significance, they do not rigidly exclude the possibility that sydnones might exist in optically active forms. (4) On the basis of structure (II) the benzene nucleus of *N*-phenylsydnone should undergo very ready substitution by cationoid reagents, as it may be regarded as a dialkylaniline, or more strictly an α-alkylphenylhydrazine. *N*-Phenylsydnone does, in fact, undergo bromination, but in the monobromo-derivative produced the bromine atom is linked to one of the carbon atoms of the sydnone ring (II; R = Br; Ar = Ph); no substitution occurs in the benzene nucleus (Kenner and Mackay, *Nature*, 1946, **158**, 909).

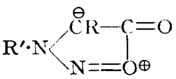
Some of the foregoing considerations led two of us (Baker and Ollis, *loc. cit.*) to put forward a modified five-membered ring structure for the sydnones which cannot be satisfactorily represented by any one purely covalent formula. This modification omits the bridge bond in (II) and substitutes a hybrid structure derived from a number of ionic states, some dipolar and some tetrapolar. Some of these contributing forms are shown in formulæ (IX—XXII). Of the eight dipolar forms, (IX) and (XII) are partly aromatic in character, and (X) and (XIII) also possess conjugated systems and may be expected to make important contributions to the hybrid. Of the four tetrapolar forms, (XVII) and (XVIII) both contain cyclic conjugated systems, and, in particular, (XVII) should contribute considerably to the whole hybrid. Formulæ are excluded which possess charges on adjacent atoms, except when one of the atoms is nitrogen in the quadricovalent state, or oxygen in the tercovalent state. In the formulæ, R = H, an alkyl or aryl group; R′ = an aryl or alkyl group.

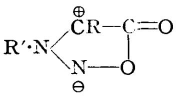

(IX.)

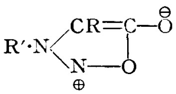

(X.)

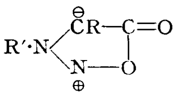

(XI.)

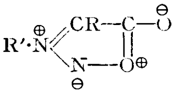

(XII.)

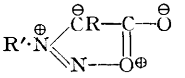

(XIII.)

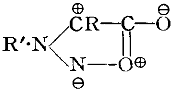

(XIV.)

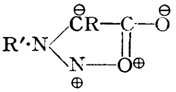

(XV.)

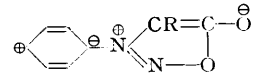

(XVI.)

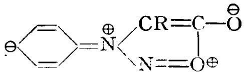

(XVII.)


(XVIII.)


(XIX.)


(XX.)

(XXI.)



(XXII.)

The bridged ring structure (II) is unlikely to make any effective contribution to the hybrid, as it would involve a much shorter distance between the CR group and the unsubstituted nitrogen atom than is possible in the above formulæ. In the case of the *N*-arylsydnones (R′ = aryl), many other possibilities of resonance occur involving the aryl nucleus; two of these are shown in formulæ (XXI) and (XXII) which are derived from (IX) and (XII). Further possible contributors to the hybrid are diradical types, but these are excluded from this discussion. The open-chain nitroso-keten type (V) has already been excluded on steric grounds. Examination of the formulæ (IX—XX) and, in particular, those [(IX), (X), (XII), (XIII), (XVII), (XVIII)] which may be expected to make considerable contributions to the hybrid, shows that although the dipoles of the different structures will be variously orientated so that the dipole of the sydnone molecule may be expected to be considerably less than that of a zwitterionic molecule with fixed charges, yet the substituted nitrogen atom will be expected to bear a large fractional positive charge, and the negative end of the sydnone dipole will be more diffusely directed towards the lactonic carbonyl grouping.

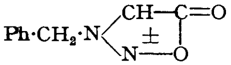
This general view of the structure of the sydnones has been fully supported by measurements of their dipole moments, preliminary mention of which has already been made (Baker, Ollis, Poole, Barltrop, Hill, and Sutton, *Nature*, 1947, **160**, 366; Earl, Leake, and Le Fèvre, *ibid.*, p. 366), and which will be the subject of a later paper. It also answers the objections to the bridged-ring structure and is consistent with the known facts of sydnone chemistry, requiring that the sydnones should (1) be virtually strainless and exhibit a general stability of aromatic type, (2) not show the properties of β-lactones, (3) possess planar molecules incapable of optical activity, (4) behave physically like molecules of fairly high dipole moment, (5) not contain a chemically reactive benzene nucleus, since the nitrogen atom directly attached to the benzene ring is approaching in character the nitrogen atom in an anilinium cation, $Ph{-}\overset{\oplus}{N}R_3$. The sydnones should possess appreciable resonance energy, and this is indicated by their difficulty of catalytic reduction, which is very slow even in the presence of platinum oxide. Their hybrid nature renders difficult the interpretation of their chemical reactions, and we feel it is unwise at this stage to attempt this either in terms of any one or more arbitrarily chosen contributing forms, or by analogy with the chemical behaviour of known compounds of essentially covalent character.

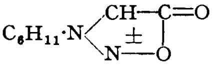
In discussing the ionic structures which contribute to the hybrid sydnone molecule, it was mentioned that forms such as (XXI) and (XXII) involving polarisation of the benzene nucleus might be involved. In order to see if such contributors were essential to the stability of the sydnone structure, the preparation of N-*benzylsydnone* (XXIII) and N-cyclo*hexylsydnone* (XXIV) was undertaken, and, as already reported (Baker, Ollis, Poole, Barltrop, Hill, and Sutton, *loc. cit.*) the syntheses proceeded normally. These two sydnones are similar to the *N*-arylsydnones in their physical properties and chemical behaviour. Contributing forms such as (XXI) and (XXII) involving polarisation of the benzene ring are, therefore, not essential for the existence of the sydnone ring. *N*-Benzylsydnone was smoothly hydrolysed by alkali to N-*nitroso*-N-*benzylglycine*, and hydrolysis with hydrochloric acid gave benzylhydrazine hydrochloride characterised as its α-nitroso-derivative and by the formation of p-*nitrobenzaldehyde benzylhydrazone*. *N*-*cyclo*Hexylsydnone behaved similarly, giving on alkaline hydrolysis *N*-nitroso-*N*-*cyclo*hexylglycine, and on acid hydrolysis *cyclo*hexylhydrazine hydrochloride.

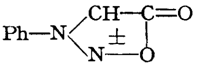
Further evidence in support of the proposed structure for the sydnones is provided by a study of their ultra-violet absorption spectra in alcoholic solution. *N*-*cyclo*Hexylsydnone (curve 1), which contains no possible conjugated system apart from the sydnone ring, shows a well-defined absorption band at 292 mμ, and *N*-benzylsydnone (curve 2) in which conjugation between the phenyl group and the sydnone nucleus is impossible, also shows absorption at exactly the same wave-length. This band at 292 mμ is therefore characteristic of the sydnone ring itself. If these two compounds had dicyclic covalent structures, as (II), they would not be expected to show strong absorption in this part of the spectrum. In *N*-phenylsydnone (curve 3), conjugation between the phenyl group and the heterocyclic nucleus causes a displacement of this band from 292 to 310 mμ, and a new band also appears at *ca.* 238 mμ owing to a similar shift of the ethylenic absorption of the benzene ring. *NC*-Diphenylsydnone (curve 4) shows a still greater displacement to 333 mμ of the absorption band characteristic of the sydnone ring, thus indicating increased conjugation. In this connection it is noteworthy that the three diaryl sydnones described in this paper all show a white fluoresence in ultra-violet light.

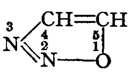
The sydnones are thus compounds exhibiting aromatic characteristics, which can be represented only as resonance hybrids of a large number of contributing ionic forms. It is impossible to represent them, even approximately, by any one covalent formula, or as a hybrid of a number of covalent formulæ, and their case is therefore fundamentally different from that of most organic compounds which can be satisfactorily represented either by a single covalent form, or as a hybrid of a few covalent forms, *e.g.*, benzene and naphthalene, or as a hybrid of covalent and ionic forms, *e.g.*, the amides. The closest analogies are provided by the aliphatic diazo-compounds, which can be represented only as hybrids of two zwitterionic forms $>\!C{=}\overset{\oplus}{N}{=}\overset{\ominus}{N}$ and $>\!\overset{\ominus}{C}{-}\overset{\oplus}{N}{\equiv}N$, and by the organic azides, which are similarly derived from the forms $R{-}N{=}\overset{\oplus}{N}{=}\overset{\ominus}{N}$ and $R{-}\overset{\ominus}{N}{-}\overset{\oplus}{N}{\equiv}N$ (see Taylor and Baker, Sidgwick's " Organic Chemistry of Nitrogen," 1942, pp. 362, 365). For molecules of this type we propose to use the adjective " meso-ionic ", and the sydnones afford an example of cyclic meso-ionic compounds.

For cyclic meso-ionic structures it is necessary to have a simple symbol to give expression to the structural considerations discussed above, and it seems convenient to adopt the sign $\pm$ proposed by Simpson (*J.*, 1946, 95) for molecules like anthranil, piazthiole, 2-substituted indazoles, and related types for which mainly meso-ionic structures had been previously proposed (Baker, *J.*, 1945, 267). *N*-Phenylsydnone is thus conveniently represented by formula (XXV).

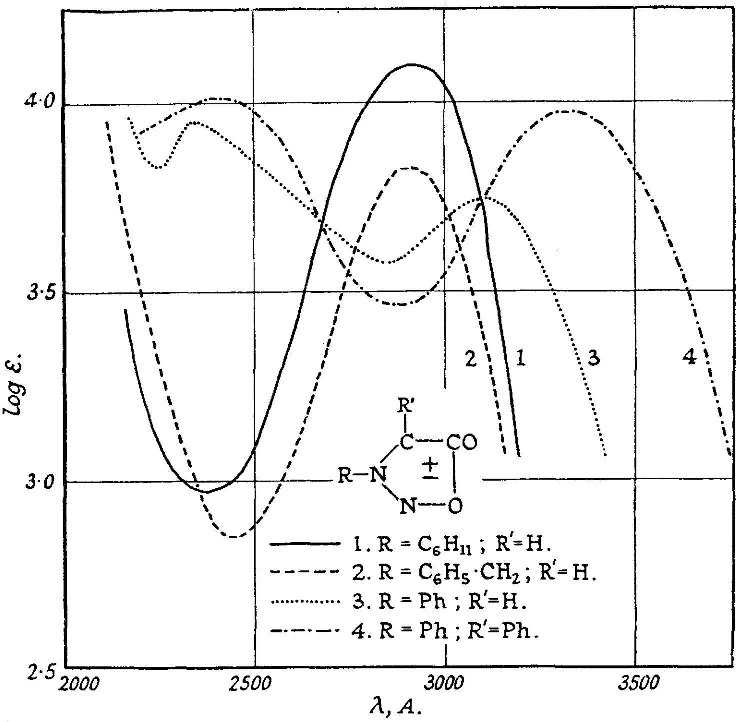

(XXIII.)


(XXIV.)

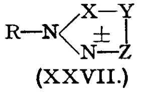

(XXV.)

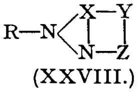

(XXVI.)

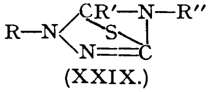
As will be indicated later, many cyclic meso-ionic compounds containing a heterocyclic 5-membered ring are possible. A number are, in fact, already described in the literature, and as the multiplication of trivial names is to be deprecated, it is necessary to adapt existing systematic nomenclature to substances of this type. *N*-Phenylsydnone (XXV) is a derivative of 1-oxa-2 : 3-diazole (XXVI), and structure (XXV) with its two unsatisfied valencies is 5-keto-3-phenyl-3 : 5-dihydro-1-oxa-2 : 3-diazole. It is suggested that this name should be prefixed by the symbol ψ to indicate the hybrid ionic structure of the compound, so that *N*-phenylsydnone becomes ψ-5-keto-3-phenyl-3 : 5-dihydro-1-oxa-2 : 3-diazole.

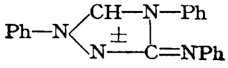


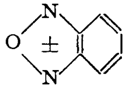
The sydnones form a special case of a group of related cyclic meso-ionic compounds which may be represented by the general formula (XXVII), where X = CH, CR, or N ; Y–Z or Z–Y = –CO–O–, –NR–CO–, –NR–C(:NR')–, or –O–C(:NR)– or any of the related mono- or di-thio-

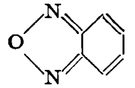

(XXVII.)


(XXVIII.)


(XXIX.)


(XXX.)

(XXXI.)



(XXXII.)

derivatives, R being an alkyl or aryl group throughout. Many compounds conforming to this type are to be found in the literature, but they have generally been regarded as bridged-ring compounds, *e.g.*, (XXVIII), or as the stereochemically unacceptable *endo*-oxy-, -thio-, or -imino-compounds, *e.g.*, (XXIX), which has been suggested as an alternative structure for the " *endo*-thiotriazolines ". The well-known reagent " nitron " is best represented by the formula (XXX) instead of as an *endo*-anilo-compound (cf. XXIX). Schönberg appears to have been the first to suggest the possibility of hybrid, ionic, cyclic structures for certain triazoles including nitron (*J.*, 1938, 824), but the wide generality of this type of molecule does not appear to have been previously recognised, though the ideas have been more precisely formulated by Jensen and Friediger (*Kgl. Danske Videnskab. Selskab*, 1943, **20**, 1; see *Chem. Abs.*, 1945, **39**, 2068) as the result of dipole moment measurements. A further class of compounds belonging to the group represented by formula (XXVII) is where Y–Z or Z–Y is part of a benzene or aromatic nucleus, in which case R–N (in, for example, the 2-substituted-indazoles or -benztriazoles) may be replaced by O, as in benzfurazan (XXXI), S, as in piazthiole and Se, as in piaselenole. In these cases, which have already received slight general consideration (Baker, *J.*, 1945, 258), the possibility exists that covalent *o*-quinonoid forms (as XXXII) may make a large contribution to the hybrid molecule.

A number of sydnones have been prepared for measurement of their dipole moments to be discussed in Part II of this series. These are N-p-*tolyl*, N-p-*chlorophenyl*-, NC-*diphenyl*-, C-*phenyl*-N-p-*chlorophenyl*-, and C-*phenyl*-N-p-*tolyl-sydnone*. Improved preparations of *C*-bromo-*N*-phenyl- and *N*-*p*-nitrophenyl-sydnone are described. *C*-Bromo-*N*-phenylsydnone can also be prepared by the bromination of *N*-phenylsydnone with *N*-bromosuccinimide in chloroform solution.

EXPERIMENTAL.

N-*Benzylaminoacetonitrile Hydrochloride*.—Benzylamine (110 c.c.) in ethanol (50 c.c.) was added with shaking to a solution of hydrogen chloride (40 g.) in ethanol (200 c.c.). After standing overnight the hydrochloride was collected and washed with ether (yield 137 g.).

A solution of potassium cyanide (63 g.) in water (150 c.c.) was added slowly with stirring and ice-cooling during 1 hour to a mixture of benzylamine hydrochloride (137 g.) in water (300 c.c.), aqueous formaldehyde (35%; 82 g.), and ether (500 c.c.). The organic layer was separated, the aqueous layer extracted with 3 portions of ether (250 c.c.), the combined ethereal solutions dried ($MgSO_4$), and a solution of hydrogen chloride (50 g.) in ether (150 c.c.) added. The crystalline precipitate was washed with ether and dried over potassium hydroxide. Crystallisation from ethanol gave N-*benzylaminoacetonitrile hydrochloride* (114 g.; 65%) as colourless plates, m. p. 171° (decomp.) (Found: C, 58·6; H, 6·2; N, 15·3; Cl, 19·5. $C_9H_{11}N_2Cl$ requires C, 59·2; H, 6·0; N, 15·3; Cl, 19·5%).

N-*Benzylglycine Hydrochloride*.—*N*-Benzylaminoacetonitrile hydrochloride (100 g.) was dissolved in concentrated hydrochloric acid which had been saturated with hydrogen chloride at 0° (350 c.c.) and left at room temperature for 1 hour. On dilution with water (250 c.c.) crystals, probably of the amide, separated, and the mixture was refluxed for 4 hours, left overnight, and the colourless plates collected and dried (88 g.; m. p. 205°). The aqueous filtrate was evaporated to dryness under reduced pressure, and the residue extracted with hot ethanol (500 c.c.). The cooled solution was filtered from ammonium chloride, and yielded a further crop (25 g.; m. p. 195—200°). Crystallisation from ethanol gave *N*-benzylglycine hydrochloride as colourless plates, m. p. 220° (slight decomp.) (the m. p. depends upon the rate of heating; Mason and Winder, *J.*, 1894, **65**, 190, give m. p. 214—215°).

N-*Nitroso*-N-*benzylglycine*.—A solution of sodium nitrite (19 g.) in water (60 c.c.) was added during 1 hour to a stirred, ice-cooled suspension of *N*-benzylglycine hydrochloride (50 g.) in water (200 c.c.). After being left for 1 hour at room temperature, the mixture was acidified to pH 4 with concentrated hydrochloric acid. The precipitate was collected and crystallised from hot water (*ca.* 1 l.) giving N-*nitroso*-N-*benzylglycine* (41·7 g.; 87%) as glistening plates, m. p. 148° (Found: C, 55·6; H, 5·4; N, 14·3. $C_9H_{10}O_3N_2$ requires C, 55·7; H, 5·2; N, 14·4%). The product gives a strong Liebermann nitroso-reaction.

N-*Benzylsydnone* (ψ-5-*Keto*-3-*benzyl*-3 : 5-*dihydro*-1-*oxa*-2 : 3-*diazole*) (XXIII).—*N*-Nitroso-*N*-benzylglycine (40 g.) and acetic anhydride (185 c.c.) were heated on the steam-bath for 5 hours, and then distilled under reduced pressure leaving a residue which solidified on standing. Crystallisation from benzene–light petroleum (b. p. 40—60°) gave colourless plates, m. p. 67°. Further recrystallisation gave pure N-*benzylsydnone* as colourless plates, m. p. 69·5° [Found: C, 61·2; H, 5·0; N, 15·9; *M* (Rast), 174. $C_9H_8O_2N_2$ requires C, 61·4; H, 4·6; N, 15·9%; *M*, 176]. It is insoluble in aqueous sodium carbonate and does not give Liebermann's nitroso-reaction. Earl, Leake, and Le Fèvre (*loc. cit.*) mentioned *N*-benzylsydnone, but gave no m. p. or details of preparation.

Alkaline Hydrolysis of N-*Benzylsydnone*.—*N*-Benzylsydnone (2 g.) was heated on the steam-bath for 3 hours with water (20 c.c.) and sodium hydroxide (1 g.). The cooled, filtered solution was acidified with hydrochloric acid, and the crystalline precipitate of *N*-nitroso-*N*-benzylglycine was collected and dried (2·05 g.; 93%), m. p. 144°, mixed m. p. 146°.

Acid Hydrolysis of N-*Benzylsydnone*.—*N*-Benzylsydnone (5 g.), water (50 c.c.), and concentrated hydrochloric acid (25 c.c.) were heated on the steam-bath for 4½ hours; solution gradually occurred, and carbon dioxide was evolved. The solution was evaporated to dryness, and the residue dried in a vacuum over potassium hydroxide and crystallised from ethanol (20 c.c.), giving benzylhydrazine monohydrochloride (2·65 g.) as colourless needles, m. p. 105—107° (Wohl and Oesterlin, *Ber.*, 1900, **33**, 2739, give m. p. 110°). Treatment of this benzylhydrazine hydrochloride (500 mg.) in water (3 c.c.) with sodium nitrite (250 mg.) gave a solid (230 mg.; 49%), crystallisation of which from benzene–light petroleum (b. p. 40—60°) gave α-*N*-nitrosobenzylhydrazine as colourless needles, m. p. 71° (Wohl and Oesterlin, *loc. cit.*, give m. p. 71°). The benzylhydrazine hydrochloride also readily gave p-*nitrobenzaldehyde benzylhydrazone* as yellow needles from ethanol, m. p. 131° (decomp.) (Found: C, 65·7; H, 5·1; N, 16·7. $C_{14}H_{13}O_2N_3$ requires C, 65·9; H, 5·1; N, 16·5%).

N-*Nitroso*-N-cyclo*hexylglycine*.—*cyclo*Hexylglycine hydrochloride was prepared from *cyclo*hexylamine hydrochloride (40 g.) by the Strecker synthesis (Zelinsky and Arzibacheff, *Ber.*, 1907, **40**, 3054), and was purified by dissolution in alcohol and precipitation of the accompanying ammonium chloride with ether. After removal of the solvents, the *N*-*cyclo*hexylglycine hydrochloride was dissolved in water (200 c.c.), and a solution of sodium nitrite (20 g.) in water (40 c.c.) was added dropwise during 30 minutes with stirring and ice-cooling. After 2 hours the solution was acidified, and the solid collected and crystallised from hot water, giving *N*-nitroso-*N*-*cyclo*hexylglycine (30 g.) as colourless needles, m. p. 117° [Zelinsky and Arzibacheff, *loc. cit.*, give m. p. 117·5—118° (decomp.)].

N-cyclo*Hexylsydnone* (*ψ*-5-*Keto*-3-cyclo*hexyl*-3 : 5-*dihydro*-1-*oxa*-2 : 3-*diazole*) (XXIV).—*N*-Nitroso-*N*-*cyclo*hexylglycine (30 g.) was dissolved in acetic anhydride (200 c.c.) and left at room temperature in the dark for 3 days. Excess of acetic anhydride was removed under reduced pressure and the solid residue was recrystallised thrice from benzene–light petroleum (b. p. 60—80°), giving N-cyclo*hexylsydnone* (17 g.; 63%) as colourless, flat needles, m. p. 64° [Found : C, 57·4; H, 7·3; N, 16·6; *M* (Rast), 165. $C_8H_{12}O_2N_2$ requires C, 57·2; H, 7·2; N, 16·7%; *M*, 168]. The product is insoluble in aqueous sodium carbonate and gives no reaction for a nitroso-group. Slight decomposition is observed after long periods.

Acid Hydrolysis of N-cyclo*Hexylsydnone*.—*N*-*cyclo*Hexylsydnone (2 g.) was heated on a steam-bath with water (3 c.c.), alcohol (3 c.c.), and concentrated hydrochloric acid (10 c.c.) for ½ hour, carbon dioxide being evolved. The solution was taken to dryness, and formic acid was detected in the distillate. The residue of *cyclo*hexylhydrazine hydrochloride had m. p. 111° (Harkins and Lochte, *J. Amer. Chem. Soc.*, 1924, **46**, 454, give m. p. 107—110°), and was characterised, by the addition of phenyl *iso*thiocyanate, as the phenylthiosemicarbazide, m. p. 146° from alcohol (Kizhner and Byelov, *J. Russ. Phys. Chem. Soc.*, 1911, **43**, 577, see *Chem. Abs.*, 1912, **6**, 347, give m. p. 143°; Harkins and Lochte, *loc. cit.*, give m. p. 148°). It was also converted into the condensation product with benzaldehyde, m. p. 183° from ethyl acetate (Harkins and Lochte record the same m. p.), the structure of which has not been established.

Alkaline Hydrolysis of N-cyclo*Hexylsydnone*.—*N*-*cyclo*Hexylsydnone (0·5 g.) was refluxed with 2N-sodium hydroxide (10 c.c.) for ½ hour, and the solution then filtered and acidified, precipitating *N*-nitroso-*N*-*cyclo*hexylglycine, m. p. and mixed m. p. 119°.

Catalytic Reduction of N-*Phenylsydnone*.—*N*-Phenylsydnone (0·5 g.) in ethanol (100 c.c.) was shaken in hydrogen in presence of Adams's platinum oxide catalyst (0·1 g.) till hydrogen uptake (230 c.c.; $3H_2$ requires 220 c.c.) ceased (3 hours). Evaporation of the filtered solution left a residue (0·46 g.) which when treated with alcoholic potassium hydroxide evolved ammonia and deposited the potassium salt of *N*-phenylglycine. The free acid after crystallisation from light petroleum (b. p. 100—120°) had m. p. 123°, and was converted into *N*-nitroso-*N*-phenylglycine, m. p. and mixed m. p. 104°.

C-*Bromo*-N-*phenylsydnone* (*ψ*-4-*Bromo*-5-*keto*-3-*phenyl*-3 : 5-*dihydro*-1-*oxa*-2 : 3-*diazole*).—(*a*) The action of bromine on *N*-phenylsydnone in acetic acid to give a bromo-derivative, m. p. 134°, has been noted by Kenner and Mackay (*Nature*, 1946, **158**, 910); we find that the reaction takes place more smoothly in acetic anhydride solution, and the formation of violet by-products is avoided.

A solution of bromine (10 g.) in acetic anhydride (25 c.c.) was added at 0° to a suspension of *N*-phenylsydnone (10 g.) in acetic anhydride (100 c.c.), and after a short time a light yellow solid had separated. The residue (12·6 g.) left after the removal of the solvents under diminished pressure was crystallised from ethanol, giving *C*-bromo-*N*-phenylsydnone (12·1 g.; 81%) as colourless needles, m. p. 140° (decomp.) (Found : C, 39·7; H, 2·1; N, 11·8; Br, 33·2. Calc. for $C_8H_5O_2N_2Br$: C, 39·8; H, 2·1; N, 11·6; Br, 33·2%).

(*b*) *N*-Phenylsydnone (1 g.) dissolved in chloroform (10 c.c.) was refluxed for ¼ hour with excess of *N*-bromosuccinimide (1·3 g.). The cooled mixture was filtered and evaporated, and the residue crystallised from alcohol, giving white needles (1 g.), m. p. 136°, undepressed when mixed with *C*-bromo-*N*-phenylsydnone prepared by the previous method.

N-p-*Tolylsydnone* (*ψ*-5-*Keto*-3-p-*tolyl*-3 : 5-*dihydro*-1-*oxa*-2 : 3-*diazole*).—A solution of *N*-nitroso-*N*-*p*-tolylglycine (prepared according to the directions of Vorländer and von Schilling, *Ber.*, 1901, **34**, 1646, for the *o*-tolyl isomer) (24 g.) in acetic anhydride (100 c.c.) was kept at room temperature for 48 hours and then poured into water. The *product*, after collection, crystallised from dilute ethanol in needles (8 g.), m. p. 142—144°. Further crystallisation from benzene gave long, lustrous, colourless needles, m. p. 144—145° (Found : C, 61·6; H, 4·6; N, 16·1. $C_9H_8O_2N_2$ requires C, 61·3; H, 4·5; N, 15·9%).

N-p-*Chlorophenylglycine Ethyl Ester*.—A mixture of ethyl chloroacetate (62 g.), *p*-chloroaniline (64 g.), ethanol (50 c.c.), and hydrated sodium acetate (60 g.) was refluxed (oil-bath at 125°) for 5 hours. Water (200 c.c.) was then added and the precipitated solid ester collected and washed. A further quantity of the ester was obtained by shaking the filtrate and washings with ether at pH 4, then neutralising and extracting with ether again, drying, and removing the ether from the second extract. The combined yields of ester were crystallised from ethanol, giving N-p-*chlorophenylglycine ethyl ester* (81 g.; 80%) as colourless plates, m. p. 88° (Found : C, 56·4; H, 5·5; N, 6·8. $C_{10}H_{12}O_2NCl$ requires C, 56·3; H, 5·6; N, 6·6%).

N-p-*Chlorophenylglycine*.—The preceding ester (53 g.), ethanol (20 c.c.), and a solution of sodium hydroxide (15 g.) in water (200 c.c.) were refluxed for ½ hour, filtered, and neutralised with concentrated hydrochloric acid (45 c.c.), and the precipitated acid collected and dried over potassium hydroxide (yield 45·5 g.; 98%). The m. p. of this material was 141° (Swalbe, Schulz, and Jochheim, *Ber.*, 1908, **41**, 3794, who prepared this acid by the Strecker reaction, give m. p. 141°).

N-*Nitroso*-N-p-*chlorophenylglycine*.—The above acid (40 g.) was suspended in water (400 c.c.), and a solution of sodium nitrite (16 g.) in water (60 c.c.) was added slowly at 0°. After 2 hours, when solution was complete, concentrated hydrochloric acid (25 c.c.) was added, and the solid nitroso-compound collected and dried over potassium hydroxide (yield, 46 g.). Recrystallisation from chloroform gave the rather unstable *N*-nitroso-*N*-*p*-chlorophenylglycine as almost colourless needles, m. p. 114°.

N-p-*Chlorophenylsydnone* (*ψ*-5-*Keto*-3-p-*chlorophenyl*-3 : 5-*dihydro*-1-*oxa*-2 : 3-*diazole*).—*N*-Nitroso-*N*-*p*-chlorophenylglycine (10 g.) and acetic anhydride (50 c.c.) were heated on the steam-bath for 90 minutes and distilled to dryness under diminished pressure, and the residue immediately crystallised from benzene–light petroleum (b. p. 60—80°), giving N-p-*chlorophenylsydnone* (8·2 g.; 82%) as light-yellow needles, m. p. 113° (Found : C, 49·1; H, 2·8; N, 14·1. $C_8H_5O_2N_2Cl$ requires C, 48·8; H, 2·6; N, 14·3%). The compound is insoluble in sodium carbonate solution, and gives no reaction for a nitroso-group. Hydrolysis with hydrochloric acid gave carbon dioxide and *p*-chlorophenylhydrazine characterised by conversion into benzaldehyde *p*-chlorophenylhydrazone, m. p. 127° (lit., m. p. 127°) and the *p*-chlorophenylhydrazone of pyruvic acid, m. p. 199° (Found : C, 50·6; H, 4·5. Calc. for $C_9H_9O_2N_2Cl$: C, 50·7; H, 4·2%) (Hewitt, *J.*, 1893, **63**, 873, gives m. p. 199°).

Ethyl α-*Bromophenylacetate.*—Phenylacetyl chloride (191 g.; b. p. 98°/14 mm.) was prepared by refluxing phenylacetic acid (200 g.), thionyl chloride (200 g.), and pyridine (1 c.c.) for 3 hours and then fractionating. To this acid chloride was added anhydrous bromine (217 g.) with stirring and irradiation with ultra-violet light during 1 hour, the temperature being then gradually raised to 60° where it was maintained for ½ hour. The resulting crude bromo-acid chloride was then carefully added to absolute ethanol (500 c.c.), excess of ethanol distilled off after standing overnight, and the ester dissolved in ether (500 c.c.), washed with aqueous sodium carbonate, dried, and distilled, finally giving ethyl α-bromophenylacetate (203 g.; 68%, b. p. 102—104°/1·5 mm., 146—150°/12 mm.) (cf. Anschutz, *Annalen*, 1907, **354**, 127, who records b. p. 150—152°/13 mm.).

α-*Anilinophenylacetic Acid.*—Ethyl α-bromophenylacetate (50 g.), aniline (19 c.c.), hydrated sodium acetate (28 g.), and ethanol (20 c.c.) were refluxed for 5 hours. After 12 hours the solid was triturated with 2N-sodium carbonate, washed with water, dried, and crystallised from light petroleum (b. p. 60—80°), giving ethyl α-anilinophenylacetate (46 g.; 86%) as needles, m. p. 87·5° (Bischoff, *Ber.*, 1897, **30**, 2305, gives m. p. 85°; Hinze, *Ber.*, 1899, **32**, 3056, m. p. 89—90°). Hydrolysis with 10% sodium hydroxide in presence of a little ethanol and precipitation at pH 4 gave α-anilinophenylacetic acid in quantitative yield, m. p. 183° (decomp.); after crystallisation from ethanol it had m. p. 185° (Hinze, *loc. cit.*, gives m. p. 183°, decomp.).

NC-*Diphenylsydnone* (ψ-5-*Keto*-3 : 4-*diphenyl*-3 : 5-*dihydro*-1-*oxa*-2 : 3-*diazole*).—Sodium nitrite (8·4 g.) was added with stirring to a solution of α-anilinophenylacetic acid (25 g.) in concentrated sulphuric acid (300 c.c.) at 0°, and after 1½ hours the mixture was poured on ice. The crude nitroso-acid was collected, washed, and heated on the steam-bath for 1 hour with acetic anhydride (90 c.c.), and cooled, water was added, and the solid was collected, washed with aqueous sodium carbonate, water, and alcohol, and dried. Crystallisation from ethanol (700 c.c.) gave NC-*diphenylsydnone* (15·5 g.) as light-yellow, thick, rhombic plates, m. p. 184·5° (Found : C, 70·7; H, 4·5; N, 11·6. $C_{14}H_{10}O_2N_2$ requires C, 70·6; H, 4·2; N, 11·8%). It is insoluble in aqueous sodium carbonate, gives no reaction for a nitroso-group, and shows a white fluorescence in ultra-violet light.

α-p-*Chloroanilinophenylacetic Acid.*—Ethyl α-*p*-chloroanilinophenylacetate was prepared by the method used for ethyl α-anilinophenylacetate; it formed needles from light petroleum (b. p. 60—80°), m. p. 88·5° (84% yield) (Bischoff, *Ber.*, 1897, **30**, 2763, records m. p. 87·8°). Alkaline hydrolysis gave α-p-*chloroanilinophenylacetic acid* (97% yield) as small, colourless needles from aqueous ethanol, m. p. 175° (decomp.) (Found : C, 63·9; H, 4·5; N, 5·5; Cl, 14·2. $C_{14}H_{12}O_2NCl$ requires C, 64·2; H, 4·6; N, 5·4; Cl, 13·6%).

C-*Phenyl*-N-p-*chlorophenylsydnone* (ψ-5-*Keto*-4-*phenyl*-3-p-*chlorophenyl*-3 : 5-*dihydro*-1-*oxa*-2 : 3-*diazole*).—Nitrosation of the preceding acid (15 g.) in concentrated sulphuric acid (300 c.c.) with sodium nitrite (4·5 g.), isolation of the crude nitroso-derivative, and conversion of it into the sydnone were carried out as in the case of *NC*-diphenylsydnone. C-*Phenyl*-N-p-*chlorophenylsydnone* (10·5 g.) was obtained by crystallisation from ethanol (50 c.c.) as thick, light-yellow plates, m. p. 124° (Found : C, 61·8 H, 3·4; N, 10·3; Cl, 13·4. $C_{14}H_9O_2N_2Cl$ requires C, 61·7; H, 3·3; N, 10·3; Cl, 13·0%).

C-*Phenyl*-N-p-*tolylsydnone* (ψ-5-*Keto*-4-*phenyl*-3-p-*tolyl*-3 : 5-*dihydro*-1-*oxa*-2 : 3-*diazole*).—This sydnone was prepared *via* ethyl α-*p*-toluidinophenylacetate (needles, m. p. 91·5° from light petroleum, b. p. 60—80°, yield 89%; Stockenius, *Jahresber.*, 1878, 781, gives m. p. 89—90°), α-*p*-toluidinophenylacetic acid (crystalline powder, m. p. 182°, decomp., from ethanol; yield 95%; von Miller and Plöchl, *Ber.*, 1896, **29**, 1739, give m. p. 178—182°, decomp.), and the nitroso-acid, prepared from α-*p*-toluidinophenylacetic acid (25 g.), concentrated sulphuric acid (250 c.c.), and sodium nitrite (7·9 g.). C-*Phenyl*-N-p-*tolylsydnone* was obtained in 64% yield from *N*-nitroso-α-*p*-toluidinophenylacetic acid as colourless needles from ethanol, m. p. 151° (Found : C, 71·5; H, 4·9; N, 11·2. $C_{15}H_{12}O_2N_2$ requires C, 71·4; H, 4·4; N, 11·1%).

N-p-*Nitrophenylsydnone* (ψ-5-*Keto*-3-p-*nitrophenyl*-3 : 5-*dihydro*-1-*oxa*-2 : 3-*diazole*).—Difficulty was experienced in nitrosating *N*-*p*-nitrophenylglycine in 36N-sulphuric acid (Eade and Earl, *loc. cit.*), but the reaction proceeds readily, and in somewhat greater yield than that claimed, in hydrochloric acid. A solution of sodium nitrite (7·7 g.) in water (25 c.c.) was added dropwise during ½ hour to a stirred, ice-cooled solution of *N*-*p*-nitrophenylglycine (20 g.) in concentrated hydrochloric acid (200 c.c.). After a total of 2 hours the nitroso-derivative was collected, washed, and dried; it crystallised from dilute ethanol in fine, light-yellow needles (21·5 g.; 93%), m. p. 149° (decomp.) (Eade and Earl record m. p. 147·5°, decomp.). Eade and Earl converted the nitroso-acid into *N*-*p*-nitrophenylsydnone by treatment with acetic anhydride at room temperature for 14 days, but an equally good yield is obtained by heating the acid with 5 times its weight of acetic anhydride for 2 hours on the steam-bath, and isolating the sydnone as previously described. It had m. p. 184° (Eade and Earl give m. p. 187—188°).

The authors' thanks are due to Dr. A. E. Gillam for a determination of the ultra-violet absorption spectrum of *N*-phenylsydnone, to Dr. J. A. Barltrop for details of the preparation of *N*-*p*-tolylsydnone, to Imperial Chemical Industries Limited for a grant and for a supply of *N*-phenylglycine, and to the Department of Scientific and Industrial Research for a maintenance allowance awarded to one of them (V. D. P.).

THE UNIVERSITY, BRISTOL.

[*Received, March* 30*th*, 1948.]