

MESO-IONIC COMPOUNDS

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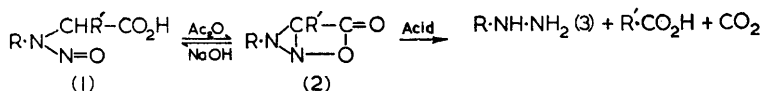
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IN 1949 the term meso-ionic was introduced to describe a class of novel heterocyclic compounds of which the sydnones are the most closely investigated members. Since the proposal was first made, the wide generality of this structural type has been recognised and several new members have been discovered, so that a review of this subject seems both opportune and desirable.

Sydnones as Meso-ionic Compounds

In 1935 Earl and Mackney¹ showed that treatment of *N*-nitroso-*N*-phenylglycine (1; R = Ph, R' = H) with warm acetic anhydride yielded a well-crystalline, neutral anhydro-derivative which was given the fused-ring structure (2; R = Ph, R' = H). Later work showed that such dehydration is a quite general reaction.² The exact nature of these anhydro-derivatives has aroused considerable interest and various structural proposals have been made.^{2, 3} The name "sydnone" has been given to this class of compound because they were first studied at the University of Sydney, and the anhydro-derivative of *N*-nitroso-*N*-phenylglycine was termed *N*-phenylsydnone.



The sydnones are hydrolysed by hot aqueous sodium hydroxide with regeneration of the original nitroso-acid, and by hot dilute acid to give an aryl- or alkyl-hydrazine (3), a carboxylic acid (formic acid in the case of *N*-phenylsydnone), and carbon dioxide.² These facts made any

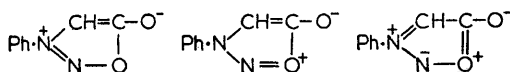
¹ Earl and Mackney, *J.*, 1935, 899.

² Eade and Earl, *J.*, 1946, 591.

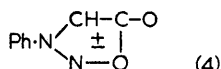
³ (a) Baker and Ollis, *Nature*, 1946, **158**, 703; (b) Kenner and Mackay, *ibid.*, p. 909; (c) Earl, *ibid.*, p. 910; (d) Baker, Ollis, Poole, Barltrop, Hill, and Sutton, *ibid.*, 1947, **160**, 366; (e) Earl, Leake, and Le Fèvre, *ibid.*, p. 366; (f) Eade and Earl, *J.*, 1948, 2307; (g) Baker, Ollis, and Poole, *J.*, 1949, 307; (h) *idem*, *J.*, 1950, 1542; Crane, *Eastman Kodak Co., Org. Chem. Bull.*, 1950, **22**, No. 2; (i) Earl, *Chem. and Ind.*, 1953, 746, 1284; (j) Hammick and Roe, *ibid.*, p. 900; (k) Orville Thomas, *ibid.*, 1955, 533; (l) Baker and Ollis, *ibid.*, p. 910; (m) Bieber, *ibid.*, p. 1055; (n) Earl, *Rec. Trav. chim.*, 1956, **75**, 346; (o) Jennen, III^e Congrès National des Sciences, Brussels, 1950; *Chimie et Industrie*, 1952, **67**; XXVIII^e Congrès International de Chimie Industrielle, Brussels, 1954, 622.

molecular rearrangement during sydnone formation most unlikely, and formed the basis of the original, covalent structure (2).^{1, 2}

This fused-ring structure was considered unacceptable by Baker and Ollis^{3a} who suggested that the sydnones could be satisfactorily represented by a modification of the structure (2) which had been tentatively proposed by Earl and Mackney. In view of the impossibility of representing the sydnones by any, even approximately satisfactory, covalent structure, the sydnones were regarded as resonance hybrids of a number of dipolar and tetrapolar forms, of which twelve were shown in the original paper; three of these are shown below for the case of *N*-phenylsydnone.



When this proposal was made, it was emphasised that the contribution of these canonical forms to the hybrid molecule would vary considerably, and it was felt that the arbitrary selection of any one of them as a structural formula would be misleading. Clearly what was required was a symbol and a general, adjectival term which would indicate that the sydnones had a mesomeric structure derived from a number of ionic, in the sense of zwitterionic, forms. The word *meso-ionic* was therefore introduced, and the symbol \pm suggested by Simpson⁴ was at first accepted. Hence, for example, *N*-phenylsydnone was referred to as a meso-ionic compound, and it was represented by formula (4) in which all the atoms taking part in the hybrid structure were shown as linked by single bonds.



It was later found that the concept of molecules of this type had been anticipated by Schönberg in 1938 in the case of the "endothiodihydrothiodiazoles" (see p. 24) and the reagent "nitron" (see p. 26).⁵ Schönberg indeed appears to have been the first to recognise the existence of compounds which cannot be represented satisfactorily by a covalent structure, but which can be properly regarded as a hybrid of electrically charged forms. The generality of this class of molecule was recognised only after the structure of the sydnones became known, although the views of Schönberg had been expanded and more precisely formulated by Jensen and Friediger⁶ in 1943.

The Term Meso-ionic and the Representation of Meso-ionic Compounds

The use of the term meso-ionic and of the early symbolism shown in formula (4) requires careful examination. Neither is justified unless existing nomenclature and formulæ are inadequate. If the sydnones had been an isolated class of compound it is doubtful whether any such suggestions

⁴ Simpson, *J.*, 1946, 95.

⁵ Schönberg, *J.*, 1938, 824.

⁶ Jensen and Friediger, *Kgl. danske Videnskab. Selskab Mat.-fys. Medd.*, 1943, 20, 1; *Chem. Abs.*, 1945, 39, 2068.

would have been necessary, but as will be seen there are many known groups of compounds, related to the sydnones, which it is otherwise impossible to classify except as "sydnone-like". The scope of the word meso-ionic needs clear definition in view of the fact that inaccuracies in its application have appeared in the literature. These have been discussed by Katritzky⁷ who also raised objections to the word meso-ionic. We believe that a satisfactory definition of the word meso-ionic is now possible and that its retention is desirable, but the special symbolism shown in formula (4) is no longer necessary because existing, accepted symbolism, widely adopted since the \pm sign was first put forward, may now be used.

The revised definition of the word meso-ionic, and the use of an accepted instead of a special symbolism, were advanced by the Reviewers in 1955,³¹ who realised the advantage of discussing these compounds in terms of molecular orbital theory. Almost exactly similar proposals were put forward a few weeks later and independently by Bieber,^{3m} the only difference being a very minor one of symbolism which is mentioned below. These new proposals emphasise the essentially *aromatic* character of the sydnones and related compounds which was explicitly recognised in 1946.^{3a}

The essential feature of all aromatic compounds is a five-, six-, or seven-membered cyclic structure with a total of six π electrons associated with all the atoms of the ring. The ring must be planar, or almost planar, and it must possess a considerable resonance energy. These conditions are satisfied in the carbocyclic series in the case of benzene with its planar six-membered ring and six π electrons. In the case of the *cyclopentadienyl* anion each of the five CH groups contributes one electron and the sextet is made up by the gain of a further electron, so that aromatic character is exhibited in the anion $C_5H_5^-$. In the seven-membered carbocyclic ring as in the tropylium cation, $C_7H_7^+$, each of the seven CH groups contributes one electron; loss of an electron then gives the sextet which therefore becomes associated with a positive charge. The negative charge may be resident on an accompanying anion as in tropylium bromide, $C_7H_7^+Br^-$, or on a covalently linked atom such as oxygen in tropone. The same conditions apply to the requirements for the development of aromatic character in heterocyclic compounds. In furan and pyrrole the heteroatoms each supply two electrons, so that in these cases the five-membered rings become aromatic when neutral. In pyridine the nitrogen atom supplies one electron, giving a neutral aromatic molecule with a six-membered ring.

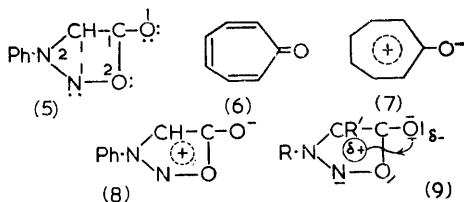
It is desirable to mention these facts in order to make clear the basis of the new formulation of the sydnones and related compounds. Reference may be made to two recent reviews, "Non-benzenoid Aromatic Compounds"⁸ and "The Development of the Concept of Aromaticity"⁹ where these matters are dealt with in much greater detail.

⁷ Katritzky, *Chem. and Ind.*, 1955, 521.

⁸ Baker and McOmie, "Progress in Organic Chemistry", ed. J. W. Cook, Butterworths, London, 1955, Vol. III, pp. 44-80.

⁹ Baker, "Perspectives in Organic Chemistry", ed. Sir A. Todd, Interscience Publ., 1956, pp. 28-67.

For *N*-phenylsydnone, as a typical representative of the class, it will be seen that before delocalisation there is a total of seven $2p_z$ electrons supplied by the atoms which make up the five-membered ring and one more such electron is available on the exocyclic oxygen atom; the origins of these electrons are shown in formula (5) by the positions of the numerals representing their numbers. The lone pairs of electrons which are accommodated in orbitals unsuitable for overlap, and which therefore are not involved in the delocalisation process, are also shown. A sextet of π electrons may now be acquired in association with the ring if one of the seven electrons initially supplied by the five annular atoms is paired with the single electron provided by the exocyclic oxygen atom. The result is that the sydnone ring becomes both positively charged and aromatic.



The situation is very similar to that occurring in tropone¹⁰ which has been represented both by the covalent structure (6) and by the polar structure (7) with its sextet of π electrons in association with a positive charge, the sextet being represented by the large inscribed circle. This symbolism, which is now widely accepted, was first used by Doering and Knox.¹¹ Formulæ (6) and (7) are both acceptable, and for this reason tropone and its derivatives are not regarded as meso-ionic, and the definition given later does not include such compounds.* It is to be noted that formula (7) does not imply that a complete negative charge is resident upon the exocyclic oxygen atom. It does, however, emphasise the aromatic, weakly ketonic, and dipolar nature of tropone, which has a considerably higher boiling point than its isomer benzaldehyde and is miscible with water.

The sydnes may similarly be very satisfactorily represented by the structural formula (8) and they may be regarded as five-membered heterocyclic analogues of tropone. The large inscribed circle represents the six π electrons occupying molecular orbitals associated with all the annular atoms, though this association will certainly be unequal; it follows that the positive charge must also be regarded as unevenly distributed, though it is probably mainly associated with the nitrogen atom to which the phenyl group is attached. Two points must be especially emphasised. First, that

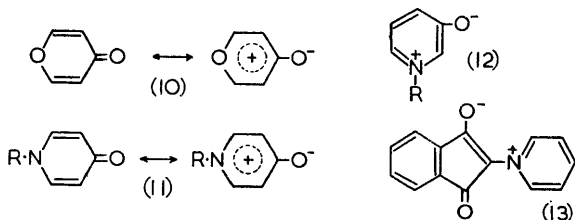
¹⁰ Pauson, *Chem. Rev.*, 1955, **55**, 9.

¹¹ Doering and Knox, *J. Amer. Chem. Soc.*, 1952, **74**, 5686.

* In the *Annual Reports on the Progress of Chemistry* (1955, **52**, 233) it is stated that the term meso-ionic should be applicable to tropone and to the betaine (12) (p. 19). In its context the statement seems to imply that this represents our view, but we have definitely stated that we are of the opposite opinion.³¹ We are informed by the Reporter, Dr. W. Wilson, that the statement in the *Annual Reports* represented solely his own view.

no covalent structure for the sydnones can be written corresponding to the covalent structure (6) for tropone, and secondly, that the use of formula (8) for the sydnones and formula (7) for tropone does *not* imply that unit positive and negative charges are associated with the ring structures and the exocyclic oxygen atoms respectively. The Reviewers prefer to use the simple formula (8) for the sydnones with the mental reservation that the charges are something less than unit charges, *i.e.*, the molecule will assume a state of compromise between the opposing tendencies towards the completely polar aromatic form and towards the neutralisation of the opposite charges. Organic chemists are well used to such reservations in interpreting, for example, the Kekulé structures for benzene, or the covalent structures usually written for the amides or the cyanides. The only difference between the proposals now put forward and those of Bieber^{3m} is that the latter prefers to incorporate these reservations in the formula for the sydnones by means of a special symbol as shown in (9), which, although fairly self-evident, needs to be explained; the lone pairs of electrons are shown by short lines.

The representation of *N*-phenylsydnone by formula (8) stresses its aromatic character and its close similarity to γ -pyrone (10) and to the γ -pyridone (11). At first sight it may apparently be also very closely related to the betaine (12), but it is not intended that such a compound should be regarded as meso-ionic, because it almost certainly possesses a high degree of charge fixation, and it may be *satisfactorily* represented by the dipolar structure (12).* Similarly, the "enol-betaines" such as (13) are not to be regarded as meso-ionic, although this description has been given to them.^{1,2}



Examples of the various known types of compound which are regarded as meso-ionic are described later, and a definition of the word in as precise terms as possible must be attempted. In its very nature it is as difficult to define as the word "aromatic", in view of the varying degrees of aromaticity which are found in passing from benzene at one end of the scale to, say, furan towards the other end. Probably the best definition of an aromatic compound is that given by Dewar¹³ who states that "an aromatic compound may be defined as a cyclic compound with a large resonance energy where all the annular atoms take part in a single conjugated system".

¹² Stafford, *J.*, 1952, 581.

¹³ Dewar, "The Electronic Theory of Organic Chemistry", Oxford, 1949, p. 160.

* See footnote, p. 18.

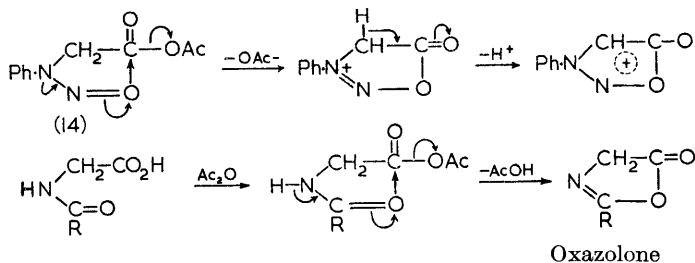
The necessarily vague phrase here is "with a large resonance energy", and no attempt to define the value of "large" in kcal. per mole would be acceptable.

It is now suggested that a compound may appropriately be called meso-ionic if it is a five- or possibly a six-membered heterocyclic compound which cannot be represented *satisfactorily* by any one co-valent or polar structure and possesses a sextet of electrons in association with all the atoms comprising the ring. The ring bears a fractional positive charge, balanced by a corresponding negative charge located on a covalently attached atom or group of atoms. The inevitable ambiguity here is the word "satisfactorily", and chemists are not likely always to agree on what may or may not be a satisfactory constitutional formula for a given compound. Indeed different formulæ may rightly be used on different occasions for the same compound according to the structural feature which it is desired to emphasise, *e.g.*, the two representations of tropone (6) and (7) have already been mentioned. As a corollary to the definition it follows that in any particular polar structure which may be written for a meso-ionic compound the charges cannot wholly neutralise one another to give a covalent structure.

The meso-ionic compounds described in this Review are all five-membered heterocyclic compounds. Although six-membered meso-ionic compounds might conceivably exist, none has as yet been definitely prepared.

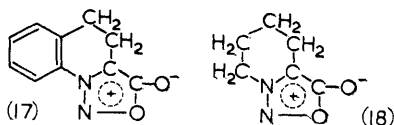
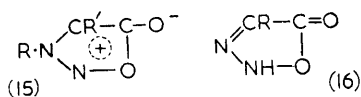
The Chemistry and Physical Properties of the Sydnones

The mechanism of the formation of *N*-phenylsydnone by the action of acetic anhydride on *N*-nitroso-*N*-phenylglycine was studied by Baker, Ollis, and Poole^{3b} who showed that the mixed anhydride (14) behaves as a true intermediate. The pure mixed anhydride was prepared by reaction of the potassium salt of *N*-nitroso-*N*-phenylglycine with acetyl chloride, and when kept for a few days at room temperature, or more rapidly when



heated in benzene solution, it was transformed into *N*-phenylsydnone. The reaction sequence may be represented as annexed, and it will be seen that it is very closely analogous to the formation of oxazolones by dehydration of α -acylamino-acids. This mechanism is also compatible with the observation that *N*-nitroso-*N*-phenylglycine yields *N*-phenylsydnone when treated either with thionyl chloride, or with trifluoroacetic anhydride which is

known to form mixed anhydrides with carboxylic acids;¹⁴ the second reaction proceeds instantaneously in ethereal solution at -5° in 93% yield. Many sydnones (15) are now known in which R may be an alkyl or aryl group [R cannot be a hydrogen atom otherwise rearrangement to the oxadiazoles (16) would be possible] and R' may be hydrogen or an alkyl or an aryl group. The existence of stable *N*-alkylsydnones such as *N*-methyl-, *N*-*n*-butyl-, *N*-cyclohexyl-, and *N*-benzyl-sydnones demonstrates that conjugation of the sydnone ring with another aromatic system is not essential. Compounds, *e.g.*, (17) and (18) in which the sydnone ring forms part of a polycyclic system have also been prepared.¹⁵ *N*-3'-Pyridylsydnone (15; R = 3-pyridyl, R' = H) is normally colourless, but exposure to sunlight causes an almost instantaneous phototropic change to a deep blue modification which slowly reverts to the colourless form.¹⁶



The sydnones are stable, and highly crystalline with the exception of a few *N*-alkyl sydnones,¹⁶ and most of them are fairly soluble in benzene. *N*-Phenylsydnone has m.p. 135° and sublimes unchanged at $110^{\circ}/1$ mm.; *N*-cyclohexylsydnone has m.p. 64° , and *N*-methylsydnone has m.p. 36° . Their lactonic character is revealed by reaction with various nucleophilic reagents, but they are much more stable than normal γ -lactones. Thus, *N*-phenylsydnone may be crystallised unchanged from boiling water, but is hydrolysed when heated with aqueous sodium hydroxide; it reacts with hot benzylamine, yielding the benzylamide of *N*-nitroso-*N*-phenylglycine, $\text{Ph}\cdot\text{N}(\text{NO})\cdot\text{CH}_2\cdot\text{CO}\cdot\text{NH}\cdot\text{CH}_2\cdot\text{Ph}$, but it is unaffected by aniline at 125° .³⁴

The sydnones undergo an interesting reaction when heated with aqueous acid, giving an alkyl- or aryl-hydrazine, a carboxylic acid, and carbon dioxide.^{1, 2} Compounds (17) and (18) cannot hydrolyse in this way; (17) gives carbon dioxide and 1-amino-1:2:3:4-tetrahydro-2-oxoquinoline.¹⁵ The probable mechanism of acid hydrolysis is shown below, and is supported by the interesting observation that a benzene solution of *N*-phenylsydnone reacts rapidly with one molecular proportion of water and hydrogen chloride or bromide in ether, giving *N*-formyl-*N*-phenylhydrazine and carbon dioxide. This is the easiest route to α -acylhydrazines.¹⁷

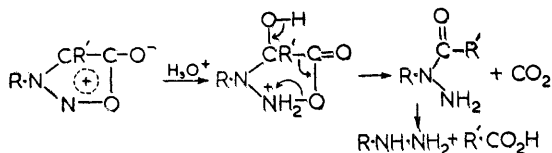
N-Phenylsydnone reacts rapidly with chlorine or bromine to give monohalogen derivatives, and the same bromo-derivative is obtained by reaction

¹⁴ Bourne, Stacey, Tatlow, and Tedder, *J.*, 1949, 2976.

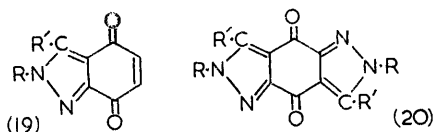
¹⁵ Hammick, Roe, and Voaden, *Chem. and Ind.*, 1954, 251.

¹⁶ Fugger, Tien, and Hunsberger, *J. Amer. Chem. Soc.*, 1955, **77**, 1843; Tien and Hunsberger, *ibid.*, p. 6604.

¹⁷ Kenner and Mackay, *Nature*, 1947, **160**, 465.

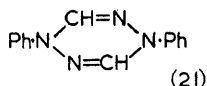


with *N*-bromosuccinimide in chloroform. In these reactions the hydrogen atom directly attached to the sydnone ring is replaced, and no substitution in the phenyl group is observed. It is also possible to nitrate *N*-phenylsydnone in concentrated sulphuric acid at -10° , to give *C*-nitro-*N*-phenylsydnone.³² These reactions demonstrate the aromatic character of the sydnone ring. The nucleophilic reactivity of sydneses is also involved in their recently discovered reaction with 1 : 4-quinones, giving the complex heterocyclic quinones (19) and (20) and carbon dioxide.¹⁸



The stability of the sydnone nucleus is clearly demonstrated by the observation that *N*-phenylsydnone resists catalytic hydrogenation except in presence of highly active catalysts. It may be slowly reduced to the ammonium salt of *N*-phenylglycine with hydrogen and Adams's platinum oxide catalyst.³⁹

In an attempt to prepare a thiosydnone, *N*-phenylsydnone was treated with phosphorus pentasulphide, but the product proved unexpectedly to be 1 : 4-diphenyl-1 : 4-dihydrotetrazine (21).¹⁹



Further evidence in support of the aromatic meso-ionic structure for the sydneses is provided by the ultraviolet absorption spectra of *N*-cyclohexyl- and *N*-benzyl sydneses which both show a well-defined absorption band at $292 \mu\mu$.^{39, 20} The position and the intensity of this band are characteristic of an aromatic system and, when further conjugation of the sydnone ring is possible, as in *N*-phenyl- or *NC*-diphenylsydnone, the expected shift to longer wavelength is observed. No detailed study of the infrared spectra of sydneses has been reported, but the published results^{16, 21} show that the position and nature of the sydnone carbonyl absorption vary considerably with the structure of the sydnone and in some cases a double band in the carbonyl region is observed. The position of the carbonyl

¹⁸ Hammick and Voaden, *Chem. and Ind.*, 1956, 739.

¹⁹ Baker, Ollis, and Poole, *J.*, 1950, 3389.

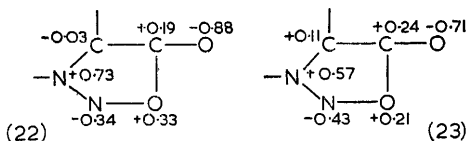
²⁰ Earl, Le Fèvre, and Wilson, *J.*, 1949, S 103.

²¹ Earl, Le Fèvre, Pulford, and Walsh, *J.*, 1951, 2207.

band varies over the range 1720—1770 cm.^{-1} , but the interpretation of this in terms of the degree of double-bond character is not possible because of the unique structural nature of the sydnones. It is however incompatible with the bicyclic structure (2), as the β -lactonic carbonyl absorption is at 1818 cm.^{-1} for β -butyrolactone.²²

Of the various physical methods which are now available for the examination of organic compounds, it was recognised at an early stage that the measurement of their dipole moments was likely to be the most revealing. An interpretation of the dipole moments of a large number of sydnones has been made by Hill and Sutton²³; cf. ^{3a} and by Earl, Leake, and Le Fèvre.^{3e, 24} *N-cyclo*Hexylsydnone, which is non-polar except for the sydnone nucleus, has a moderately large dipole moment of 6.7 D in benzene. A comparison of the dipole moments of *N*-phenyl- (6.48 D), *N-p*-chlorophenyl- (5.01 D), and *N-p*-tolylsydnone (6.89 D) with those of chlorobenzene (1.55 D) and toluene (0.4 D) shows that the dipole of the sydnone structure has its negative pole directed towards the carbonyl-oxygen atom. Further analysis showed that the five-membered ring was almost certainly flat, and this coupled with the magnitude and direction of the sydnone group moment provided strong support for their formulation as meso-ionic compounds.

This very satisfactory agreement made a more quantitative theoretical treatment of the sydnones very desirable. This was done and the formal charge distribution on the various atoms of the sydnone ring was calculated by the molecular-orbital method. The results obtained by Hill, Sutton, and Longuet-Higgins²⁵ are summarised in formula (22) and, after some refinement, the results given in formula (23) were obtained by Orgel, Cottrell, Dick, and Sutton.²⁶ Both calculations show that the ring bears an aggregate



positive charge of the order 0.7—0.9 balanced by a negative charge on the exocyclic oxygen atom. These calculations indicate that there is a substantial charge transfer from the sydnone ring and that the bonding of the carbonyl group has quite a high degree of single-bond character (the two values given for the calculated π bond order are 0.37 and 0.59). This is in complete agreement with the meso-ionic structure. It is important to recognise that a meso-ionic compound does not necessarily possess a large dipole moment,²⁷ and that such a moment is not necessarily indicative of a meso-ionic structure.

²² Taufen and Murray, *J. Amer. Chem. Soc.*, 1945, **67**, 754.

²³ Hill and Sutton, *J.*, 1949, 746; 1953, 1482.

²⁴ Earl, Leake, and Le Fèvre, *J.*, 1948, 2269.

²⁵ Hill, Sutton, and Longuet-Higgins, *J. Chim. phys.*, 1949, **46**, 244.

²⁶ Orgel, Cottrell, Dick, and Sutton, *Trans. Faraday Soc.*, 1951, **47**, 113.

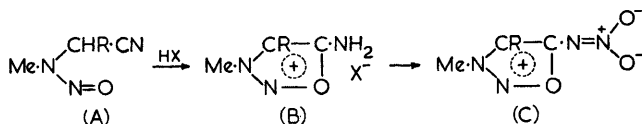
²⁷ Kaufmann, Ernsberger, and McEwan, *ibid.*, 1956, **78**, 4197.

Katritzky⁷ has recommended that if a systematic name for the sydnones is required the nomenclature for betaines should be employed. Thus, *N*-phenylsydnone becomes anhydro-5-hydroxy-3-phenyl-1-oxa-2:3-diazolinium hydroxide.

Survey of Known Meso-ionic Compounds

As expected, heterocyclic compounds with structures analogous to those of the sydnones can exist, and in fact many such compounds are known, but when they were first described they were often given either bridged-ring or other stereochemically impossible *endo*-types of structure. Since the generality of the meso-ionic type of structure was first recognised, several new examples have been discovered. In this survey of meso-ionic compounds it has been felt desirable to classify them by the trivial names under which many of them were first described, but if necessary the betaine nomenclature could be applied.

Sydnone Imines.—Brookes and Walker* have found that various *N*-methylamino-*N*-nitroso-acetonitriles (A) react with acids to give salts (B) of sydnone imines. Thus the hydrochloride (B; X = Cl) is precipitated in high yield when the nitrosamine (A) is treated with ethereal hydrogen chloride, and the nitrate (B; X = NO₃) is similarly formed when an equimolecular proportion of concentrated nitric acid is used. This nitrate is dehydrated by acetic anhydride or concentrated sulphuric acid to the meso-ionic compound (C) in which the exocyclic electron-accepting group is nitramine.



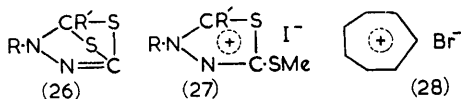
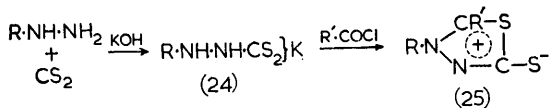
Under very mildly basic conditions, the salts (B) do not yield either free sydnone imines or the sydnones, but undergo hydrolysis to the open-chain nitroso-amides, Me·N(NO)·CHR·CO·NH₂.

"*Endo-thiodihydrothiodiazoles*."—These compounds were first prepared in 1895 by Busch and his co-workers²⁸ who gave them the *endo*-structure (26), but in 1938 it was suggested by Schönberg⁵ that they should be represented by a hybrid structure involving charged forms. It is now clear that they are best represented by the meso-ionic structure (25). They were prepared by Busch by reaction of an acid chloride with the potassium salt of an *N*-aryl-*N'*-dithiocarboxyhydrazine (24); for the synthesis of compounds unsubstituted in position 5 (*i.e.*, 25 where R' = H), the potassium salts are treated with ethyl formimidate hydrochloride or more conveniently with sodium dithioformate in aqueous solution.²⁹

²⁸ Busch and co-workers, *Ber.*, 1895, **28**, 2635; *J. prakt. Chem.*, 1899, **60**, 218, 228; 1903, **67**, 201, 216, 246, 257.

²⁹ Baker, Ollis, Phillips, and Strawford, *J.*, 1951, 289.

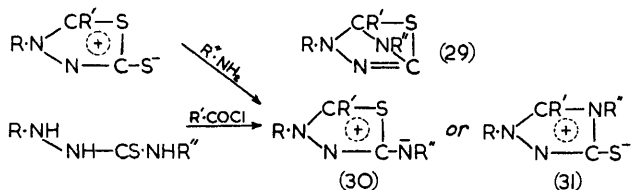
* P. Brookes and J. Walker (unpublished work), to whom we are indebted for this re-publication information.



These thiadiazoles (25) are bright yellow stable compounds with high melting points, and they are sparingly soluble in the usual organic solvents. They cannot be dethionated with mercuric oxide even in boiling benzene, and they react exothermally with methyl iodide to give products which were first given covalent structures, but it is obvious from a consideration of their physical properties that they are salts (27); they behave as strong binary electrolytes in aqueous or alcoholic solution. The structural relation between these salts (27) and tropylium bromide (28) is very close in that in neither case does the covalent form exist, owing to the stability of the cation with its associated six π electrons.

The meso-ionic character of the "endo-thiodihydrothiadiazoles" is shown by their large dipole moments; the diphenyl compound (25; R = R' = Ph) has a dipole moment ⁶ of 8.8 D. The dipole moments of several members of this series have been measured by Edgerley and Sutton ³⁰ and, from the dipole moments of the *N*-phenyl (25; R = Ph, R' = H), *N*-*p*-chlorophenyl (25; R = *p*-Cl-C₆H₄, R' = H), and *N*-*p*-tolyl (25; R = *p*-Me-C₆H₄, R' = H) derivatives which are 8.36, 7.09, and 8.70 D respectively, it is clear that there is a high degree of charge transfer from the five-membered ring to the exocyclic sulphur atom.

"*Endo-thiotriazolines*."—The "endo-thiodihydrothiadiazoles" react with primary amines giving substances which were originally formulated as in (29).²⁸ It is now clear that they are meso-ionic compounds for which two isomeric structures are possible, (30) or (31). These compounds may also be formed from acid chlorides and 1:4-diarylthiosemicarbazides, and the tendency to form the aromatic system is so great that they are even formed from benzaldehyde and 1:4-diarylthiosemicarbazides.

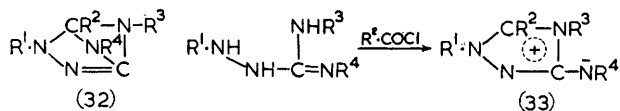


The dipole moment ⁶ of the compound (30 or 31; R = R'' = Ph, R' = Me) is 8.4 D.

"*Endo-imino- and Endoxy-triazolines*."—These compounds, prepared

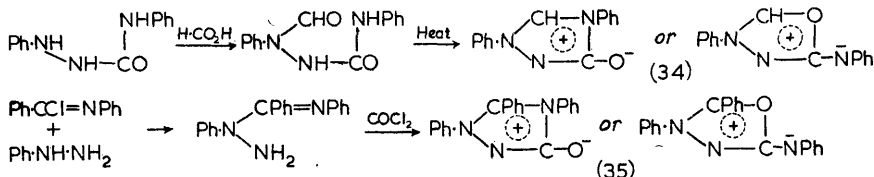
³⁰ Edgerley and Sutton, personal communication.

from substituted guanidines and acid chlorides (or where $R^2 = H$ by using formic acid), were originally given the structure (32), but this must now be replaced by the meso-ionic formula (33).³¹

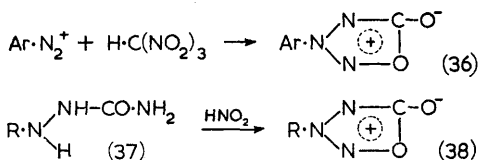


These compounds are yellow basic substances whose nitrates are usually very insoluble in water. The nitric acid precipitant "nitron" (dipole moment³² 7.2 D) is the triphenyl derivative (33) ($R^1 = R^3 = R^4 = Ph$, $R^2 = H$), and it was recognised by Schönberg⁵ as having a hybrid structure. It was originally given the "endo-imino" structure (32), and is unfortunately still usually given this sterically impossible formula.

"Endoxytriazolines" (34) and (35) have been prepared by Busch and his co-workers³³ by the annexed routes.



The 3-aryloxatriazoles (36) may be prepared by treating nitroform with diazonium salts,³⁴ and recently it has been shown³⁵ that *N*-alkylsemicarbazides (37) and nitrous acid give the 3-alkyloxatriazoles (38). 3-Aryloxatriazoles cannot be prepared by the latter reaction because the intermediate *N*-aryl-*N*-nitrososemicarbazides undergo loss of nitroxyl, giving the arylazocarbamides.³⁶



"Tetrazoles."—Methylation of 5-amino-2-methyltetrazole with methyl benzenesulphonate yields a monomethyl derivative which has the meso-ionic structure (39).³⁷; cf. 27 The hydrochloride and hydrobromide of the

³¹ Busch *et al.*, *Ber.*, 1905, **38**, 856, 4049; *J. prakt. Chem.*, 1906, **74**, 501, 533.

³² Warren, *J.*, 1938, 1100.

³³ Busch *et al.*, *J. prakt. Chem.*, 1903, **67**, 263; *Ber.*, 1910, **43**, 3008.

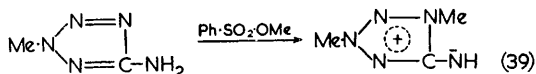
³⁴ Ponzio, *Gazzetta*, 1933, **63**, 471.

³⁵ Boyer and Canter, *J. Amer. Chem. Soc.*, 1955, **77**, 1280.

³⁶ Widman, *Ber.*, 1895, **28**, 1925.

³⁷ Brydon, Henry, Finnegan, Boschan, McEwan, and Van Dolah, *J. Amer. Chem. Soc.*, 1953, **75**, 4863; Henry, Finnegan, and Lieber, *ibid.*, 1954, **76**, 2894.

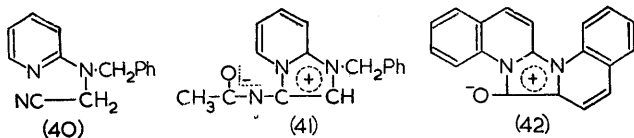
tetrazole (39) are isomorphous and it was possible to carry out an X-ray analysis of the compound without making any previous assumptions con-



cerning its structure. The preliminary results show that the five-membered ring is planar and is definitely not bridged. Normal tetrazoles show only end absorption in the ultraviolet region, but this hydrochloride shows aromatic-type absorption (λ_{max} . 254 m μ , $\epsilon = 2600$ in H₂O).

Polycyclic Meso-ionic Compounds

Several compounds are known in which a meso-ionic ring forms part of a polycyclic aromatic system. For example, the nitrile (40) when treated with acetic anhydride gives a monoacetyl derivative which is basic and no longer contains a C \equiv N group (infrared spectrum); it regenerates the nitrile on mild hydrolysis and forms a methiodide. A meso-ionic structure was proposed for this compound,³⁸ and it may now be represented by formula (41). In the methiodide the methyl group is attached to the exocyclic nitrogen atom, because hydrolysis with dilute sulphuric acid gives methylamine.



Similar meso-ionic compounds in which the benzyl group is replaced by phenyl, ethyl, or various heterocyclic groups have been prepared. The acylation may also be effected by benzoyl chloride or benzenesulphonyl chloride to give the corresponding N-acyl derivatives.

The compound (41) has a structure which is analogous to those discussed previously. Thus the atoms comprising the two rings of the bicyclic structure (41) have, before delocalisation, eleven electrons in their $2p_z$ orbitals, so that the establishment of an aromatic system involving ten electrons (cf. naphthalene) requires the displacement of one of these electrons to the exocyclic acylamide grouping, giving the structure (41).

It has also been suggested that the pigment Besthorn's Red has the meso-ionic structure (42).^{37, 39}

Substances no longer regarded as Meso-ionic

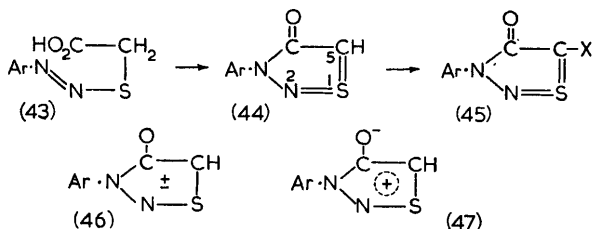
In a few cases the meso-ionic structures which have been proposed for certain compounds have been replaced by others. The (arylazothio)acetic

³⁸ Bristow, Charlton, Peak, and Short, *J.*, 1954, 4748.

³⁹ Krollpfeiffer and Schneider, *Annalen*, 1937, 530, 34; Hammick and Brown, *Nature*, 1949, 164, 831.

acids (43) give anhydro-compounds when treated with acetic anhydride and pyridine. These anhydro-compounds are weak bases, stable to mineral acids, and they react with electrophilic reagents in position 5. Thus direct bromination and nitration give the derivatives (45; X = Br and NO₂), and arylation with diazonium salts in neutral or alkaline solution gives the 5-aryl derivatives.

Originally these anhydro-compounds were regarded as hybrids derived from ionic forms,⁴⁰ and were represented by a structure (46) which according to the current proposals for meso-ionic compounds would be formulated as in formula (47). Recently it has been suggested⁴¹ that their formulation as (47) is unsatisfactory because they are soluble in non-polar solvents and react with electrophilic reagents in position 5. This observation we believe to be incorrect. Many meso-ionic compounds have large dipole moments and yet are quite readily soluble in benzene. Moreover, reaction with electrophilic reagents does not require "a degree of negativity on the 5 carbon atom" as suggested, but it does demonstrate that the negative charge associated with the exocyclic oxygen atom can in fact be made available in this position to permit the generation of a transition state suitable for substitution by electrophilic reagents. However, there is another consideration which presumably excludes these compounds from being represented as meso-ionic. If *dsp*² hybridisation of the sulphur atom occurs in these compounds⁴² they may perhaps be regarded as satisfactorily represented by the covalent structures (44) and (45) and accordingly they would not be termed meso-ionic. It is recognised, however, that this exclusion is somewhat artificial because the substances are very closely related to the sydnones, in that the annular atoms in formulæ (44) and (45) have seven 2*p*_z electrons and a sextet may be formed by electron-transfer to the oxygen atom.



Statements which have appeared in the literature make it necessary to point out that the electron distribution in a molecule cannot be determined unequivocally by a study of its chemical reactions. Physical measurements are far more reliable.

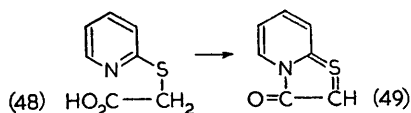
Dehydration of (2-pyridylthio)acetic acid (48) with acetic anhydride

⁴⁰ Kendall and Duffin, Congress Handbook, XIVth Internat. Congr. Pure Appl. Chem., 1955, p. 320.

⁴¹ Duffin and Kendall, *J.*, 1956, 3189.

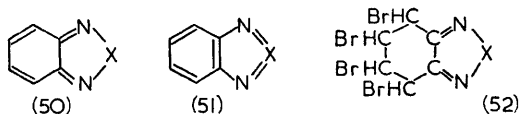
⁴² Longuet-Higgins, *Trans. Faraday Soc.*, 1949, **45**, 173; Craig, Maccoll, Nyholm, Orgel, and Sutton, *J.*, 1954, 333.

gives a substance first formulated as a thiophen and later as a keten. A detailed investigation by Duffin and Kendall⁴³ showed that it was a bicyclic compound which they first represented as a hybrid molecule derived from a number of dipolar forms, but later they preferred to represent it by formula (49). The structure is very similar to that of the anhydro-derivatives of the (arylazothio)acetic acids, so that their representation by the covalent structure (49) instead of as a meso-ionic compound may be justified, although it should be emphasised that it is very closely similar to the anhydro-derivatives (41), as is shown by their aromatic character.



These substances are yellow and their ultraviolet spectra have been investigated by Knott.⁴⁴ They are fairly stable, but hydrolysis with 50% aqueous sulphuric acid yields the parent acid.

Previously it has been suggested that the compounds benzofurazan (50; X = O), piazthiole (50; X = S), and piaselehole (50; X = Se) should be regarded as having partially meso-ionic structures.^{3a} We are now of the opinion, however, that this is undesirable because the *o*-quinonoid structures (50) are quite suitable for them. For piazthiole and piaselehole too, formula (51), involving the higher valency states of sulphur and selenium, can also be used. On the other hand, the *o*-quinonoid structures (50) may be considered adequate for all these compounds because they react additively⁴⁵ with bromine to give tetrabromides (52).



⁴³ Duffin and Kendall, *J.*, 1951, 734; 1956, 361.

⁴⁴ Knott, *J.*, 1955, 918.

⁴⁵ Hammick, Edwardes, and Steiner, *J.*, 1931, 3308; Calcott-James, De Witt, and Ollis, unpublished results.