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MESO-IONIC HETEROCYCLES (1976–1980)

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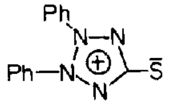
I. INTRODUCTION

It is one hundred years since Emil Fischer and Emil Besthorn described the preparation of dehydrodithizone (**1**) and thus provided the first example of a meso-ionic compound.[1] This initial contribution was soon followed by the pioneering work of Max Busch who, during the period 1895–1905, described the preparation and chemical properties of a number of meso-ionic heterocycles (e.g. **2–5**).[2] Later, three important further developments paved the way for extensive investigations which were to follow: (i) Earl and Mackney (1935) prepared *N*-phenylsydnone (**6**; R=Ph) by cyclodehydration of *N*-nitroso *N*-phenylglycine;[3] (ii) Schonberg (1938) recognised that the derivatives (**2**) and (**5**), which had been formulated as bicyclic compounds by Busch, were resonance hybrids of several dipolar canonical forms;[4] (iii) Baker and Ollis (1946) demonstrated that the sydnones (**6**) belong to a large family of heterocycles which includes the derivatives (**2–5**) and which they described as meso-ionic (*meso*meric + *ionic*).[2] The possible existence of other meso-ionic compounds was predicted by Baker and Ollis and subsequently many new systems have been prepared. Pre-eminent among these are the munchnones (**7**) whose preparation and cycloaddition reactions have been described by Huisgen (1964).[5] The recognition that the munchones (**7**) react as 1, 3-dipoles soon led to the investigation of other meso-ionic systems and was largely responsible for the extensive studies of meso-ionic compounds which have been reported over the last two decades.

The chemistry of meso-ionic compounds was comprehensively reviewed by Ollis and Ramsden in 1976.[6] In the period 1976–1981 considerable progress has been made in this area of chemistry. The purpose of this Report is primarily to up-date the earlier review while the number of references is still manageable. The literature up to the end of 1980 has been covered.



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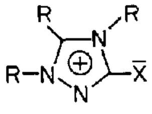
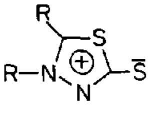


2 X=NR
3 X=O
4 X=S



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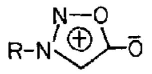

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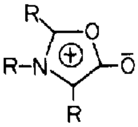

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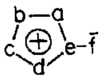
II. MESO-IONIC COMPOUNDS OF TYPES A AND B

The definition of the term meso-ionic and the possible types of meso-ionic compounds have been discussed in detail elsewhere.[6] Although the original definition of the term meso-ionic recognised that some 6-membered rings could be described as meso-ionic, more recently it has been recommended that the name should be restricted to 5-membered rings. The following modified definition has been proposed:

"*a compound may be appropriately called meso-ionic if it is a five-membered heterocycle which cannot be represented satisfactorily by any one covalent or polar structure and possesses a sextet of electrons in association with the five atoms comprising the ring*".[6]

In accord with this definition meso-ionic compounds are represented by formulae of the general type (**8**) where a–f are atoms or groups derived from carbon or heteroatoms.



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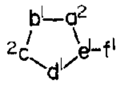

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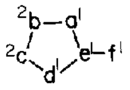

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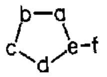

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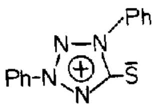

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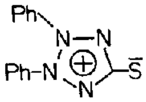

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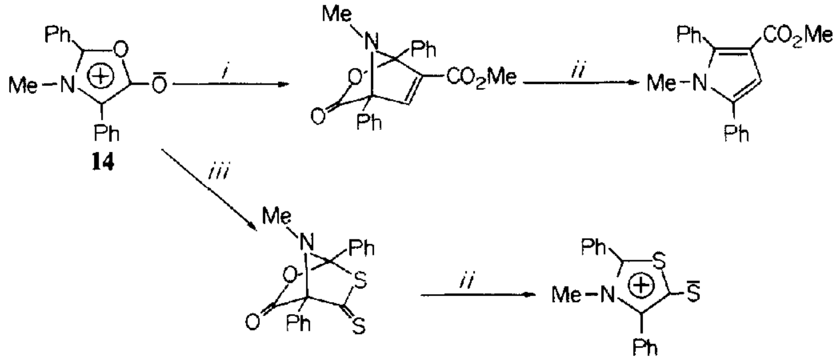
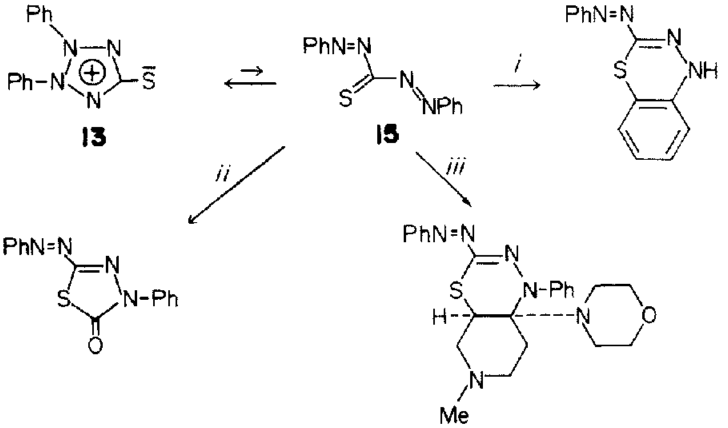
The different types of heterocycle having the σ-skeleton (**11**) have been discussed by Ollis and Ramsden.[6] Analysis of these possible systems shows that there are two types of meso-ionic heterocycle having structures (**9**) or (**10**), where the superscripts indicate the origin of the eight π-electrons. These meso-ionic systems are referred to as type A (**9**) or type B (**10**). The 1, 2, 3, 4-tetrazolium-5-thiolate (**12**) is an example of a type A meso-ionic system whereas the isomeric dehydrodithizone (**13**) belongs to type B. The two general types of meso-ionic compound show quite distinct chemical properties.

A major aspect of the chemistry of type A meso-ionic compounds is their participation in 1, 3-dipolar cycloaddition reactions. Scheme 1 shows two examples of typical cycloaddition reactions of 2, 4-diphenyl-3-methyl-1, 3-oxazolium-5-olate (**14**).[5]



Reagents: i, $HC\equiv C.CO_2Me$; ii, spontaneous elimination of CO_2; iii, CS_2
Scheme 1.

The chemical properties of type B meso-ionic compounds are quite different to those of type A. An important feature of type B meso-ionic heterocycles is their facile ring opening to give acyclic valence tautomers. For example, many of the reactions of dehydrodithizone (**13**) are consistent with a mechanism in which valence tautomerism (**13**→**15**; Scheme 2) precedes reaction.[6]



Reagents: i, hot $MeCO_2H$; ii, $Fe_2(CO)_{10}$; iii, 1,2,5,6-tetrahydro-1-methyl-4-morpholinopyridine
Scheme 2.

III. THE CHEMISTRY OF MESO-IONIC COMPOUNDS OF TYPE A (1976–1980)

These systems are discussed in the order given in Table 1. Since the review by Ollis and Ramsden in 1976,[6] derivatives of 12 new type A meso-ionic systems have been reported bringing the total number of known systems up to 60.

Table 1. Known meso-ionic heterocycles of type A(**9**)

Parent System	Heterocycle	Atom or group[a]					
		a	b	c	d	e	f
Dioxoles							
1,3-Dioxolium-4-olates	(**16**)	O	CR	O	CR	C	O
Oxazoles							
1,3-Oxazolium-4-olates	(**19**)	NR	CR	O	CR	C	O
1,3-Oxazolium-4-aminides	(**28**)	NR	CR	O	CR	C	NR
1,3-Oxazolium-5-olates	(**29**)	O	CR	NR	CR	C	O
1,3-Oxazolium-5-aminides	(**53**)	O	CR	NR	CR	C	NR
Oxathioles							
1,3-Oxathiolium-4-olates	(**62**)	S	CR	O	CR	C	O
1,3-Oxathiolium-5-olates	(**67**)	O	CR	S	CR	C	O
Diazoles							
1,3-Diazolium-4-olates	(**70**)	NR	CR	NR	CR	C	O
1,3-Diazolium-4-aminides	(**78**)	NR	CR	NR	CR	C	NR
1,3-Diazolium-4-thiolates	(**80**)	NR	CR	NR	CR	C	S
1,3-Diazolium-4-methylides	(**88**)	NR	CR	NR	CR	C	CXY

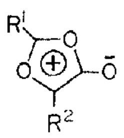
Table 1 (*Contd*)

Parent System	Heterocycle	Atom or group[a] a	b	c	d	e	f
Thiazoles							
1,3-Thiazolium-4-olates	**(90)**	NR	CR	S	CR	C	O
1,3-Thiazolium-4-aminides	**(114)**	NR	CR	S	CR	C	NR
1,3-Thiazolium-5-olates	**(115)**	S	CR	NR	CR	C	O
1,3-Thiazolium-5-aminides	**(127)**	S	CR	NR	CR	C	NR
1,3-Thiazolium-5-thiolates	**(128)**	S	CR	NR	CR	C	S
Selenazoles							
1,3-Selenazolium-4-olates	**(134)**	NR	CR	Se	CR	C	O
Dithioles							
1,3-Dithiolium-4-olates	**(140)**	S	CR	S	CR	C	O
1,3-Dithiolium-4-aminides	**(146)**	S	CR	S	CR	C	NR
Oxadiazoles							
1,2,3-Oxadiazolium-5-olates	**(149)**	O	N	NR	CR	C	O
1,2,3-Oxadiazolium-5-aminides	**(175)**	O	N	NR	CR	C	NR
1,2,3-Oxadiazolium-5-thiolates	**(178)**	O	N	NR	CR	C	S
1,3,4-Oxadiazolium-2-olates	**(181)**	O	CR	NR	N	C	O
1,3,4-Oxadiazolium-2-aminides	**(187)**	O	CR	NR	N	C	NR
1,3,4-Oxadiazolium-2-thiolates	**(190)**	O	CR	NR	N	C	S
1,3,4-Oxadiazolium-2-methylides	**(193)**	O	CR	NR	N	C	CXY
Oxathiazoles							
1,3,2-Oxathiazolium-5-olates	**(195)**	O	N	S	CR	C	O
Triazoles							
1,2,3-Triazolium-4-olates	**(202)**	NR	N	NR	CR	C	O
1,2,3-Triazolium-4-aminides	**(205)**	NR	N	NR	CR	C	NR
1,2,3-Triazolium-4-thiolates	**(206)**	NR	N	NR	CR	C	S
1,2,4-Triazolium-3-olates	**(207)**	NR	CR	NR	N	C	O
1,2,4-Triazolium-3-aminides	**(219)**	NR	CR	NR	N	C	NR
1,2,4-Triazolium-3-thiolates	**(220)**	NR	CR	NR	N	C	S
1,2,4-Triazolium-3-methylides	**(226)**	NR	CR	NR	N	C	CXY
1,2,4-Triazolium-3-selenolates	**(227)**	NR	CR	NR	N	C	Se
Thiadiazoles							
1,2,3-Thiadiazolium-4-olates	**(230)**	NR	N	S	CR	C	O
1,2,3-Thiadiazolium-5-olates	**(231)**	S	N	NR	CR	C	O
1,2,3-Thiadiazolium-5-aminides	**(233)**	S	N	NR	CR	C	NR
1,2,3-Thiadiazolium-5-thiolates	**(237)**	S	N	BR	CR	C	S
1,2,3-Thiadiazolium-5-methylides	**(240)**	S	N	NR	CR	C	CXY
1,2,4-Thiadiazolium-3-olates	**(241)**	NR	CR	S	N	C	O
1,2,4-Thiadiazolium-3-aminides	**(245)**	NR	CR	S	N	C	NR
1,3,4-Thiadiazolium-2-olates	**(247)**	S	CR	NR	N	C	O
1,3,4-Thiadiazolium-2-aminides	**(252)**	S	CR	NR	N	C	NR
1,3,4-Thiadiazolium-2-thiolates	**(254)**	S	CR	NR	N	C	S
1,3,4-Thiadiazolium-2-methylides	**(257)**	S	CR	NR	N	C	CXY
Oxatriazoles							
1,2,3,4-Oxatriazolium-5-olates	**(258)**	O	N	NR	N	C	O
1,2,3,4-Oxatriazolium-5-aminides	**(259)**	O	N	NR	N	C	NR
1,2,3,4-Oxatriazolium-5-thiolates	**(261)**	O	N	NR	N	C	S
Tetrazoles							
1,2,3,4-Tetrazolium-5-olates	**(263)**	NR	N	NR	N	C	O
1,2,3,4-Tetrazolium-5-aminides	**(264)**	NR	N	NR	N	C	NR
1,2,3,4-Tetrazolium-5-thiolates	**(265)**	NR	N	NR	N	C	S
1,2,3,4-Tetrazolium-5-methylides	**(267)**	NR	N	NR	N	C	CXY
1,2,3,4-Tetrazolium-5-selenolates	**(269)**	NR	N	NR	N	C	Se
Thiatriazoles							
1,2,3,4-Thiatriazolium-5-olates	**(271)**	S	N	NR	N	C	O
1,2,3,4-Thiatriazolium-5-aminides	**(273)**	S	N	NR	N	C	NR
1,2,3,4-Thiatriazolium-5-thiolates	**(274)**	S	N	NR	N	C	S
1,2,3,4-Thiatriazolium-5-methylides	**(275)**	S	N	NR	N	C	CXY
Dithiadiazoles							
1,3,2,4-Dithiadiazolium-5-olate	**(276)**	S	N	S	N	C	O
1,3,2,4-Dithiadiazolium-5-aminides	**(280)**	S	N	S	N	C	NR

[a] The grouping a and c each contribute 2 electrons tothe π-electron system of the heterocycle; b, d, e, and f each contribute 1 electron.

A. *Dioxoles*

1. 1, 3-*Dioxolium-4-olates* (**16**).



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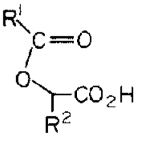

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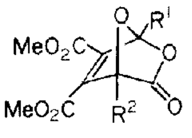

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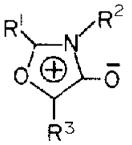
Cyclodehydration of *O*-acetylmandelic acid (**17**; R^1=Me, R^2=Ph) in the presence of dimethyl acetylenedicarboxylate gives 2-methyl-5-phenyl-3, 4-dimethoxycarbonyl furan (32%). This reaction probably proceeds *via* the meso-ionic 1, 3-dioxolium-4-olate (**16**; R^1=Me, R^2=Ph) and its 1, 3-dipolar cycloadduct (**18**; R^1=Me, R^2=Ph). This is the first report of a meso-ionic 1, 3-dioxolium-4-olate (**16**).[7]

B. *Oxazoles*

1. 1, 3-*Oxazolium-4-olates* (**19**).



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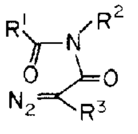

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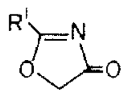

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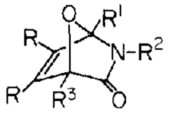

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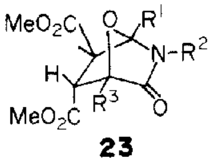

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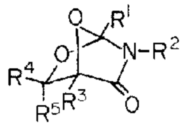

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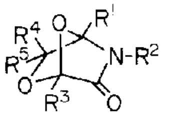

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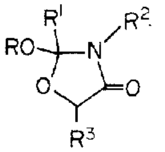

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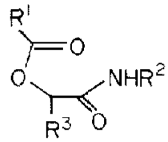

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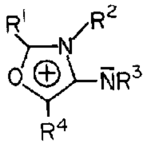
Examples of this meso-ionic system (**19**) were first described in 1974 and were obtained by cupric acetylacetonate catalysed thermal cyclisation of the diazo-ketones (**20**).[8,9] The 1, 3-oxazolium-4-olates (**19**) are reactive 1, 3-dipolarophiles. With acetylenes they form the primary adducts (**22**) which undergo thermal elimination of an isocyanate molecule (R^2NCO) to give the corresponding furan. 4(5*H*)-Oxazolones (**21**) also react with acetylenes giving furans and evidence that these reactions proceed *via* the meso-ionic valence tautomers (**19**; R^2=R^3=H) has been presented.[10] 1, 3-Dipolar cycloadducts are also formed with olefinic dipolarophiles: compound (**19**; R^1=Ph, R^2=Me, R^3=*p*. $C_6H_4 \cdot NO_2$) and dimethyl fumarate, in hot benzene, gave a quantitative yield of the adduct (**23**; R^1=Ph, R^2=Me, R^3=*p* · $C_6H_4 \cdot NO_2$).[8,11]

An interesting feature of the chemistry of the 1, 3-oxazolium-4-olates (**19**) is their formation of 1, 3-dipolar cycloadducts with carbonyl compounds. The 2, 3-diphenyl derivative (**19**; R^1=R^2=Ph, R^3=H) reacts with aromatic ketones and aldehydes giving the adducts (**24**). Surprisingly, when benzil is used as 1, 3-dipolarophile, the regiospecificity is reversed giving the adduct (**25**; R^1=R^2=R^4=Ph, R^3=H; R^5=COPh).[12] Reaction of the *p*-nitrophenyl derivative (**19**; R^1=Ph, R^2=Me, R^3=*p* · $NO_2 \cdot C_6H_4$) with tetrachloro-*o*-benzoquinone gives a [4 + 4] cycloadduct.[13]

In contrast to the isomeric 1, 3-oxazolium-5-olates (**29**) (Section III B, 3) which undergo nucleophilic attack at the carbon atom associated with the exocyclic oxygen atom, the 1, 3-oxazolium-4-olate (**19**; R^1=Ph, R^2=Me, R^3=*p* · $NO_2 \cdot C_6H_4$) reacts with alcohols giving the adducts (**26**; R^1=Ph, R^2=Me, R^3=*p* · $NO_2 \cdot C_6H_4$). When the nucleophile is water, cleavage of the initial adduct (**26**) gives a quantitative yield of *N*-methyl-α-benzoyloxy-α-*p*-nitrophenyl acetamide (**27**; R^1=Ph, R^2=Me, R^3=*p* · $NO_2 \cdot C_6H_4$).[14]

2. 1, 3-*Oxazolium-4-aminides* (**28**).



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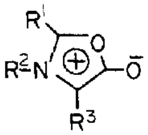
No new work on this system (**28**) has been reported since the subject was last reviewed.[6]

3. 1, 3-*Oxazolium-5-olates* (*Munchnones*) (**29**).



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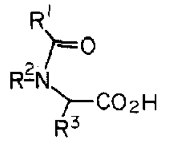

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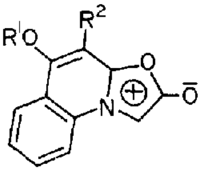

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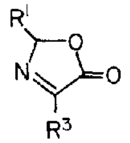

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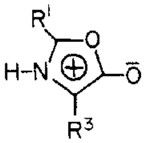

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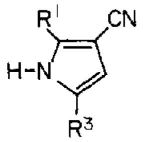

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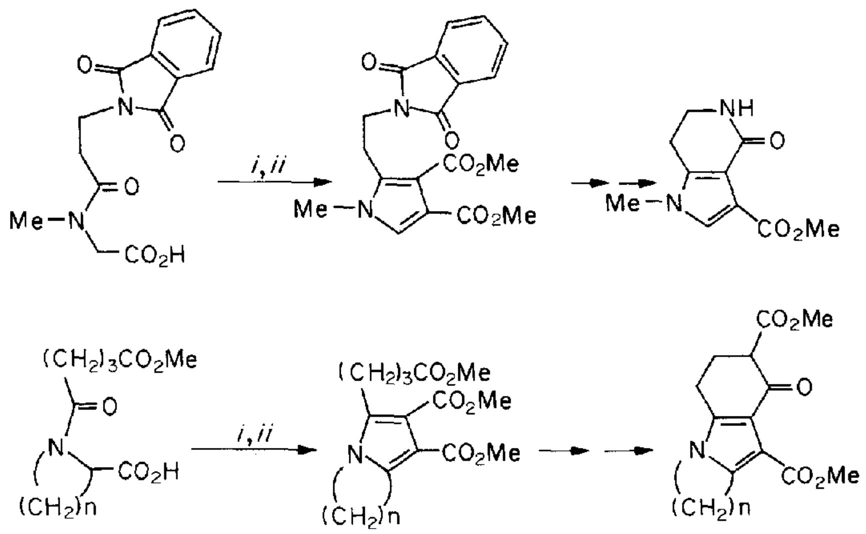
1, 3-Oxazolium-5-olates (**29**) are prepared by cyclodehydration of *N*-acylamino acids (**30**) and have been the subject of considerable study. Recently an alternative synthetic route has been described. Treatment of acyltetracarbonyl ferrate salts [ArCOFe(CO)$_4^-$M$^+$] with imidoyl chlorides ($R^2N{=}CCl\cdot Ar$) gives the meso-ionic 1, 3-oxazolium-5-olates (**29**; $R^1{=}R^3{=}Ar$, $R^2{=}Ar$ or alkyl) in good yield. This reaction fails to give alkyl derivatives (**29**; R^1 or R^3=alkyl).[15]

4-Unsubstituted munchnones (**29**; $R^3{=}H$) are usually too unstable to be isolated and the preparation of the unsubstituted polycyclic derivatives (**31**; $R^1{=}COMe$, $p\cdot Me\cdot C_6H_4SO_2$; $R^2{=}H$, Me) using the cyclodehydration route is therefore of interest: these compounds undergo electrophilic substitution at position 4.[16,17]

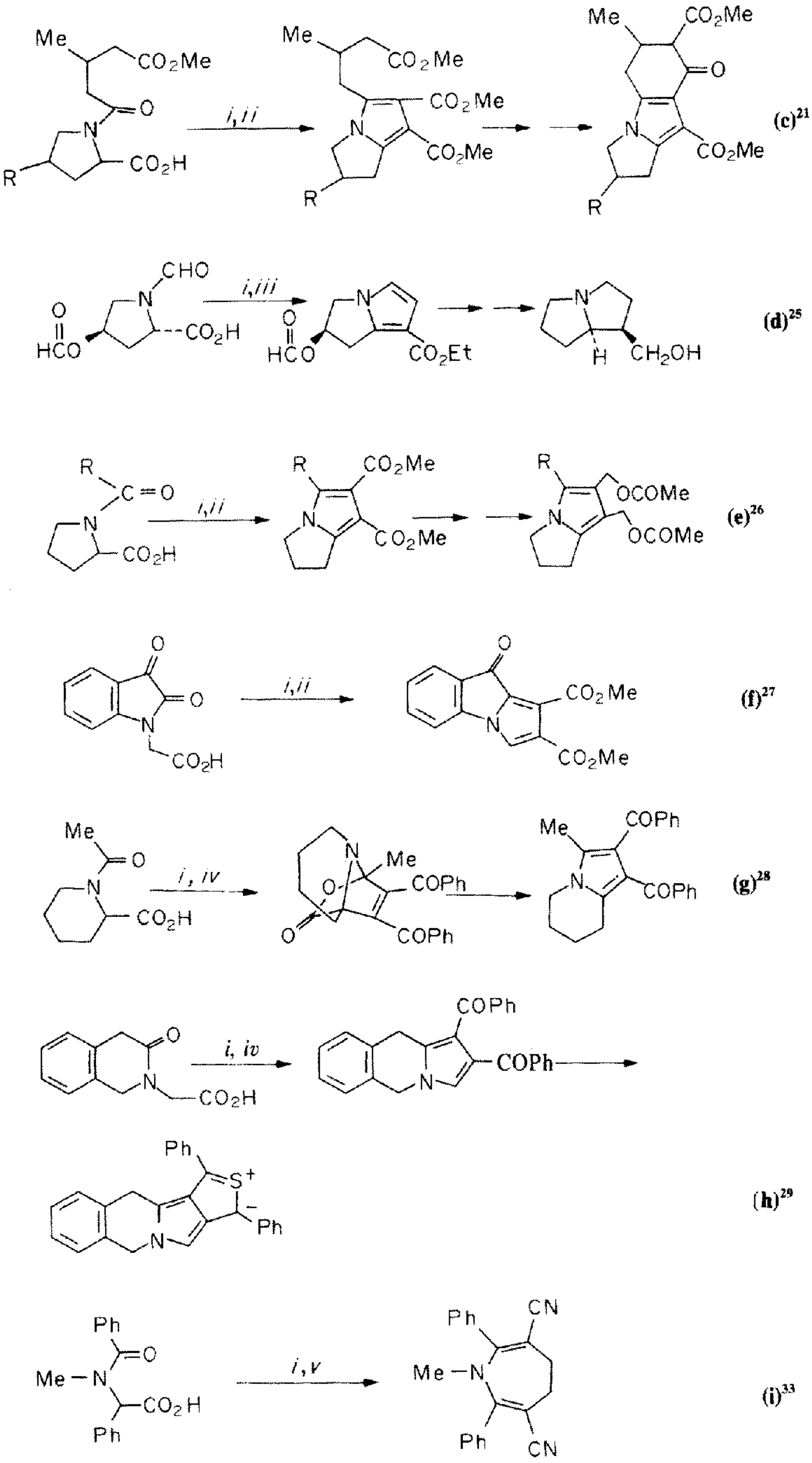
1, 3-Dipolar cycloadditions of meso-ionic 1, 3-oxazolium-5-olates (**29**) are valuable synthetic reactions. Often it is unnecessary to isolate the meso-ionic reagent. Either the oxazolone (**32**) may be used as a source of its meso-ionic tautomer (**33**) or the meso-ionic species can be generated *in situ* by cyclodehydration of *N*-acylamino acids (**30**). It is interesting to note that both the oxazolone (**32**; $R^1{=}R^3{=}Ph$), m.p. 103.5–104.5°, and the meso-ionic tautomer (**33**; $R^1{=}R^3{=}Ph$), m.p. 113–115°, have been isolated and characterised.[18]

The most important source of the 1, 3-oxazolium-5-olate synthon (**29**) is still the cyclodehydration of *N*-acylamino acids.[19–33] Some recent examples of the use of munchnones (**29**) as *in situ* intermediates in organic synthesis are given in Scheme 3. These reactions include syntheses of (i) natural products; (ii) compounds of potential value in chemotherapy and (iii) novel heterocyclic systems. It is notable that the use of dibenzoylacetylene as the 1, 3-dipolarophile led to the first isolable 1 : 1 cycloadduct of a munchnone and an acetylene (Scheme 3; reaction g).[28]



(a)[19]

(b)[20]

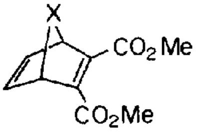


Reagents: i, Ac_2O; ii, dimethyl acetylenedicarboxylate; iii, $HC{\equiv}C.CO_2Et$; iv, $PhCO.C{\equiv}C.COPh$; v, 1,2-dicyanocyclobutene.

Scheme 3.

Reactions with olefines have also led to novel products. Cyclodehydration of *N*-acylaminoacids (**30**; R^2=H) in the presence of 2-chloroacrylonitrile affords, after elimination of carbon dioxide and hydrogen chloride from the initial adduct, 3-cyanopyrroles (**34**) in good yield. This pyrrole synthesis is particularly useful if the substituents (**34**; R^1 and R^3) are the same or when the cycloaddition is regiospecific.[34]

With the oxabicycloheptadiene (**35**; X=O), the 1, 3-oxazolium-5-olate (**29**; R^1=R^3=Ph, R^2=Me) undergoes non-selective addition to the double bonds: spontaneous fragmentation of the resulting adducts leads to pyrrole derivatives and the olefin (**35**; X=O) is thus behaving as a masked acetylene.[35] With the azabicycloheptadene (**35**; X=N·SO_2·C_6H_4·*p*·Me), compound (**29**; R^1=R^3=Ph, R^2=Me) adds specifically to the unsubstituted double bond.[36] In a similar reaction, compound (**29**; R^1=R^3=Ph, R^2=Me) and cyclopentadienequinone (**36**) give the acid (**38**) formed by cleavage of the initial adduct (**37**). Treatment of compound (**38**) with aqueous base results in oxidative decarboxylation giving the pyrrole derivative (**39**) and pyrolysis in hot benzene gives compound (**40**).[37–40] Reactions with several other quinones have also been described.[41]



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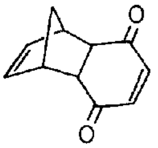

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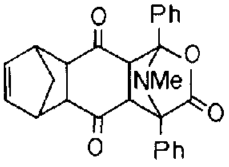

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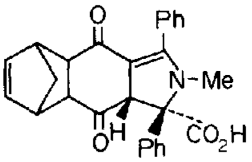

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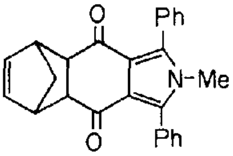

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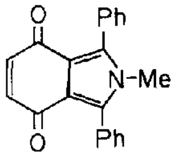
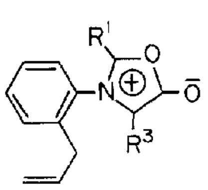


40

Intramolecular additions of olefines to munchnones have been reported. For derivatives of the type (**41**), the regioselectivity of the addition (i.e. **42** or **43**) depends upon the substituents on the meso-ionic ring (**41**; R^1 and R^3).[42] The use of diphenylcyclopropenone and its thione as dipolarophile affords 4-pyridones and 4-thiopyridones, respectively.[43,44] When the munchnones (**29**) are reacted with carbon disulphide, the initial cycloadduct (**45**) eliminates carbon dioxide providing a useful synthesis of meso-ionic 1, 3-thiazolium-5-thiolates (**44**) (see Section III E, 5).[45,46] If isocyanates are used as 1, 3-dipolarophile, the primary adduct (**46**) is stable and can be isolated.[47]



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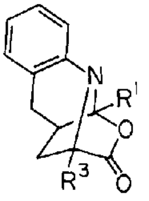

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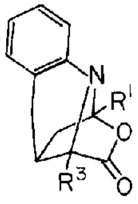

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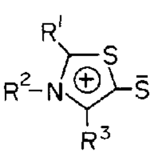

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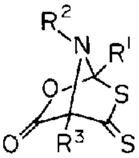

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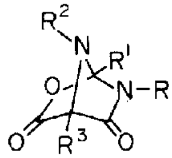
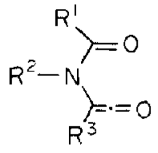


46

An interesting aspect of the munchnones (**29**) is that in addition to their reactivity as 1, 3-dipoles, they also have the capacity to react in terms of a [4+4] cycloaddition.[48,49] In this context, *o*-quinones react with 3-methyl-1, 3-oxazolium-5-olates (**29**; R^2=Me) giving the adducts (**48**; X=O).[48,49] Quinone imines give similar adducts (**48**; X=NSO_2Ph)[48] and cinnamaldehyde anils give α-pyridones.[50] Compound (**29**; R^1=R^3=Ph, R^2=Me) reacts with 2, 2-dimethyl-3-dimethylamino azirine yielding the oxazoline derivative (**49**) whose structure has been confirmed by X-ray crystallography.[51,52] Hydrolysis of munchnones (**29**) is comparable to that of a ketene: compound (**29**; R^1=EtS, R^2=Me, R^3=$COCF_3$) undergoes hydrolysis and decarboxylation to give compound (**50**; R^1=EtS, R^2=CF_3).[53]

The photochemistry of the 1, 3-oxazolium-5-olates (**29**) has only recently received attention. Irradiation of compound (**29**; R^1=Ph, R^2=Me, R^3=H) in chloroform–ethanol affords the ester (**50**; R^1=Ph, R^2=OEt), possibly by photo-generation of the ketene tautomer (**47**).[54] Photo-oxidation of the derivative (**29**; R^1=R^3=Ph, R^2=Me) gives *N*-methyldibenzamide (**51**; R^1=R^3=Ph, R^2=Me) as the major product. This reaction (**29**→**51**) is rationalised by assuming initial formation of the endoperoxide (**52**).[55] Interestingly, oxazolones (**32**) also undergo photo-oxidation to dibenzamides (**51**) in solvents in which the meso-ionic tautomer (**33**) might be expected to predominate.[55,56]



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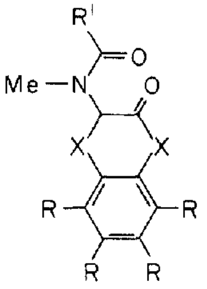

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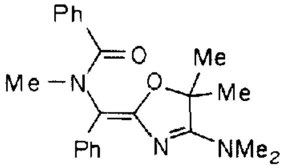

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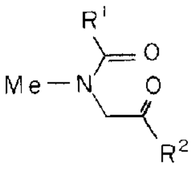

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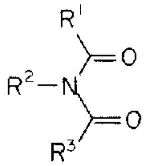

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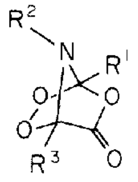
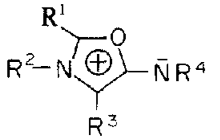


52

4. 1, 3-*Oxazolium-5-aminides* (**53**).



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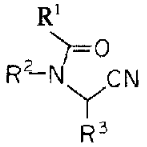

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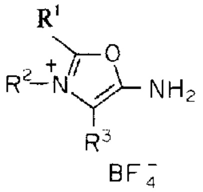

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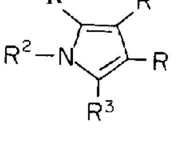

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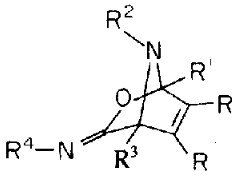

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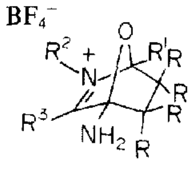
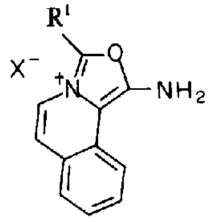


58

Cyclodehydration of the nitriles (**54**; R^3=H) using trifluoroacetic anhydride gives the *N*-trifluoroacetyl-1, 3-oxazolium-5-aminides (**53**; R^3=H, R^4=$COCF_3$): the *N*-acylated structure of these products has been confirmed by ^{13}C-NMR spectroscopy.[57] Treatment of these meso-ionic derivatives (**53**; R^3=H, R^4=$COCF_3$) with dimethyl acetylenedicarboxylate gives 3, 4-dimethoxycarbonyl-pyrroles (**56**; R=CO_2Me) in good yield.[57] Cyclisation of the nitriles (**54**; $R^3 \neq H$) with tetrafluoroboric acid similarly gives the 5-amino oxazolium tetrafluoroborates (**55**). The free meso-ionic systems (**53**; R^4=H) have not been isolated but in solution a small equilibrium concentration can be trapped by acetylenes to give good yields of the pyrroles (**56**) *via* the 1, 3-dipolar cycloadducts (**57**). The meso-ionic system is not trapped, however, by alkenes. In this case, a Diels–Alder cyclo-addition to the oxazolium salt (**55**) takes place giving 2-aroylpyrroles (**56**; R^1=ArCO, R^2=H) *via* the Diels–Alder cyclo-adducts (**58**).[58]



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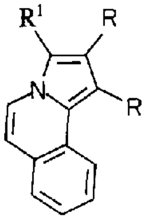

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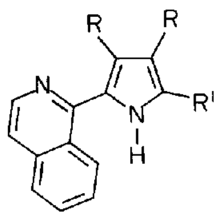

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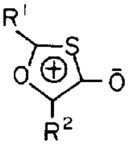
A similar behaviour towards alkynes and alkenes has been observed for Reissert salts. These have been shown to have the 5-amino-1,3-oxazolium structure (**59**).[59] Reaction with alkynes leads to pyrrolo[1, 2-*a*] isoquinolines (**60**) whereas treatment with alkenes gives the 1-(2-pyrrolo) isoquinolines (**61**).[60] In a similar manner, addition of acetylenes to phthalazine Reissert salts gives pyrrolo [2, 1-*a*] phthalazines.[61]

C. *Oxathioles*

1. 1, 3-*Oxathiolium*-4-*olates* (**62**).



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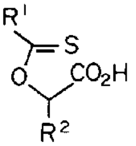

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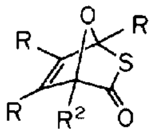

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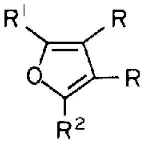

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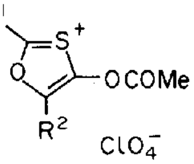
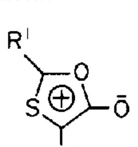


66

The 1, 3-oxathiolium-4-olates (**62**) have not been isolated but they can be generated *in situ* by cyclodehydration of the acids (**63**; R^1=NR_2 or SR) using acetic anhydride or dicyclohexylcarbodiimide. The meso-ionic product (**62**) can be trapped by a variety of acetylenic 1, 3-dipolarophiles to give furans (**65**) *via* the primary adducts (**64**). Treatment of the acid (**63**; R^1=SMe, R^2=Ph) with acetic anhydride and perchloric acid affords the isolable oxathiolium perchlorate (**66**; R^1=SMe, R^2=Ph).[62,63]

2. 1, 3-*Oxathiolium*-5-*olates* (**67**).



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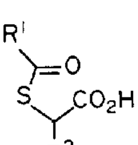

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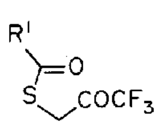
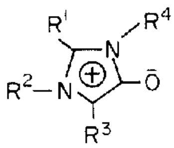


69

Cyclodehydration of aroylthioglycollic acids (**68**; R^1=Ar, R^2=H) using trifluoroacetic anhydride yields the red crystalline 1, 3-oxathiolium-5-olates (**67**; R^1=Ar, R^2=$COCF_3$).[64,65] These novel meso-ionic derivatives (**67**) are readily hydrolysed to the thioesters (**69**). The diphenyl derivative (**67**; $R^1 = R^2 =$ Ph) has been generated in solution either by cyclodehydration of benzoylphenylthioglycollic acid (**68**; $R^1 = R^2 =$ Ph)[65] or by condensation of thiobenzoic acid (PhCO·SH) with α-bromophenylacetyl chloride (PhCHBr·COCl).[66] This derivative (**67**; $R^1 = R^2 =$ Ph) can be trapped by dimethyl acetylenedicarboxylate to give 3, 4-dimethoxycarbonyl-2, 5-diphenylthiophene.[65,66]

D. *Diazoles*

1. 1, 3-*Diazolium*-4-*olates* (70).



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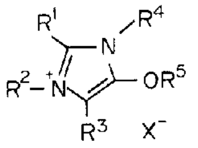

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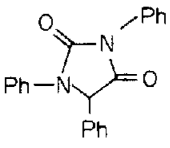

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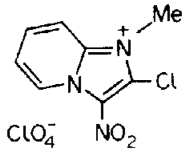

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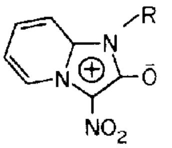

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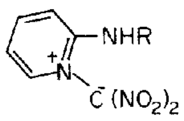
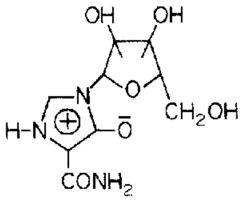


75

Recent studies on the preparation of this ring system (**70**) have utilised the base catalysed condensation of *N*, *N'*-disubstituted amidines ($R^2NH \cdot CR^1 = NR^4$) with α-bromoacylchlorides ($R^3CHBr \cdot COCl$) which gives good yields of the meso-ionic derivatives (**70**). In accord with their meso-ionic structure, reaction of 1, 3-diazolium-4-olates (**70**) with electron deficient alkynes gives pyrroles. Hydrolysis of the 2-methylmercapto derivative (**70**; R^1 = SMe, $R^2 = R^3 = R^4$ = Ph) gives the imidazoline dione (**72**). Meerwein alkylation gives the 4-ethoxydiazolium salts (**71**; R^5 = Et).[67,68]

Demethylation of 4-methoxy-1, 2, 3-trimethyl-5-nitro-diazolium perchlorate (**71**; R^1=R^2=R^4=R^5= Me, $R^3 = NO_2$, $X = ClO_4$) affords the unstable 5-nitro derivative (**70**; $R^1 = R^2 = R^4$ = Me, $R^3 = NO_2$).[69] In contrast, the benz-derivative (**74**; R=Me), obtained by treatment of the salt (**73**) with aqueous potassium carbonate, is quite stable. The meso-ionic tautomer (**74**; R=H) appears to be more stable than the corresponding hydroxy tautomer: methylation of compound (**74**; R=H) gives the *N*-methyl derivative (**74**; R=Me). Nitration (HNO_3/H_2SO_4) of the bicyclic meso-ionic derivatives (**74**) gives the dinitromethylides (**75**).[70] Meso-ionic 1, 3-diazolium-4-olates react with tetrachloro-*o*-benzoquinone to give [4 + 4] cycloadducts, the structure of one of which has been verified by X-ray crystallography.[13]



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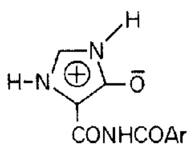

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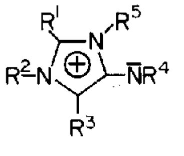
The structure of the derivative (**76**) has been investigated by X-ray analysis. This compound (**76**) is known as Bredinin and is a potential immuno-suppressant.[72–74] Acylation of the meso-ionic derivatives (**77**) also leads to compounds of pharmaceutical interest.[75,76]

2. 1, 3-*Diazolium-4-aminides* (**78**).



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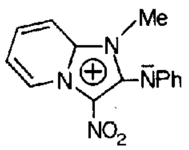

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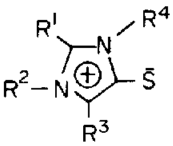
There have been no new studies on derivatives of the monocyclic system (**78**) but the orange bicyclic derivative (**79**) has been prepared by treatment of the perchlorate (**73**) with aniline in the presence of triethylamine.[70]

3. 1, 3-*Diazolium-4-thiolates* (**80**).



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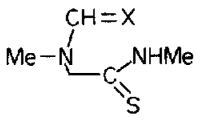

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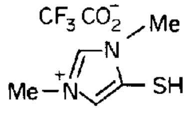

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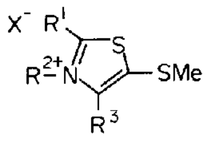

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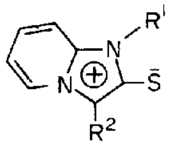

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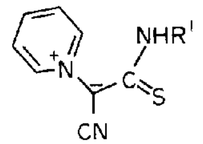

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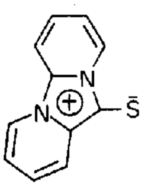

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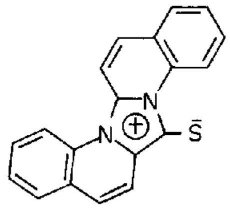

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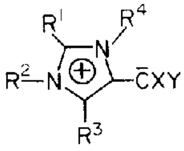
The formyl (**81**; X = O) and thioformyl derivatives (**81**; X = S) cyclise in aqueous trifluoroacetic acid yielding the 1, 3-diazolium trifluoroacetate (**82**) which upon deprotonation gives the meso-ionic derivative (**80**; $R^1 = R^3 = H$, $R^2 = R^4 = Me$). The thioformyl derivative (**81**; X = S) also yields this product (**80**; $R^1 = R^3 = H$, $R^2 = R^4 = Me$) by treatment with Amberlite IRA 400 ion exchange resin in the OH form.[77,78]

The mechanism of formation of meso-ionic 1, 3-diazolium-4-thiolates (**80**) from 5-methylthio-1,3-thiazolium salts (**83**) and primary amines has been investigated. This reaction proceeds better with aliphatic amines than with aromatic amines: a mechanism has been proposed.[78,79]

The yellow, bicyclic system (**84**; $R^1 = Me$, $R^2 = NO_2$) has been prepared by treatment of the perchlorate (**73**) with sodium hydrosulphide and triethylamine in water.[70] Treatment of the pyridinium methylides (**85**) with mercuric oxide gives the corresponding cyano derivatives (**84**; $R^2 = CN$).[80]

An amusing reaction is the formation of the red tricyclic derivative (**86**) by reaction of 2-picoline with sulphur dioxide and benzoyl chloride in pyridine solution. This reaction was first reported in 1907 but the structure of the product was not recognised. A similar reaction using quinaldine affords compound (**87**) which is the thio-derivative of the dye Besthorn's red.[81]

4. 1, 3-*Diazolium-4-methylides* (**88**).



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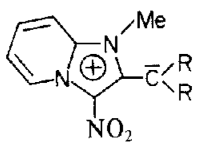

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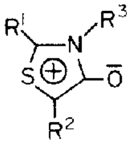
Treatment of the 2-chloro-3-nitroimidazo[1, 2-*a*]pyridinium perchlorate (**73**) with malononitrile or diethyl malonate in the presence of triethylamine gives the orange-red meso-ionic derivatives (**89**; R = CN) and (**89**; R = CO_2Et) respectively. These are the first reported examples of this class of meso-ionic system (**88**).[70]

E. *Thiazoles*

1. 1, 3-*Thiazolium-4-olates* (**90**).



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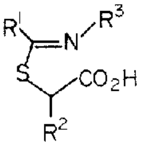

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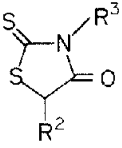

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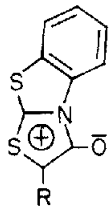

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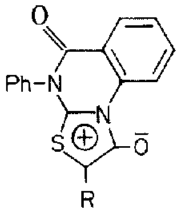

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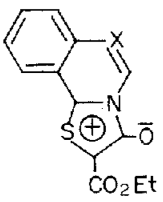

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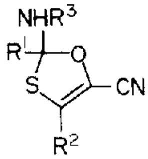

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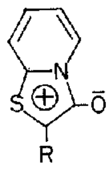

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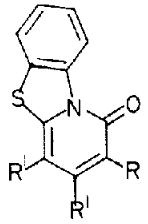


98

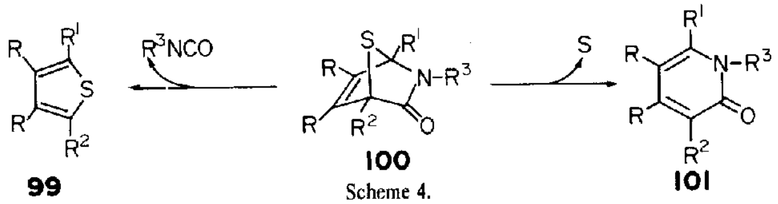
The meso-ionic 1, 3-thiazolium-4-olates (**90**) have received considerable attention since 1975. Dehydration of the acids (**91**) continues to be an important method for preparing polycyclic derivatives. Recent examples include the preparation of the systems (**93**) and (**94**).[82,83] A second preparative route involves alkylation of rhodanines (**92**) followed by treatment with base: several 2-thioalkyl derivatives have recently been prepared by this method.[84]

Two new routes to this ring system have been described. Complications often encountered using the cyclodehydration synthesis (**91**→**90**) have led to the introduction of an alternative preparation which involves reaction of α-haloacyl chlorides ($R^2CHX \cdot COCl$) with *N*-monosubstituted thioamides ($R^1CS \cdot NHR^3$). This route enables a wide variety of substituents to be incorporated into the heterocyclic ring. Both monocyclic and polycyclic derivatives have been prepared by this method.[66,82,85-87] In a similar approach, reaction of isoquinolinyl-1-thiol or quinazolinyl-4-thiol with ethylbromomalonate yields the thiazolo[2, 3-*a*] isoquinolinium-3-olate (**95**, X=CH) and the thiazolo [3, 2-*c*] quinazolinium-3-olate (**95**; X=N) respectively.[88,89]

An alternative route utilises the reaction of *gem*-dicyano epoxides with thioamides and leads to the formation of the red meso-ionic 1, 3-thiazolium-4-olates (**90**; R^1 = aryl, alkyl, CN, S-aryl, NR_2; R^2 = aryl; R^3-alkyl or aryl) in good yield. The mechanism of the multi-step process has been discussed and is believed to involve a tetrahedral intermediate (**96**) which rearranges to the meso-ionic product (**90**) with elimination of hydrogen cyanide.[90–93]

Several examples of electrophilic substitution at the 5-position of meso-ionic 1, 3-thiazolium-4-olates have been described. Reaction of 2-pyridinylthioglycollic acid and derivatives with acetic anhydride affords the acylated products, e.g. (**97**; $R = COCH_2S \cdot C_5H_4N$).[85,94,95] The unsubstituted system (**97**; R = H) has been shown to readily undergo electrophilic substitution with diazonium salts and aldehydes.[96,97] Derivatives of this system may be useful as dyes.[98] Similar results have been obtained in the thiazolo [3, 2-*a*] quinolinium-1-olate system.[99,100]

Cycloaddition reactions of meso-ionic 1, 3-thiazolium-4-olates (**90**) have attracted considerable attention. With acetylenes two possible modes of fragmentation of the primary adduct (**100**) can occur (Scheme 4): Loss of a molecule of isocyanate generates a thiophene (**99**) whereas loss of sulphur affords a pyridone derivative (**101**). In general, monocyclic 1, 3-thiazolium-4-olates (**90**) react with alkynes to give thiophenes (**99**)[66] but this mode of reaction is suppressed by ring annelation and polycyclic 1, 3-thiazolium-4-olates give pyridone derivatives. For example, the polycyclic system (**93**) reacts with acetylenes to give the derivatives (**98**)[82] and similar products have been obtained using other polycyclic derivatives.[86,87] Surprisingly, the thiazolo[3, 2-*a*]quinolinium-1-olate system yields pyrrolo[1, 2-*a*] quinolines on reaction with acetylenes: a mechanism has been proposed for this unusual reaction.[85]

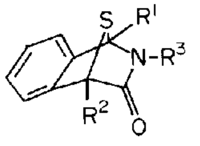


Scheme 4.

4-Hydroxythiazoles react with diethyl acetylenedicarboxylate giving the adducts (**100**; $R^3 = C(CO_2Et) = CH \cdot CO_2Et$) which fragment either to a thiophene (**99**) or a pyridone (**101**) depending upon the nature of the substituents. These reactions involve initial formation of the meso-ionic intermediates (**90**; $R^3 = C(CO_2Et) = CH \cdot CO_2Et$).[101,102] The mode of fragmentation of the benzyne adducts (**102**) can be controlled by the reaction conditions: thermal fragmentation gives isobenzothiophenes (**103**) whereas extrusion of sulphur occurs on photochemical irradiation giving isoquinolones (**104**).[30]

Several studies of the cycloaddition of olefines to meso-ionic 1, 3-thiazolium-4-olates (**90**) have been reported. The "masked acetylene" (**35**; X = O) gives a mixture of cycloadducts which upon heating undergo double fragmentation affording thiophenes.[35] Similar reactions have been observed using azabicycloheptadienes (**35**; X = N · Tosyl)[36] and a tricyclodecatriene.[103] An X-ray study of the cycloadduct formed between the meso-ionic 1, 3-thiazolium-4-olate (**90**; $R^1 = R^3 = Ph$, $R^2 = C_6H_4 \cdot p \cdot Cl$) and dimethyl maleate has shown it to possess the constitution (**105**) in which the ester groups have exostereo-chemistry.[104] Dimethyl maleate and dimethyl fumarate also react with the meso-ionic tautomers of 4-hydroxythiazoles generating 1 : 1 cycloadducts.[101,104] A number of polycyclic meso-ionic 1, 3-thiazolium-4-olates have been treated with a variety of olefinic dipolarophiles and the thermal decomposition of the primary adducts has been described.[82,85–87] Diphenylcyclopropenone and diphenylcyclopropenethione afford the cycloadducts (**106**): thermolysis of these adducts (**106**) leads to a variety of products.[43] Reaction of 1, 3-thiazolium-4-olates (**90**) with isocyanates or isothiocyanates gives adducts of the general structure (**107**). Attempts to prepare the 6-membered cross-conjugated mesomeric betaines (**108**) by removal of the sulphur bridge were unsuccessful.[47]

Some oxidation reactions of this system (**90**) have recently been reported.[105]



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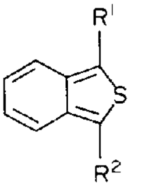

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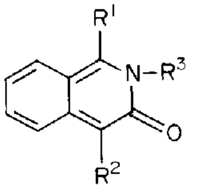

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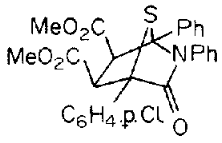

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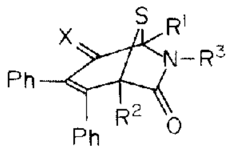

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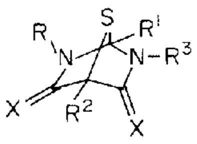

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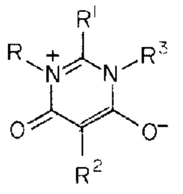

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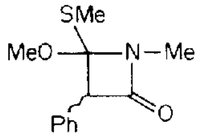

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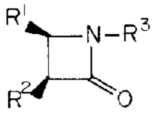
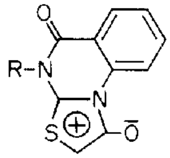


110

Several studies of the photochemistry of meso-ionic 1, 3-thiazolium-4-olates (**90**) have been reported.[54,55] Photolysis of compound (**90**; $R^1 = SMe$, $R^2 = Ph$, $R^3 = Me$) in methanol solution generates the β-lactam (**109**) as a mixture of diasterioisomers.[84] A better method of converting meso-ionic 1, 3-thiazolium-4-olates (**90**) to β-lactams involves treatment with Raney nickel. Using this reagent, desulphurisation of the derivative (**90**; $R^1 = R^2 = R^3 = Ph$) in a variety of solvents afforded the *cis*-β-lactam (**110**; $R^1 = R^2 = R^3 = Ph$) in excellent yield. This transformation (**90** → **110**) has been carried out on other meso-ionic 1, 3-thiazolium-4-olates (**90**) and the mechanism has been discussed.[106,107]

The effect of substituents on the colour of the polycyclic derivatives (**111**) has been discussed.[108] With alcohols these systems give the adducts (**112**).[109] A kinetic study of the acid catalysed hydrolysis of the derivatives (**113**) has been reported.[110]



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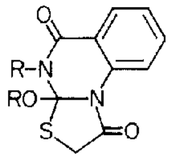

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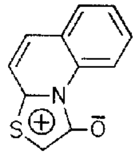

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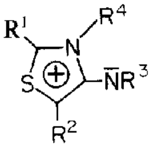
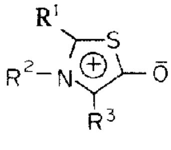
2. 1, 3-*Thiazolium-4-aminides* (**114**).



114

No new work on this system (**114**) has been reported since the subject was last reviewed.[6]

3. 1, 3-*Thiazolium-5-olates* (**115**).



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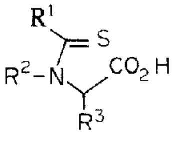

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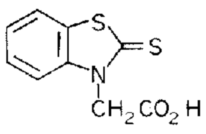

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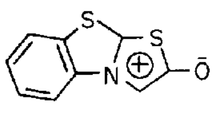

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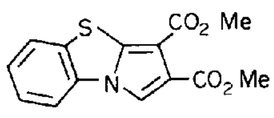

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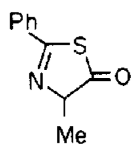

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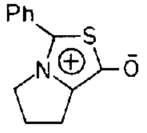

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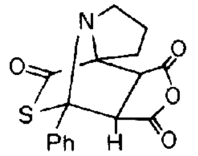

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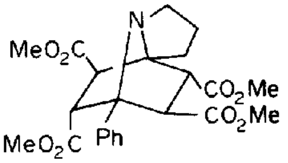

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The 1, 3-thiazolium-5-olates (**115**) are well known and have continued to receive attention. Cyclodehydration of *N*-thioacylglycines (**116**) is the best route to this system and this method has been used to prepare a series of monocyclic derivatives unsubstituted at position 4 (**115**; $R^1 = R^2 = Ar$, $R^3 = H$).[111] Electrophilic substitution gives 4-acyl derivatives (**115**; $R^1 = R^2 = Ar$, $R^3 = COMe$ or COPh).[111] A similar cyclodehydration of the acid (**117**) using acetic anhydride generates the unstable polycyclic meso-ionic 1, 3-thiazolium-5-olate (**118**) which is trapped by dimethyl acetylenedicarboxylate yielding the pyrrolo [2,1-*b*] benzothiazole (**119**).[82]

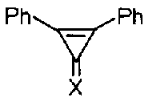
It has been demonstrated that the 5(4*H*) thiazolone (**120**) is in equilibrium with the meso-ionic tautomer (**115**; $R^1 = Ph$, $R^2 = H$, $R^3 = Me$) which can be trapped by dimethyl acetylenedicarboxylate to give 3, 4-dimethoxycarbonyl-2-methyl-5-phenylpyrrole (66%).[112]

Addition reactions with other dipolarophiles have been investigated. Compound (**115**; $R^1 = R^3 = Ph$, $R^2 = Me$) and benzyne give 1, 3-diphenyl-2-methyl isoindole in low yield.[30]

Oxabicyclo [2.2.1] heptane (**35**; X=O) and compound (**115**; R^1=R^3=Ph, R^2=Me) give mainly 2, 5-diphenyl-1-methyl pyrrole.[35]

With maleic anhydride, compound (**121**) gives the primary adduct (**122**) whereas with dimethyl fumarate the same compound gave the adduct (**123**).[113]

Two groups have investigated the reaction between the meso-ionic compounds (**115**; $R^1 = Ar$, R^2=Me, R^3=H, Ph) and the diphenylcyclopropene derivatives (**124**; X=O, S, $NSO_2{\cdot}C_6H_4{\cdot}p{\cdot}CH_3$, $C(CN)_2$, $C(CN){\cdot}CO_2Et$).[43,44] With the thione (**124**; X=S), pyrid-4-thiones (**125**) were obtained. Additions with heterocumulenes and *o*-quinones have also been described.[113,48]



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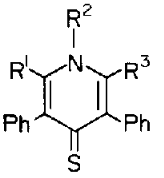

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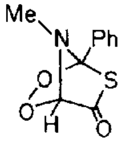

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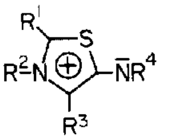
Irradiation of the derivative (**115**; $R^1 = Ph$, $R^2 = Me$, $R^3 = H$) in methanol solution yields the methyl ester of the acid (**116**, $R^1 = Ph$, $R^2 = Me$, $R^3 = H$) and similar results have been reported for the derivative (**115**; $R^1 = SMe$, $R^2 = Me$, $R^3 = COCF_3$). Interestingly, in the presence of oxygen, partial formation of the oxygen adduct (**126**) occurs: this adduct (**126**) then undergoes fragmentation giving carbonoxysulphide and *N*-formyl-*N*-methylbenzamide.[53,54]

4. 1, 3-*Thiazolium-5-aminides* (**127**).



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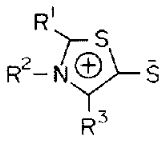
No new work on this system (**127**) has been reported since the subject was last reviewed.[6]

5. 1, 3-*Thiazolium-5-thiolates* (**128**).



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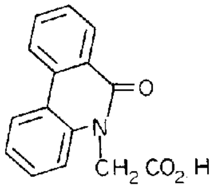

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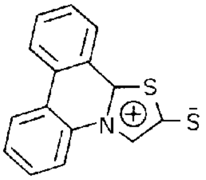

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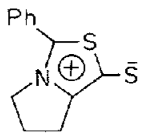

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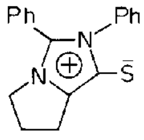

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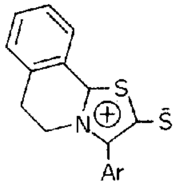

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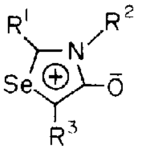
Treatment of the acid (**129**) with phosphorus pentasulphide in boiling pyridine yields the polycyclic 1, 3-thiazolium-5-thiolate (**130**). However, attempts to extend this method to other meso-ionic 1,3-thiazolium-5-thiolates failed.[46] Treatment of meso-ionic 1, 3-oxazolium-5-olates (**29**) (Section III B, 3) or 1, 3-thiazolium-5-olates (**115**) (Section III E, 3) with carbon disulphide remains the best route to this system (**128**).[46,113] Reactions of 3, 4-dihydro isoquinolinium methylide salts with carbon disulphide in the presence of base generates meso-ionic 1, 3-thiazolium-5-thiolates (**133**). The mechanism of this transformation has been discussed in detail.[114]

In general, meso-ionic 1,3-thiazolium-5-thiolates (**128**) are regarded as unreactive towards 1,3-dipolarophiles. Compound (**131**) did react with phenylisothiocyanate to give the 1, 3-diazolium-4-thiolate (**132**) and with dimethylfumarate to give adduct (**123**).[115]

F. *Selenazoles*

1. 1, 3-*Selenazolium-4-olates* (**134**).



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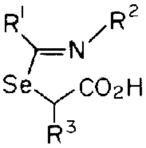

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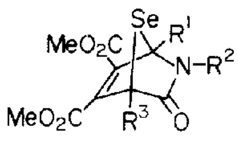

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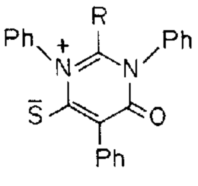

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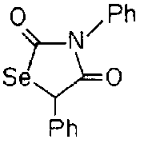

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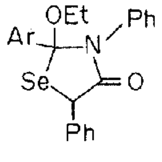

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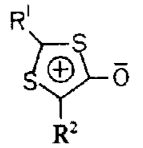
The first example of a selenium containing meso-ionic compound (**134**; $R^1 = R^2 = R^3 = Ph$) was described in 1975 and was obtained by cyclodehydration of the α-selenoacid (**135**; $R^1 = R^2 = R^3 = Ph$).[116] More recently, a variety of meso-ionic 1, 3-selenazolium-4-olates (**134**) have been prepared by condensation of selenoamides ($R^1C=Se \cdot NHR^2$) with α-bromoacyl chlorides ($R^3CHBr \cdot COCl$).[117] With dimethyl acetylenedicarboxylate, the 1, 3-selenazolium-4-olates (**134**) yield 2-pyridones by elimination of selenium from the initial adducts (**136**). The derivative (**134**; $R^1 = p \cdot MeO \cdot C_6H_4$, $R^2 = R^3 = Ph$) and phenylisothiocyanate undergo a similar reaction giving the cross-conjugated mesomeric betaine (**137**; $R = p \cdot MeO \cdot C_6H_4$). Compound (**134**; $R^1 = SMe$, $R^2 = R^3 = Ph$) undergoes hydrolysis to the selenazolidine dione (**138**) and reaction of compound (**134**; $R^1 = p \cdot MeO \cdot C_6H_4$; $R^2 = R^3 = Ph$) with alcohol gives the adduct (**139**; $Ar = p \cdot MeO \cdot C_6H_4$).[117]

G. *Dithioles*

1. 1, 3-*Dithiolium-4-olates* (**140**).

The meso-ionic 1, 3-dithiolium-4-olates (**140**) can be generated either by condensation of dithiobenzoic acids ($ArCS_2H$) with α-haloacyl halides ($R^2CHX \cdot COX$)[66] or by cyclodehydration of the dithioester derivatives (**141**).[118,119] A compound previously assigned the 4-unsubstituted structure (**140**; $R^1 = Ph$, $R^2 = H$)[120] has been shown to be incorrectly formulated.[119,121] The product, m.p. 185–186°, obtained by treatment of thiobenzoylthioglycollic acid (**141**; $R^1 = Ph$, $R^2 = H$) with boron trifluoride etherate and acetic anhydride has been reformulated as the intramolecular cyclo-adduct (**142**)[121] and is not the meso-ionic derivative (**140**; $R^1 = Ph$, $R^2 = COCH_2S_2CPh$) as previously described.[119]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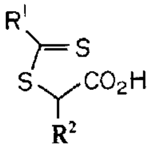
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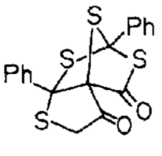
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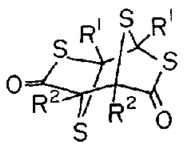
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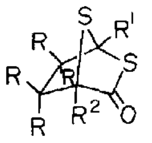
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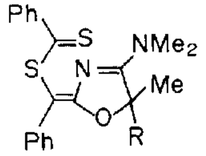
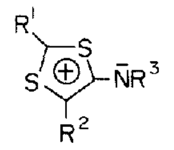

145

An interesting aspect of some 1, 3-dithiolium-4-olates (**140**) is their reversible dimerisation (**140** → **143**). The dimeric structures (**143**) have been confirmed by X-ray crystallography. In solution, equilibrium between the colourless dimers (**143**) and the red monomers (**140**) is established and the meso-ionic monomer can be trapped by 1, 3-dipolarophiles.[122,123]

The meso-ionic derivatives (**140**) are very reactive 1, 3-dipoles. Reaction with acetylenes furnishes substituted thiophenes.[119,124–126] Regioselective additions of unsymmetrical alkynes and alkenes have been rationalised by frontier orbital theory.[126,127] Addition of benzyne generates isobenzothiophenes.[30] The 1:1 cycloadducts (**144**) have been obtained by reaction with a wide variety of olefinic 1,3-dipolarophiles, including *N*-phenylmaleimide,[119,123,128] acrylonitrile,[119] ethylacrylate,[119] maleic anhydride,[123,128] dimethyl maleate,[128] dimethyl fumarate,[128] 1, 2, 3-triphenylcyclopropene,[129] *p*-quinone,[129] 7-oxa-bicycloheptadienes,[35] 7-aza-bicycloheptadienes,[36] diphenylcyclopropenone derivatives (**124**),[44] and tricyclodecatriene.[103] Primary adducts are also formed with hetero double bonds such as formaldehyde[130] and 2, 3-diphenylazirine.[119] 2-Dimethylamino-azirines, however, have been found to give the adducts (**145**) which may be formed by initial valence tautomerism of the meso-ionic precursor (**140**).[52]

Photo-oxygenation of the diphenyl derivative (**140**; $R^1 = R^2 = Ph$) gives a low yield of the dimer (**143**; $R^1 = R^2 = Ph$) together with dibenzoyldisulphide.[55] The same derivative (**140**; $R^1 = R^2 = Ph$) with aniline yields the meso-ionic 1, 3-thiazolium-4-olate (**90**; $R^1 = R^2 = R^3 = Ph$) (see Section III E, 1).[131]

2. 1, 3-*Dithiolium-4-aminides* (**146**).



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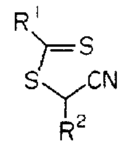

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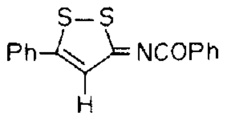

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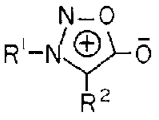
Treatment of the nitrile (**147**; R^1 = morpholino, R^2 = Ph) with acetyl chloride followed by deprotonation gives the meso-ionic derivative (**146**; R^1 = morpholino, R^2=Ph, R^3=COMe) in good yield.[125] Mechanistic aspects of the photochemical rearrangement (**146**; R^1 = Ph, R^2 = H, R^3 = COPh→**148**) have been described.[132]

H. *Oxadiazoles*

1. 1, 2, 3-*Oxadiazolium-5-olates* (*Sydnones*) (**149**).



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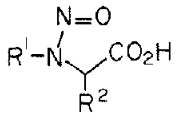

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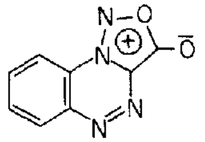

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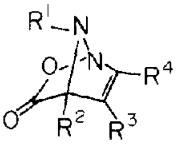

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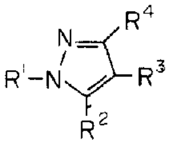

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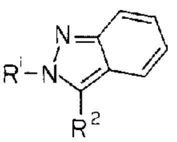


154

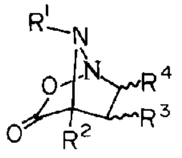
Cyclodehydration of *N*-nitroso-α-amino-acids (**150**) remains the sole synthetic route available for the preparation of sydnones (**149**).[3] Recent examples include the synthesis of 3-methyl sydnone (**149**; R^1 = Me, R^2 = H) by cyclisation of the acid (**150**; R^1 = Me, R^2 = H) using trifluoroacetic anhydride[133] and similar preparations of several 3-benzylsydnones (**149**; R^1 = $ArCH_2$, R^2 = H, Ph).[134] For 4-unsubstituted derivatives (**149**; R^2 = H), modification of the ring substituents can be achieved by electrophilic substitution and a number of novel sydnones (**149**; R^1 = Ar, Me_2N, piperidino and morpholino, R^2 = COMe, Br, SMe, SPh, SO · Ph, CN and CH=NOH) have been made in this way.[135] Anodic halogenation of 4-unsubstituted sydnones gives 3-aryl-4-bromo and 4-chlorosydnones (**149**; R^1 = Ar, R^2 = Br, Cl) but fluoridation and iodination were not successful.[136] 4-Iodo-3-(3′-pyridyl)sydnone (**149**; R^1 = 3-pyridyl, R^2 = I) has been prepared from the unsubstituted sydnone and *N*-iodo succinimide.[137]

Earlier work has demonstrated that nitration of 3-phenylsydnone (**149**; R^1 = Ph, R^2 = H) yields the 4-nitro derivative (**149**; R^1 = Ph, R^2 = NO_2)[138] whereas nitration of 3-(4′-tolyl) sydnone (**149**; R^1 = *p* · Me · C_6H_4, R^2 = H) occurs on the tolyl substituent.[139] Recently, nitration of 3-benzylsydnone has been shown to give 3-(3′-nitrobenzyl) sydnone (**149**; R^1 = *m* · NO_2 · $C_6H_4CH_2$, R^2=H) and nitration of 3,4-diphenylsydnone (**149**; R^1=R^2=Ph) gave 3-phenyl-4(4′-nitrophenyl)syndnone (**149**; R^1=Ph. R^2= *p*·NO_2·C_6H_4).[140] Further examples of electrophilic substitution of 4-unsubstituted sydnones (**149**; R^2 = H) include introduction of diazo substituents: intramolecular addition gives the tricyclic derivative (**151**).[141] 4-Acetylsydnones (**149**; R^1 = Ar, $ArCH_2$, R^2 = COMe) are formed by acetylation using a mixture of acetic anhydride and 85% phosphoric acid[142] and can be converted into 4-diazo acetylsydnones (**149**; R^1 = Ar, R^2 = $COCHN_2$).[143,144] 4-Chlorosulphonation readily yields 4-chlorosulphonylsydnones (e.g. **149**;

$R' = \mathrm{Ph}$, $R^2 = \mathrm{SO_2Cl}$)[145] and 4-formylation is achieved under Vilsmeier-Haack conditions.[146] These products (**149**; $R^1 = \mathrm{Ar}$, $R^2 = \mathrm{CHO}$) have been converted to olefines using the Wittig reaction.[146]

An alternative route to 4-olefinic sydnones involves metalation, reaction with a ketone and subsequent dehydration of the intermediate alcohol.[147–150] In another method, 4-hydroxymethylation is accomplished by treating the 4-unsubstituted sydnones with formaldehyde/NaBr affording some of the derivatives (**149**; $R^1 = \mathrm{Ar}$, $R^2 = \mathrm{CH_2OH}$).[151] Use of excess formaldehyde or formaldehyde in the presence of sulphuric acid gives *bis*-sydnones linked by a methylene group.[152] *Bis*-sydnones linked at the 4-position by a sulphur atom have been prepared by the action of thionyl chloride on 4-unsubstituted sydnones[153] and 3, 3′-diphenyl-4, 4′-*bis*-sydnone has been prepared by treating 4-bromo-3-phenylsydnone (**149**; $R^1 = \mathrm{Ph}$, $R^2 = \mathrm{Br}$) with copper bronze.[154] Synthesis of 3, 4-*bis*(4-sydnonylcarbonyl) furoxans is achieved by treating the sydnones (**149**; $R^1 = \mathrm{Me, Ph}$, $R^2 = \mathrm{CO \cdot CH_2 \cdot CO \cdot CO_2 \cdot Me}$) with fuming nitric acid.[155]

1, 3-Dipolar cycloaddition reactions of sydnones continue to receive attention. Reaction with acetylenes is a well established route to pyrazoles (**153**). Recent papers describe (i) preparation of 3-benzoylpyrazoles (**153**; $R^1 = \mathrm{PhCH_2}$, *iso*-Bu, $R^2 = \mathrm{CH_2CO_2Me}$, $R^3 = \mathrm{H}$, $R^4 = \mathrm{PhCO}$) using benzoylacetylene;[156] (ii) 5-chloropyrazoles (**153**; $R^1 = \mathrm{PhCH_2}$, $R^2 = \mathrm{Cl}$, $R^3 = R^4 = \mathrm{CO_2Me}$) using 4-chlorosydnones[157] and (iii) *N*-amino pyrazoles (**153**; $R^1 = \mathrm{NMe_2}$, morpholino, piperidino) using *N*-amino-sydnones (**149**; $R^1 = \mathrm{NMe_2}$, morpholino, piperidino).[158] Gotthardt and Reiter have investigated both thermally[159] and photochemically[160] induced reactions of a wide variety of sydnones with acetylenes. Thermal cycloaddition generates the adducts (**152**) which undergo loss of carbon dioxide generating the pyrazoles (**153**).[159] Photochemical reaction of sydnones with acetylenes also gives pyrazoles but by a different mechanism (see Scheme 5 and related discussion). Photochemical addition is a useful adjunct to the thermal reaction since the pyrazoles formed are isomeric to those formed thermally. 3-Benzyl-4-phenylsydnone (**149**; $R^1 = \mathrm{PhCH_2}$, $R^2 = \mathrm{Ph}$) and 4-methyl-3-phenylsydnone (**149**; R^1=Ph R^2=Me) react thermally with benzyne giving the benzo[*c*]pyrazoles (**154**; $R^1 = \mathrm{PhCH_2}$, $R^2 = \mathrm{Ph}$) (68%) and (**154**; $R^1 = \mathrm{Ph}$, $R^2 = \mathrm{Me}$) (64%), respectively.[30]



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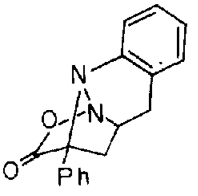

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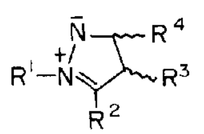

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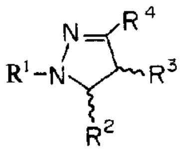

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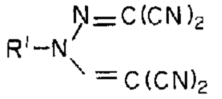

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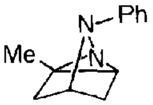

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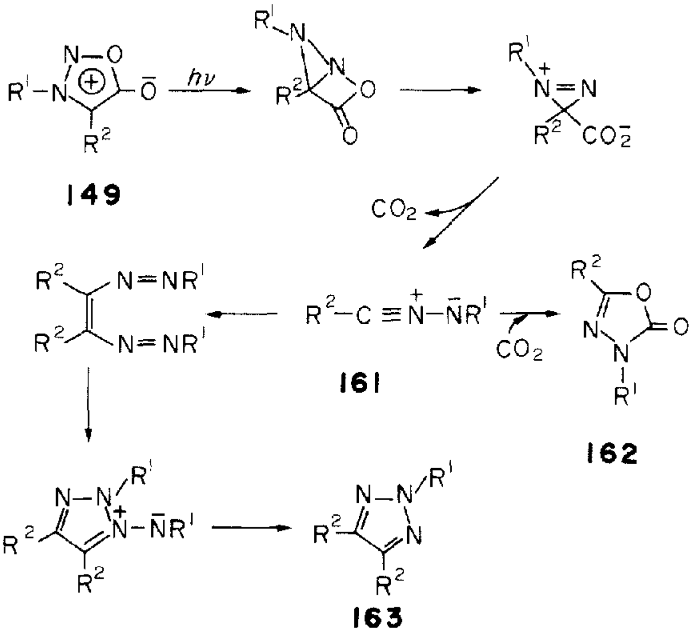
With olefinic dipolarophiles, sydnones (**149**) yield unstable 1 : 1 adducts (**155**) which can only be isolated in special circumstances: intramolecular 1, 3-dipolar cycloaddition of the sydnone (**149**; $R^1 = 2'$-allylphenyl, $R^2 = \mathrm{Ph}$) yields the bridged adduct (**156**).[161,162] More usually, cycloreversion involving loss of carbon dioxide giving the dipolar species (**157**) occurs and proton transfer then yields pyrazolines (**158**).[163,164] In the presence of dipolarophiles the intermediate (**157**) may be trapped: reaction of 3-phenylsydnone with isoprene generates some of the caged product (**160**) together with 3-isopropenyl-1-phenyl pyrazole.[165] An alternative method of fragmentation of the dipolar intermediates (**157**) has been observed when the dipolarophile is tetracyanoethylene;[166–168] the species [**157**; $R^3 = R^4 = \mathrm{(CN)_2}$] undergoes CC-bond cleavage yielding [(dicyanovinyl)hydrazono] malononitriles (**159**).

Photolysis of sydnones continues to attract interest.[169–171] In the absence of external trapping agents, irradiation of sydnone derivatives usually yields either 1, 2, 3-triazoles (**163**) and/or 1, 3, 4-oxadiazol-2-ones (**162**) as major products. Recent mechanistic proposals for the formation of these products are shown in Scheme 5. This mechanism avoids high energy antiaromatic diazirene intermediates which have previously been proposed. The formation of various minor photolysis products can also be rationalised using this mechanism as a basis (Scheme 5).[170,171] Evidence that formation of the nitrileimines (**161**) involves creation of a bond between the 2 and 4-positions in photoexcited sydnones (**149**) has been provided by the observation that syndones labelled with ^{15}N at position 2 give 1, 2, 3-triazoles (**163**) in which the label is incorporated at both the 1 and 3 positions.[170]

The intermediacy of the nitrileimines (**161**) has been demonstrated by trapping with dipolarophiles. Acetylenes yield pyrazoles[160] which are isomeric to those formed thermally from the sydnone and the acetylene. With alkenes, 2-pyrazolines are generated.[160] For example, 3, 4-diphenylsydnone (**149**; $R^1 = R^2 = Ph$) on irradiation in the presence of cyclopentadiene affords the 2-pyrazoline (**164**)[160] and 2-vinylpyridine and 3-methyl-4-phenylsydnone (**149**; $R^1 = Me$, $R^2 = Ph$) yield the 2-pyrazoline (**165**).[172] For unsymmetrical alkenes, the observed regioselectivity of addition has been interpreted qualitatively in terms of M.O. perturbation theory.[160] In the presence of carbon disulphide, irradiation of diphenylsydnone (**149**; $R^1 = R^2 = Ph$) yields the adducts (**166**; R = Ph) and (**167**).[160] 3-Methyl-4-phenylsydnone (**149**; $R^1 = Me$, $R^2 = Ph$) similarly yields compound (**166**; R = Me) with carbon disulphide and the triazole (**168**) with phenyl isocyanate.[172] Irradiation of diphenylsydnone (**149**; $R^1 = R^2 = Ph$) in the presence of tetracyclone gives the oxadiazospiro compound (**169**).[173] The mechanism of formation of the unusual photoproduct (**170**), formed from 3-*t*-butyl-4-phenylsydnone (**149**; $R^1 = t$-Bu, $R^2 = Ph$), has been unravelled.[170]

Miscellaneous studies of the photochemistry of sydnones include the Z/E photoisomerism of 4-styrylsydnones[174,175] and 4-azomethine sydnones.[176] Irradiation of 3-morpholino-4-thiophenyl sydnone (**149**; R^1 = morpholino, R^2 = SPh) results in a remarkable rearrangement yielding the tetrapolar product (**171**).[177,178] In some cases, photooxygenation of sydnones has been shown to yield *N*, *N*′-diaroylhydrazines in addition to triazoles.[179]



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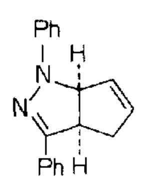
Scheme 5.



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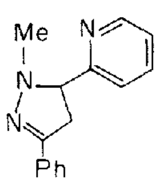

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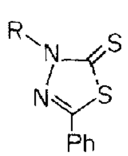

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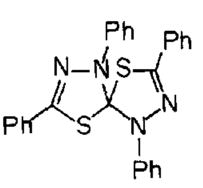

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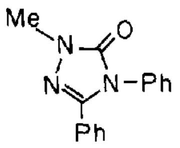

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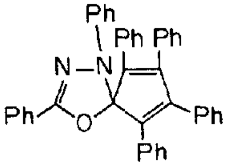

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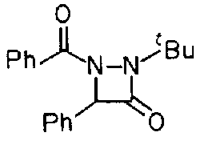

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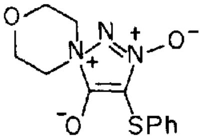

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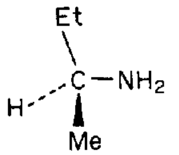
Acid catalysed hydrolysis of sydnones (**149**) yielding hydrazines provides a useful method of converting amines to hydrazines and has been used to synthesise the optically active (-)-(S) hydrazine (**173**) from the (+)-(S) amine (**172**).[180] Alkylhydrazines for oxidative studies have also been prepared by this method.[181]

The kinetics of base catalysed decomposition of 3-carboxyalkyl sydnones (**149**; $R^1 = (CH_2)_nCO_2H$, R^2=H) have been studied.[182] Other chemical studies on sydnones include: (i) reaction with 1,3,2-dioxaborolane-4-ones forming 1:1 adducts;[183] (ii) ring opening with triethylborane giving compounds of the type (**174**);[184] (iii) silylation of 4-lithiosydnones (**149**; R^2 = Li) to give 4-silasydnones.[185]



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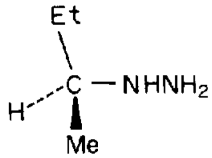

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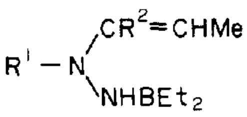
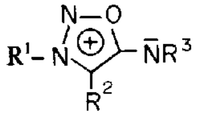


174

Physical and spectral properties of the sydnones have been the subject of several recent papers. X-Ray studies have been reported for 3-phenyl-4-(3-methyl-1-buten-2-yl) sydnone (**149**; R^1 = Ph, $R^2 = CH_2 = \overset{|}{C}\text{-}[CH(CH_3)_2]$),[186] 4-bromo-3-(3-pyridyl)sydnone (**149**; R^1 = 3-pyridyl, R^2 = Br),[187] 4(1-cyclohexenyl)-3-phenylsydnone (**149**; R^1 = Ph, R^2 = 1-cyclohexenyl),[188] 3(2-aminophenyl)sydnone (**149**; R^1 = o-$NH_2 \cdot C_6H_4$, R^2=H),[205] and the tricyclic derivative (**151**).[205] ^{14}N- and ^{15}N-NMR studies are in agreement with the meso-ionic formulation of sydnones.[189,190] Mass spectra[135,191] and UV spectra[192] have been recorded. Quantum yields and fluorescence decay times have been measured for several sydnones undergoing photoreactions.[193] The photochromic properties of sydnones have been the subject of several papers.[194–201] Dielectric constants, viscosities, densities and refractive indices have been recorded for several liquid 3-alkylsydnones:[202] 3-methylsydnone has been described as a good non-aqueous solvent which promotes ionisation of solutes.[203] The polarographic behaviour of several sydnones has also been studied[204] and theoretical investigations of the structure of sydnones have been described.[206–208]

The biological activity of sydnones was reviewed in 1967[209] and notable activity up to 1976 has been summarised.[6] Recent investigations of sydnones have claimed anti-inflammatory,[210–213] antimicrobial,[212–214] antimalarial[215] and CNS activity,[216] or a combination of activities.[217–219] A number of cephalosporin derivatives of sydnones have been prepared.[220–230]

2. 1, 2, 3-*Oxadiazolium-5-aminides* (*Sydnone imines*) (**175**).



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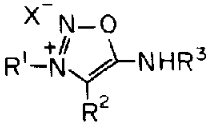

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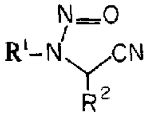

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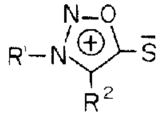
A comprehensive review of the chemistry and pharmacological properties of the sydnone imines (**175**) has been published recently.[231] The *N*-unsubstituted sydnone imines (**175**; $R^3 = H$) are unstable and isolable only as the salts (**176**; $R^3 = H$) which are prepared by acid-catalysed cyclisation of the appropriately substituted *N*-nitroso-α-amino acetonitriles (**177**):[232–234] the mechanism of this cyclisation has been examined in detail.[235–236] Reaction of the 5-amino-oxadiazolium salts (**176**; $R^3 = H$) with isocyanates[234,237] or acetic anhydride[238] yields *N*-carbamoyl and *N*-acetyl sydnone imines (**175**; $R^3 =$ CONHR or COMe) respectively. Cyclodehydration of *N*-nitroso-α-amino acetonitriles (**177**) with an acylating agent in the presence of triethylamine is a good method of preparing the *N*-acyl derivatives (**175**; $R^3 = COR$).[239,240]

Electrophilic halogenation of 4-unsubstituted sydnone imines affords 4-halo derivatives but halogenation of aryl substituents may also occur.[241] Alkaline hydrolysis of sydnone imines[242,243] and the mechanism of polarographic reduction[244] of *N*-acyl derivatives have been investigated. Various spectroscopic properties have been studied including ^{14}N-NMR,[189] IR[238] and UV spectra.[245]

Much work on sydnone imines (**175**) has been prompted by the pharmacological properties of Sydnophen (**176**; $R^1 = CHMe \cdot CH_2Ph$, $R^2 = R^3 = H$, $X = Cl$) and Sydnocarb (**175**; $R^1 = CHMe \cdot CH_2Ph$, $R^2 = H$, $R^3 = CONHPh$) which have significant psychotropic properties. Extensive studies of their properties have been reported.[246–277] Another sydnone imine of pharmacological interest is Molsidomine (**175**; $R^1 =$ *N*-morpholino, $R^2 = H$, $R^3 = CO_2Et$) which possesses haemodynamic properties.[278–289]

Work continues on the preparation of new sydnone imines and the investigation of their pharmacological activity.[290,291] *N*-Nitrososydnone imines (**175**; $R^1 = NO$) have been used as cross-linking agents in epoxy resins.[292–294]

3. 1, 2, 3-*Oxadiazolium-5-thiolates* (**178**).



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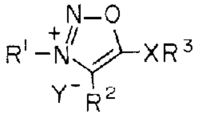

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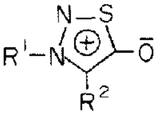

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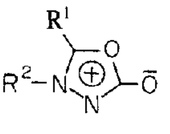
O-Alkylation of sydnones (**149**; $R^1 = Ph, Me$; $R^2 = H, Me, Ph$) with triethyloxonium tetrafluoroborate yields the corresponding salts (**179**; $X = O$, $R^3 = Et$, $Y = BF_4$) which on treatment with sodium hydrosulphide at low temperature afford the yellow meso-ionic 1, 2, 3-oxadiazolium-5-thiolates (**178**; $R^1 = Ph, Me$; $R^2 = H, Me, Ph$). This novel meso-ionic system (**178**); rearranges to the isomeric 1,2,3-thiadiazolium-5-olates (**180**) in ethanolic ammonia. With methyl iodide the meso-ionic derivatives (**178**) give the oxadiazolium iodides (**179**; $X = S$, $R^3 = Me$, $Y = I$).[295]

4. 1, 3, 4-*Oxadiazolium-2-olates* (*Isosydnones*) (**181**).

The isosydnones (**181**) are usually prepared by condensation of *N*-acyl-*N*-aryl (or alkyl) hydrazines [$R^1CO \cdot N(R^2)NH_2$] with phosgene. In a similar approach the bicyclic system (**182**) has been prepared by reaction of 4, 6-diphenyl-*N*-amino-α-pyridone (**183**) with *N*, *N'*-carbonyl diimidazole.[296] The same system (**182**) is also formed by treatment of compound (**183**) with arylisocyanates and pyrolysis of the resulting semicarbazide (**184**).[296]

In a different approach, isosydnones (**181**) have been prepared in excellent yield by treatment of 1,3,4-oxadiazolium-2-thiolates (**190**) (Section III H, 6) with 2, 4-6-trimethylphenyl cyanate.[297]

The mechanism and kinetics of the acid hydrolysis of isosydnones (**181**) to *N*-aroyl-*N*-arylhydrazines have been discussed.[298] Reaction of the derivatives (**181**; $R^1 = Ph$, $R^2 = Me, Ph$) with the dihydroisoquinoline-*N*-imines (**185**) yields the triazoloisoquinolines (**186**).[299] An X-ray spectroscopic study of 4, 5-diphenylisosydnone (**181**; $R^1 = R^2 = Ph$) has been reported.[205]



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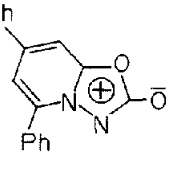

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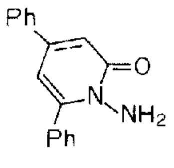

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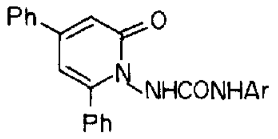

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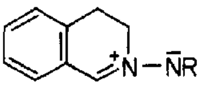

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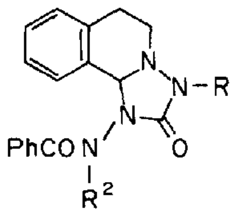

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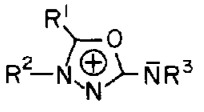

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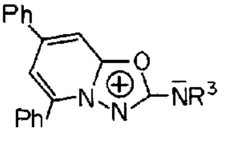

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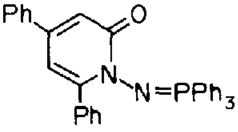

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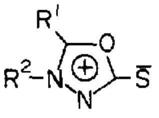
5. 1, 3, 4-*Oxadiazolium-2-aminides* (**187**).

Treatment of the *N*-aminopyridone (**183**) with triphenylphosphine dibromide gives the phosphine imine (**189**) which with aryl isocyanates or aryl isothiocyanate yields the bicyclic 1, 3, 4-oxadiazolium-2-aminides (**188**). Alternatively, de-oxygenation of the semicarbazides (**184**) using triphenylphosphine also yields the derivatives (**188**).[296]

6. 1, 3, 4-*Oxadiazolium-2-thiolates* (**190**).



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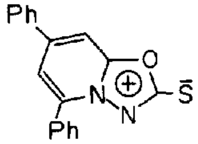

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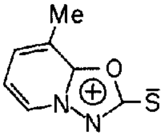

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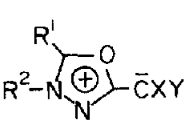
The bicyclic system (**191**) has been prepared by reaction of the phosphine imine (**189**) with carbon disulphide.[296] Compound (**192**) has been made by condensation of 1-amino-3-methyl pyrid-2-one with thiophosgene.[300]

The monocyclic derivatives (**190**) have been converted to 1,3,4-oxadiazolium-2-olates (**181**) by treatment with 2, 4, 6-trimethylphenyl cyanate.[297] Reaction of the compound (**190**; $R^1 = Ph$, $R^2 = Me$) with 3, 4-dihydroisoquinolin-*N*-imine (**185**; R = H) yields the 1, 2, 4-triazolium-3-thiolate (**194**) (59%).[299]

7. 1, 3, 4-*Oxadiazolium-2-methylides* (**193**).

No new work on this meso-ionic system (**193**) has been reported since the subject was last reviewed.[6]



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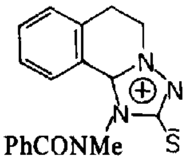

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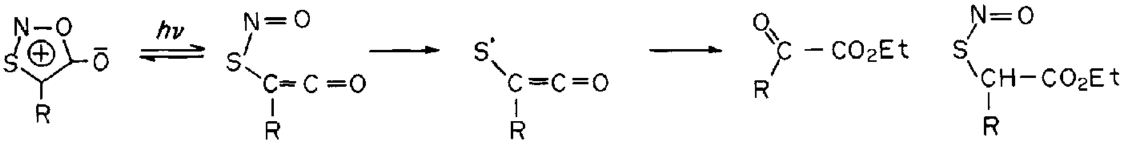
I. *Oxathiazoles*

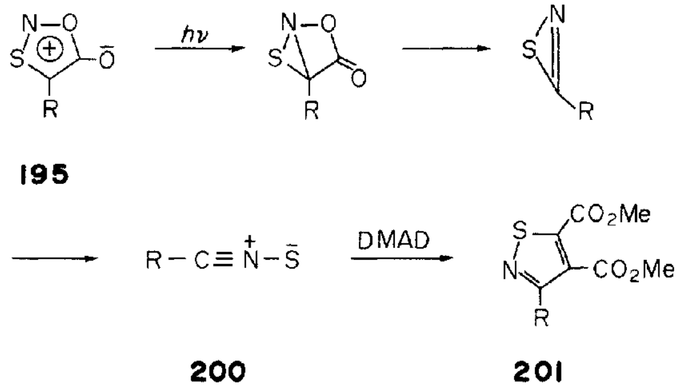
1. 1, 3, 2-*Oxathiazolium-5-olates* (**195**).



195 **196** **197** **198** **199**

Scheme 6.

The photochemistry of the phenyl derivative (**195**; R = Ph) has attracted special attention. Two photochemical processes can be distinguished. In the first process (Scheme 6) photolysis of the meso-ionic ring (**195**) reversibly generates the acyclic valence tautomer (**196**) which can be identified spectroscopically at low temperature.[301] Photochemical N-S bond cleavage then generates the radical (**197**) which is photooxidised and trapped by ethanol yielding the ester (**198**). The plausible intermediate (**199**) is not involved in the mechanism of formation of the ester (**198**).[302] A second photochemical pathway (Scheme 7) competes with the first pathway under some conditions and yields benzonitrile *via* the nitrile sulphide (**200**).[301,303-305] Evidence for the intermediacy of the nitrile sulphide (**200**) has been provided by UV spectroscopy[303] and by trapping with dimethyl acetylenedicarboxylate yielding 3-phenyl-4, 5-dimethoxycarbonyl isothiazole (**201**; R = Ph).[303]

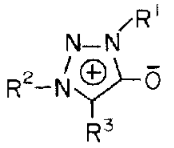


195 **200** **201**

Scheme 7.

J. *Triazoles*

1. 1, 2, 3-*Triazolium-4-olates* (**202**).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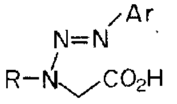
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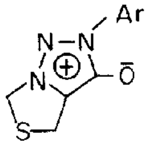
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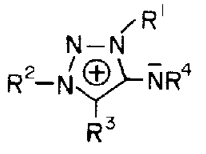
Treatment of aryldiazonium salts with α-aminoacids yields the arylazoaminoacetic acids (**203**) which are cyclodehydrated (Ac_2O/pyridine) giving meso-ionic 1,2,3-triazolium-4-olates (**202**; $R^1 = Ar$, $R^2 =$ alkyl, $R^3 = H$) in good yield. The compounds (**202**; $R^1 = Ar$, $R^2 =$ alkyl, $R^3 = H$) and some bicyclic derivatives (e.g. **204**) have been described as potent herbicides.[306,307]

2. 1, 2, 3-*Triazolium-4-aminides* (**205**).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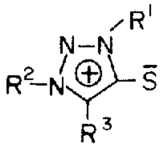
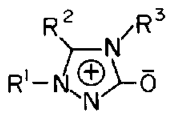

206

No new studies on this meso-ionic system (**205**) have been reported since the subject was last reviewed.[6]

3. 1, 2, 3-*Triazolium-4-thiolates* (**206**).

An X-ray structure determination of compound (**206**; $R^1 = R^2 = Me$, $R^3 = H$) has been reported.[308]

4. 1, 2, 4-*Triazolium-3-olates* (**207**).



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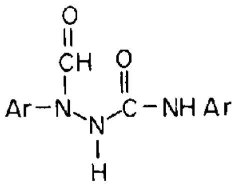

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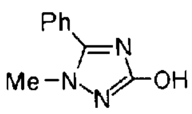

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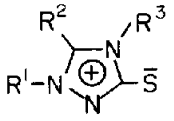

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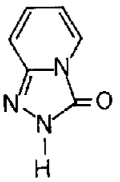

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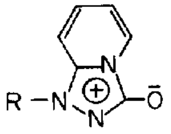


212

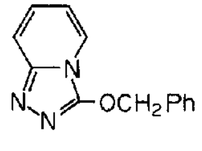
Meso-ionic 1,2,4-triazolium-3-olate derivatives (**207**) have been prepared by a wide variety of methods. Thermal ring closure of 1, 4-diaryl-1-formyl semicarbazides (**208**) yields 5-unsubstituted systems (**207**; $R^1 = R^3 = Ar$, $R^2 = H$).[169] An alternative synthesis is exemplified by the cycloaddition of phenylisocyanate to 3-phenylsydnone (**149**; $R^1 = Ph$, $R^2 = H$) giving compound (**207**; $R^1 = R^3 = Ph$, $R^2 = H$).[169] Methylation of the hydroxytriazole (**209**) with methyl iodide in aqueous sodium hydroxide gives primarily the meso-ionic product (**207**; $R^1 = R^3 = Me$, $R^2 = Ph$).[309] Treatment of meso-ionic 1,2,4-triazolium-3-thiolates (**210**) (Section III J, 6) with 2,4,6-trimethylphenyl cyanate also yields 1,2,4-triazolium-3-olates (**207**).[297]

Bicyclic systems (**212**) have also been prepared. Benzylation of 1, 2, 4-triazolo [4, 3-*a*] pyridin-3(2*H*)-one (**211**) yields some of the meso-ionic product (**212**; $R = PhCH_2$). A better method of preparing these compounds (**212**; R = alkyl) from (**211**) involves the following procedure: (i) trimethylsilylation; (ii) alkylation in the presence of $HgBr_2$ and (iii) decomposition of the $HgBr_2$ complex with H_2S or ion-exchange resin.[310] The system (**212**; R = Me) has been made by reaction of 1-methyl-1-(2-pyridyl) hydrazine with phosgene.[311]

The benzyloxytriazolopyridine (**213**) undergoes thermal rearrangement to the meso-ionic isomer (**212**; $R = PhCH_2$).[310] In contrast, the meso-ionic derivatives (**207**; $R^1 = Me$, $R^2 = SMe$, $R^3 = Ar$) rearrange to the 5-thioxo-1, 2, 4-triazolin-3-ones (**214**) on heating.[312] Pyrolysis of 1, 4, 5-triaryl-1, 2, 4-triazolium-3-olates (**207**; $R^1 = R^2 = R^3 = Ar$) yields *N*-(diarylmethylene) anilines (**215**).[169]

Photolysis of meso-ionic 1, 2, 4-triazolium-3-olates (**207**) has been investigated in some detail. The mixture obtained from photolysis of the 1, 4-diphenyl derivative (**207**; $R^1 = R^3 = Ph$, $R^2 = H$) consisted of benzimidazole (18%), azobenzene (4%) and methyl phenylcarbamate (25%).[169] The mechanisms of these transformations have been discussed. Irradiation of the triphenylderivative (**207**; $R^1 = R^2 = R^3 = Ph$) is believed to yield a polycyclic product having structure (**216**) or (**217**).[169]

A variety of polycyclic meso-ionic 1, 2, 4-triazolium-3-olates (**218**; X = O) have been prepared as anti-inflammatory agents.[313] 1, 2, 4-Triazolium-3-olate derivatives of cephalosporins have been patented as potential antibacterial agents.[314]



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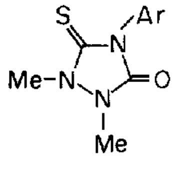

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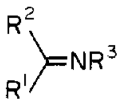

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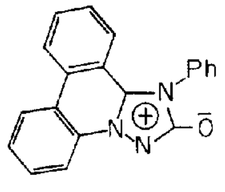

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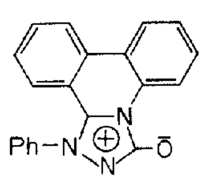

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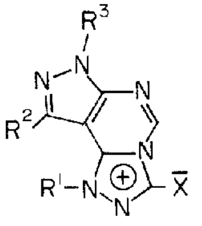

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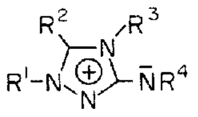


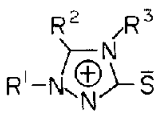
219

5. 1, 2, 4-*Triazolium-3-aminides* (**219**).

The structure of nitron (**219**; $R^1 = R^3 = R^4 = Ph$; $R^2 = H$) has been determined by X-ray crystallography. The results are consistent with its meso-ionic formulation.[315]

Meso-ionic 1, 2, 4-triazolium-3-benzylidenehydrazinides (**219**; $R^4 = N{=}CHAr$) have been prepared by reaction of 4-aryl-1,1-dibromo-2,3-diazabuta-1,3-dienes ($Br_2C{=}NN{=}CHAr$) with *N*-amino-*N*-methyl-*N'*-phenylbenzamidine.[316]

6. 1, 2, 4-*Triazolium-3-thiolates* (**220**).



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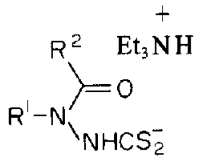

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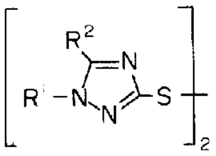

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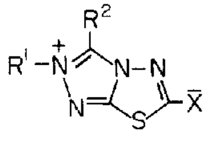

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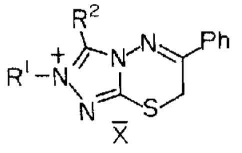

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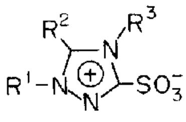


225

Rearrangement of the meso-ionic 1, 3, 4-thiadiazolium-2-benzylidenehydrazinides (**252**; $R^1 = Ph$, $R^2 = Me$ or Ph, $R^3 = N{=}CH{\cdot}p{\cdot}ClC_6H_4$ (Section III K, 9) in ethanolic ammonia solution gives the hydrazone derivatives (**220**; $R^1 = Me$ or Ph, $R^2 = Ph$, $R^3 = N = CH{\cdot}p{\cdot}Cl{\cdot}C_6H_4$) which are readily hydrolysed to the 4-amino derivatives (**220**; $R^3 = NH_2$).[316] 4-Amino-1, 2, 4-triazolium-3-thiolates (**220**; $R^3 = NH_2$) have also been prepared by reaction of the dithiocarbazates (**221**) with chloroacetic acid followed by cyclisation with hydrazine.[317,318] Treatment of the derivative (**220**; $R^1 = R^2 = Ph$, $R^3 = NH_2$) with nitrous acid yields the disulphide (**222**; $R^1 = R^2 = Ph$).[319] Alkylations and acylations of the *N*-amino derivatives (**220**; $R^3 = NH_2$) have been reported.[318] Condensation of these derivatives, (**220**; $R^3 = NH_2$) with phosgene yields the mesomeric betaines (**223**; X = O) and the derivatives (**223**; X = NCOPh, NSO_2Ph)

have been similarly prepared.[320,321] Treatment of the 4-amino derivatives (**220**; $R^3 = NH_2$) with phenacyl bromide affords the salts (**224**).[322]

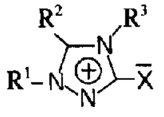
Syntheses of several bicyclic and polycyclic 1, 2, 4-triazolium-3-thiolates have been described[311,323-326] and antiinflammatory activity has been claimed.[313] Cephalosporin derivatives have been synthesised as anti-bacterial agents.[314]

Oxidation of the derivatives (**220**; $R^1 = Me$ or $PhCH_2$, $R^2 = H$, $R^3 = Ph$) gives the sulphonates (**225**).[327]

7. 1, 2, 4-*Triazolium-3-methylides* (**226**).

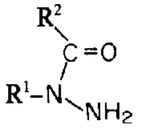
No new work on this meso-ionic system (**226**) has been reported since the subject was last reviewed.[6]

8. 1, 2, 4-*Triazolium-3-selenolates* (**227**).



226 X = CR₂

227 X = Se



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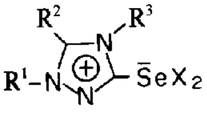
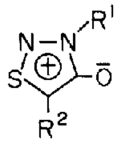


229

Reaction of the hydrazide derivatives (**228**) with phenylisoselenocyanate (PhNCSe) yields the meso-ionic 1, 2, 4-triazolium-3-selenolates (**227**).[328] Oxidation of compound (**227**; $R^1 = Me$, $R^2 = H$, $R^3 = Ph$) in the presence of magnesium perchlorate yields 1-methyl-4-phenyl-1, 2, 4-triazolium perchlorate.[329] Bromination of these compounds results in expansion of the selenium co-ordination sphere giving the derivatives (**229**; X = Br).[329] Chloro (**229**; X = Cl) and thiocyano (**229**; X = SCN) derivatives have been similarly prepared.[327]

K. *Thiadiazoles*

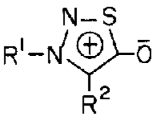
1. 1, 2, 3-*Thiadiazolium-4-olates* (**230**).



230

The 5-unsubstituted derivative (**230**; $R^1 = p\cdot MeO\cdot C_6H_4$, $R^2 = H$) undergoes electrophilic substitution giving 5-formyl, 5-chloro, 5-dimethylaminomethyl and 5-methythio derivatives (**230**; $R^1 = p\cdot MeO\cdot C_6H_4$, $R^2 = CHO$, Cl, Me_2NCH_2 or SMe). The 5-formyl derivative (**230**; $R^1 = p\cdot MeO\cdot C_6H_4$, $R^2 = CHO$) has been converted into the novel meso-ionic 1, 2, 3-thiadiazolium-5-aminide (**233**; $R^1 = p\cdot MeO\cdot C_6H_4$, $R^2 = OMe$, $R^3 = CO_2Et$) (Section III K, 3).[330]

2. 1, 2, 3-*Thiadiazolium-5-olates* (**231**).



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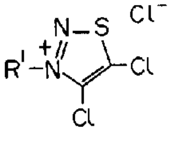


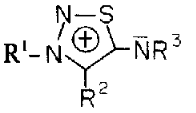
232

A general route to this new meso-ionic system (**231**) involves rearrangement of the isomeric meso-ionic 1, 2, 3-oxadiazolium-5-thiolates (**178**) (Section III H, 3) in hot ethanolic ammonia.[295] This general type of rearrangement of type A meso-ionic systems has been reviewed.[6] The system (**231**) is readily alkylated at the exocyclic oxygen atom by Meerwein's reagent.[295]

The first examples of this system to be reported were 3-aryl-4- chloroderivatives (**231**; $R^1 = Ar$, $R^2 = Cl$) prepared by hydrogen peroxide oxidation of the dichlorothiadiazolium salts (**232**; $R^1 = Ar$).[331]

The 4-chloro-3-phenyl derivative (**231**; $R^1 = Ph$, $R^2 = Cl$) prepared by this method is identical with a sample prepared by chlorination of the 4-unsubstituted compound (**231**; $R^1 = Ph$, $R^2 = H$).[295]

3. 1, 2, 3-*Thiadiazolium-5-aminides* (**233**).



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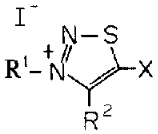
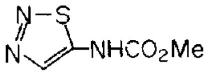


234 X = SMe

235 X = NHMe

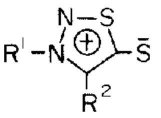


236

The methiodide (**234**; $R^1 = Ph$, $R^2 = H$) prepared from the meso-ionic 1, 2, 3-thiadiazolium-5-thiolate (**237**; $R^1 = Ph$, $R^2 = H$) (Section III K, 4) reacts with methylamine giving compound (**235**; $R^1 = Ph$, $R^2 = H$). Deprotonation of this salt gives the yellow meso-ionic 1, 2, 3-thiadiazolium-5-aminide (**233**; $R^1 = Ph$, $R^2 = H$, $R^3 = Me$).[295]

Alkylation of the meso-ionic 1, 2, 3-thiadiazolium-4-olate (**230**; $R^1 = p\cdot MeO\cdot C_6H_4$, $R^2 = NHCO_2Et$) (Section III K, 1) with excess methyl fluorosulphonate and subsequent deprotonation yields the derivative (**233**; $R^1 = p\cdot MeO\cdot C_6H_4$, $R^2 = OMe$, $R^3 = CO_2Et$).[330] A third example of this system (**233**) has been prepared by alkylation of the 1, 2, 3-thiadiazole (**236**). The structure of this product (**233**; $R^1 = Me$, $R^2 = H$, $R^3 = CO_2Me$) has been confirmed by X-ray crystallography.[332]

4. 1, 2, 3-*Thiadiazolium-5-thiolates* (**237**).



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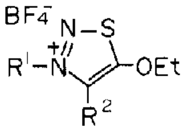

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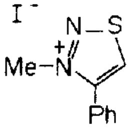
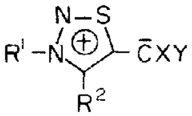


239

The first examples of this meso-ionic system (**237**) have been prepared by treatment of the salts (**238**) with sodium hydrosulphide at −70°C.[295] Alternatively, treatment of the iodide (**239**) with cold methanolic sodium methoxide yields compound (**237**; $R^1 = Me$, $R^2 = Ph$) whose structure has been confirmed by X-ray crystallography. A mechanism has been proposed for this unexpected reaction (**239**→**237**; $R^1 = Me$, $R^2 = Ph$).[333,334]

Compound (**237**; $R^1 = Ph$, $R^2 = H$) is methylated by methyl iodide affording the salt (**234**; $R^1 = Ph$, $R^2 = H$) which is a useful intermediate for preparing 1, 2, 3-thiadiazolium-5-aminides (**233**) (Section III K, 3) and 1, 2, 3-thiadiazolium-5-methylides (**240**) (Section III K, 5).[295]

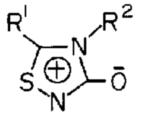
5. 1, 2, 3-*Thiadiazolium-5-methylides* (**240**).



240

Only a single member of this class has been reported. Treatment of the 1, 2, 3-thiadiazolium salt (**234**; $R^1 = Ph$, $R^2 = H$) with malononitrile in the presence of triethylamine yields the orange-yellow derivative (**240**; $R^1 = Ph$, $R^2 = H$, $X = Y = CN$).[295]

6. 1, 2, 4-*Thiadiazolium-3-olates* (**241**).



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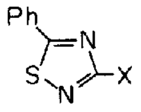
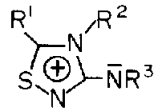


242 X = OH
243 X = NH_2
244 X = $NHSO_2 \cdot C_6H_4 \cdot 4Me$

Methylation of 3-hydroxy-5-phenyl-1, 2, 4-thiadiazole (**242**) using methyl toluene-4-sulphonate yields a variety of methylated products including a small amount (10%) of the meso-ionic 1, 2, 4-thiadiazolium-3-olate (**241**; R^1 = Ph, R^2 = Me) which has been fully characterised.[335] Alkaline hydrolysis of this compound gives *N*-benzoyl-*N*-methyl urea (12%) and *N*-methylbenzamide (24%).[335]

7. 1, 2, 4-*Thiadiazolium-3-aminides* (**245**).



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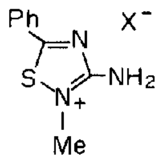
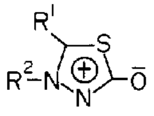


246

Methylation of the 3-sulphonamido-1, 2, 4-thiadiazole (**244**) using methyl fluorosulphonate yields all three possible *N*-monomethylated nitrogen compounds including the meso-ionic 1, 2, 4-thiadiazolium-3-aminide (**245**; R^1 = Ph, R^2 = Me, $R^3 = SO_2 \cdot C_6H_4 \cdot 4Me$) (18.5%).[335]

A report[336] of the synthesis of compound (**245**; R^1 = Ph, R^2 = Me, R^3 = H) by methylation of compound (**243**) and deprotonation has been shown to be incorrect. Methylation, in fact, gives the 2-methyl salt (**246**; X = I) which in the presence of base undergoes a Dimroth rearrangement.[337]

8. 1, 3, 4-*Thiadiazolium-2-olates* (**247**).



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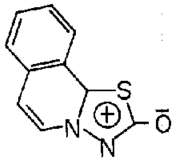

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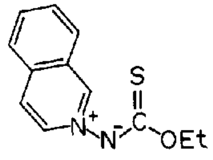

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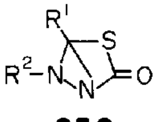

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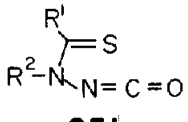
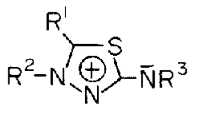


251

A new synthesis of the meso-ionic system (**247**) involves treatment of the corresponding meso-ionic 1, 3, 4-thiadiazolium-2-thiolate (**254**) (Section III K, 10) with 2, 4, 6-trimethylphenyl cyanate.[297] The tricyclic system (**248**) has been obtained by irradiation of the isoquinolinium-*N*-imide derivative (**249**).[338,339] Upon prolonged irradiation in ethanol solution compound (**248**) undergoes further reaction giving 1-ethoxycarbonylaminoisoquinoline.[338]

The photochemical behaviour of the 1, 3, 4-thiadiazolium-2-olates (**247**) has been reinvestigated.[340] Two competing processes each involving valence tautomerism have been identified. Formation of the bicyclic tautomer (**250**) leads to generation of a nitrile-imine and carbon oxysulphide: formation of the acyclic tautomer (**251**) leads to thioamide derivatives.[340]

9. 1, 3, 4-*Thiadiazolium-2-aminides* (**252**).



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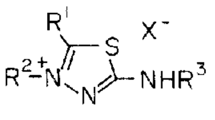
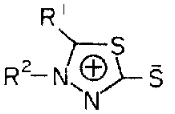


253

Reaction of 2-amino-4, 5-dimethyl-1, 3, 4-thiadiazolium iodide (**253**; $R^1 = R^2 = Me$, $R^3 = H$, $X = I$) with one equivalent of diethyl benzoylphosphonate [$(EtO)_2PO \cdot COPh$] yields the meso-ionic 1, 3, 4-thiadiazolium-2-aminide (**252**; $R^1 = R^2 = Me$, $R^3 = COPh$) as the major product (36%).[341] This product was identical with a sample prepared by condensation of *N*-methyl-*N*-thioacetylhydrazine ($MeCS \cdot NMe \cdot NH_2$) with benzoylisothiocyanate.[341]

1, 3, 4-Thiadiazolium-2-aminides possessing the novel exocyclic benzylidenehydrazinide grouping (**252**; $R^3 = N = CHR$) have been prepared by condensation of dibromodiazabutadienes ($ArCH{=}N \cdot N{=}CBr_2$) with *N*-thiobenzoyl hydrazines ($PhCS{\cdot}NR{\cdot}NH_2$) and deprotonation of the resulting 1,3,4-thiadiazolium bromides (**253**; $R^1 = Ph$, $R^2 = Me$ or Ph, $R^3 = N{=}CHAr$).[316] In aqueous ethanolic ammonia solution, rearrangement of the meso-ionic derivative (**252**; $R^1 = Ph$, $R^2 = Me$, $R^3 = N{=}CH \cdot pClC_6H_4$) to the isomeric meso-ionic 1, 2, 4-triazolium-3-thiolate (**220**; $R^1 = Me$, $R^2 = Ph$, $R^3 = N{=}CH \cdot pClC_6H_4$) is observed.[316] The same derivative (**252**; $R^1 = Ph$, $R^2 = Me$, $R^3 = N{=}CH \cdot pClC_6H_4$) forms a 1, 3-dipolar cycloadduct with 4-phenyl-1, 2, 4-triazoline-3,5-dione.[316]

10. 1, 3, 4-*Thiadiazolium-2-thiolates* (**254**).



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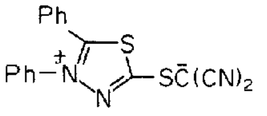

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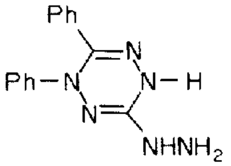
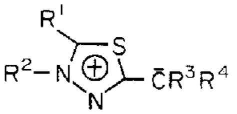


256

Meso-ionic 1, 3, 4-thiadiazolium-2-thiolates (**254**) are well known. Several new tricyclic derivatives have been prepared.[326] The diphenyl derivative (**254**; $R^1 = R^2 = Ph$) yields the interesting zwitterion (**255**) with tetracyanoethylene oxide[342] and the 3-amino-tetrazine (**256**) with hydrazine.[343] Photolysis of compound (**254**; $R^1 = Ph$, $R^2 = Me$) in moist acetonitrile gives *N*-methylthiobenzamide.[340]

The effect of solvent on the electronic absorption spectra of several systems has been discussed.[344] Some derivatives have been claimed as anti-convulsants.[345,346]

11. 1, 3, 4-*Thiadiazolium-2-methylides* (**257**).

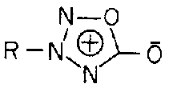


257

Treatment of *N*-methyl-*N*-thiobenzoylhydrazide with phenylthioacetylthioglycolic acid ($PhCH_2CS \cdot SCH_2CO_2H$) yields the derivative (**257**; $R^1 = R^3 = PH$, $R^2 = ME$, $R^4 = CS \cdot CH_2PH$), the structure of which has been determined by X-ray crystallography.[347]

L. *Oxatriazoles*

1. 1, 2, 3, 4-*Oxatriazolium-5-olates* (**258**).



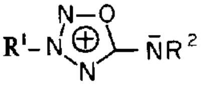
258

An X-ray analysis of the 3-phenyl derivative (**258**; R = Ph) is in agreement with the meso-ionic structure.[348] Further support for the structure of these compounds has been provided by their mass spectra[349] and electric dipole moments.[350]

Irradiation of compound (**258**; R = Ph) yields phenyl azide by a mechanism which involves phenyl migration and not an antiaromatic triazene intermediate. A second, minor, pathway yields phenylisocyanate and nitrous oxide.[351] The kinetics of acid hydrolysis of the 3-methyl (**258**; R = Me) and 3-isopropyl (**258**; R = isoPr) derivatives have been investigated.[352,353]

Some aryl derivatives (**258**; R = Ar) have been claimed to have pesticidal and herbicidal activity.[354]

2. 1, 2, 3, 4-*Oxatriazolium-5-aminides* (**259**).



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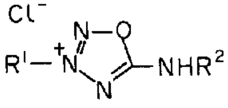
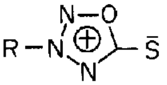


260

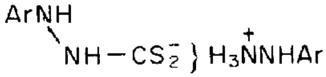
Nitrosation of 1, 4-diarylthiosemicarbazides yields the 1, 2, 3, 4-oxatriazolium chlorides (**260**) which are deprotonated by dry ammonia affording the meso-ionic 1, 2, 3, 4-oxatriazolium-5-aminides (**259**; R^1 and R^2 = Ar).[355] In hot ethanolic sodium hydroxide solution these diaryl derivatives (**259**; R^1 and R^2 = Ar) rearrange to meso-ionic 1, 2, 3, 4-tetrazolium-5-olates (**263**) (Section III M, 1). Meso-ionic systems possessing four heteroatoms are usually unreactive towards 1, 3-dipolarophiles. It is interesting to note, therefore, that the diphenyl compound (**259**; $R^1 = R^2$ = Ph) with *p*-chlorophenylisocyanate yields the *p*-chlorophenyl derivative (**259**; R^1 = Ph, $R^2 = p\text{-Cl}\cdot C_6H_4$) (55%)—presumably *via* cycloaddition and cycloreversion.[355]

Recent physical studies on this meso-ionic system (**259**) include: (i) an X-ray investigation of the diphenyl compound (**259**; $R^1 = R^2$ = Ph);[356] (ii) measurements of electric dipole moments of three diaryl derivatives;[350] and (iii) a discussion of their mass spectral fragmentation pattern.[349] Some derivatives have been claimed to possess pesticidal and herbicidal properties.[354]

3. 1,2,3,4-*Oxatriazolium-5-tholates* (**261**).



261



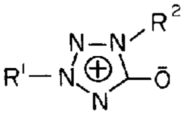
262

3-Aryl-1, 2, 3, 4-oxatriazolium-5-thiolates (**261**) have been prepared by nitrosation of the dithiocarbazinic acid salts (**262**).[357] The meso-ionic structure is supported by their mass spectra[349] and electric dipole moments.[350]

1, 2, 3, 4-Oxatriazolium-5-thiolates (**261**) are isomerised to meso-ionic 1, 2, 3, 4-thiatriazolium-5-olates (**271**) (Section III N, 1) in hot ethanolic ammonia solution.[357] Pesticidal and herbicidal activity has been claimed for compounds of this type.[354]

M. *Tetrazoles*

1. 1, 2, 3, 4-*Tetrazolium-5-olates* (**263**).



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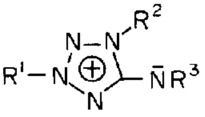


264

Diaryl derivatives (**263**; R^1 and R^2 = Ar) have been prepared by rearrangement of meso-ionic 1,2,3,4-oxatriazolium-5-aminides (**259**) (Section III L, 2) in ethanolic alkali and by treatment of potassium arylhydrazonomethanedisulphonates with aryldiazonium chlorides.[355] The diphenyl compound (**263**;

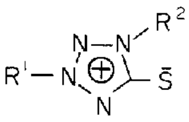
R^1=R^2=Ph) has also been made (45%) by thermal rearrangement of the type B meso-ionic 1,2,3,4-tetrazolium-5-olate (**307**; $R^1 = R^2$ = Ph) (Section IV G, 1).[141,358]

The meso-ionic structure (**263**) is supported by mass spectral[349] and electric dipole moment studies.[350] Pesticidal and herbicidal activities have been claimed.[354]

2. 1, 2, 3, 4-*Tetrazolium-5-aminides* (**264**).

No new studies on this system (**264**) have been reported since the subject was last reviewed.[6]

3. 1, 2, 3, 4-*Tetrazolium-5-thiolates* (**265**).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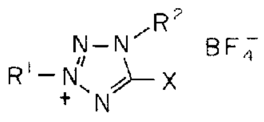
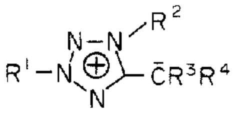

266

Treatment of the tetrazolium tetrafluoroborates (**266**; R^1 and R^2 = Ar, X = OEt) with sodium sulphide in dimethylformamide affords the 1, 3-diaryl-1, 2, 3, 4-tetrazolium-5-thiolates (**265**; R^1 and R^2 = Ar).[359] In a similar fashion, the derivative (**265**; R^1 = Et, R^2 = Ph) has been prepared by reaction of the salt (**266**; R^1 = Et, R^2 = Ph, X = SMe) with sodium hydrosulphide in methanol solution.[360,361] The diphenyl derivative (**265**; $R^1 = R^2$ = Ph) is obtained in low yield by thermal rearrangement of dehydrodithizone (Section IV G, 3).[141,358]

Recent structural studies on this meso-ionic system (**265**) include: (i) an X-ray investigation of the diphenyl derivative (**265**; $R^1 = R^2$ = Ph);[205] (ii) an analysis of the ^{13}C-NMR spectrum of compound (**265**; R^1 = Et, R^2 = Ph);[360] (iii) electric dipole moment measurements[350] and (iv) an analysis of the mass spectral fragmentation pattern.[349]

4. 1, 2, 3, 4-*Tetrazolium-5-methylides* (**267**).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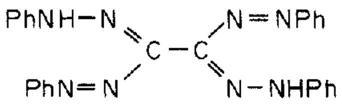
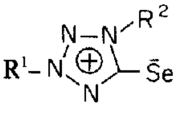

268

Diformazyl, the product obtained by Bamberger and co-workers in 1893 by treatment of the acids [$RCH_2CH_2CO_2H$; R = MeCO, or $HO_2C(CH_2)_2CO$] with phenyldiazonium hydroxide,[362,363] has recently been shown to be the meso-ionic compound (**267**; $R^1 = R^2$ = Ph, $R^3 = R^4 = N_2Ph$) and not the biformazan (**268**) as originally formulated.[364] The structure (**267**; $R^1 = R^2$ = Ph, $R^3 = R^4 = N_2Ph$) has been confirmed by an X-ray analysis of its hydrochloride salt. Ozonolysis of diformazyl (**267**; $R^1 = R^2$ = Ph, $R^3 = R^4 = N_2Ph$) yields 1, 3-diphenyl-1, 2, 3, 4-tetrazolium-5-olate (**263**; $R^1 = R^2$ = Ph) (Section III M, 1).[364]

Reaction of the tetrazolium tetrafluoroborates (**266**; R^1 and R^2 = Ar, X = OEt) with malononitrile in triethylamine yields the derivatives (**267**; R^1 and R^2 = Ar, $R^3 = R^4$ = CN).[365] The electric dipole moment[350] and mass spectrum[349] of compound (**267**; $R^1 = R^2$ = Ph, $R^3 = R^4$ = CN) (μ = 9.54D) support its meso-ionic structure.

5. 1, 2, 3, 4-*Tetrazolium-5-selenolates* (**269**).

This novel selenium containing meso-ionic heterocycle has recently been synthesised. Treatment of the 5-methylthiotetrazolium salt (**270**) with sodium hydrogen selenolate (NaSeH) yields 3-ethyl-1-phenyl-1, 2, 3, 4-tetrazolium-5-selenolate (**269**; R^1 = Et, R^2 = Ph).[360,361]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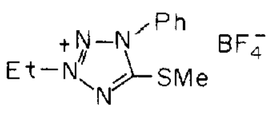
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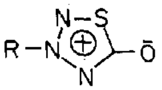
N. *Thiatriazoles*

1. 1, 2, 3, 4-*Thiatriazolium-5-olates* (**271**).



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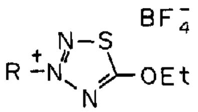


272

273

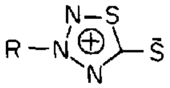
Examples of this system (**271**) have been prepared by rearrangement of meso-ionic 1,2,3,4-oxatriazolium-5-thiolates (**261**) (Section III L, 3) is hot ethanolic ammonia.[357]

Studies on their mass spectral fragmentation patterns[349] and electric dipole moments[350] have been reported. Treatment with triethyloxonium tetrafluoroborate gives the thiatriazolium salts (**272**).[357] Some derivatives of this meso-ionic system (**271**) have been claimed to have useful pesticidal and herbicidal activity.[354]

2. 1, 2, 3, 4-*Thiatriazolium-5-aminides* (**273**).

The meso-ionic 1, 2, 3, 4-thiatriazolium-5-aminides (**273**; R^1 and $R^2 = Ar$) have been prepared by reaction of the salts (**272**) with aromatic amines followed by treatment with base.[359]

3. 1, 2, 3, 4-*Thiatriazolium-5-thiolates* (**274**).



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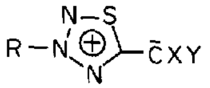


275

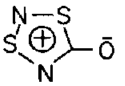
Treatment of the 5-ethoxy-1, 2, 3, 4-thiatriazolium tetrafluoroborates (**272**; R = Ar) with sodium sulphide in aqueous dimethyl formamide yields the meso-ionic 1, 2, 3, 4-thiatriazolium-5-thiolates (**274**).[357] The structure (**274**) is supported by mass spectrometry.[349]

4. 1, 2, 3, 4-*Thiatriazolium-5-methylides* (**275**).

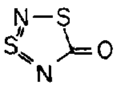
Treatment of the salts (**272**; R = Ar) with malononitrile in the presence of triethylamine yields the meso-ionic 1, 2, 3, 4-thiatriazolium-5-methylides (**275**; X = Y = CN).[365] Mass spectra[349] and electric dipole moments [350] have been measured.

O. *Dithiadiazoles*

1. 1, 3, 2, 4-*Dithiadiazolium-5-olate* (**276**).



276



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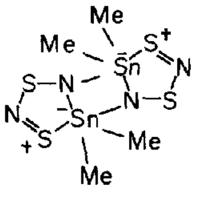

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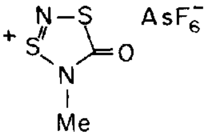
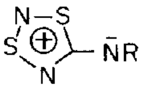


279

This new heterocycle has recently been synthesised by two different methods. Reaction of the dimeric 1, 3, 2, 4, 5-dithiadiazastannole (**278**) with excess phosgene or carbonyldifluoride gives the heterocycle (**276**) in moderately good yield (*ca.* 50%).[366] Alternatively, treatment of *N, N'-bis* (trimethylsilyl)sulphur diimide ($Me_3SiN = S = NSiMe_3$) with 1-(chlorothio)formyl chloride ($ClCO \cdot SCl$) also gives compound (**276**) (46%).[367]

The structure of this meso-ionic compound **(276)** has been confirmed by an X-ray analysis.[368] The extent of the participation of sulphur *d*-orbitals in the bonding of this heterocycle **(276 ↔ 277)** is not clear. With Lewis acids, 1 : 1 adducts (BF_3, SO_3, AsF_5, $SbCl_5$ SbF_2Cl_3) or 2 : 1 adducts ($SnCl_4$, $TiCl_4$) are formed by complexing through the oxygen atom.[368,369] Interestingly, methylation of this heterocycle **(276)** using $MeOSO^+AsF_6^-$ results in *N*-methylation giving the salt **(279)**.[370]

2. 1, 3, 2, 4-*Dithiadiazolium-5-aminides* **(280)**.



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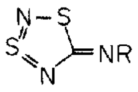

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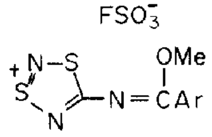


282

The derivatives **(280)** have been prepared by reaction of *N*-acyl-1-(chlorothio)formimidoyl chlorides ($RCO \cdot N = CCl \cdot SCl$) with *N, N'-bis* (trimethylsilyl)sulphur diimide ($Me_3SiN = S = NSiMe_3$).[367,371] The structure of compound (**280**; $R = p Me \cdot C_6H_4 \cdot CO$) has been confirmed by an X-ray study.[367,372] The extent of *d*-orbital participation in the π-bonding of these molecules (i.e. **280↔281**) is not clear. Methylation (FSO_3Me) of the derivatives (**280**; $R = COAr$) results in *O*-methylation to give the salts **(282)**.[367,371]

IV. THE CHEMISTRY OF MESO-IONIC COMPOUNDS OF TYPE B (1976–1980)

These systems are discussed in the order given in Table 2. Since the review by Ollis and Ramsden in 1976,[6] derivatives of 4 new type B meso-ionic systems have been reported bringing the total number of known systems up to 13.

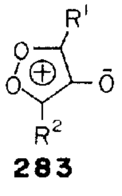
Table 2. Known meso-ionic heterocycles of type B(**10**)

		Atom or Group[a]					
Parent System	Heterocycle	a	b	c	d	e	f
Oxazoles							
1,2-Oxazolium-4-olates	**(285)**	CR	O	NR	CR	C	O
1,2-Oxazolium-4-aminides	**(287)**	CR	O	NR	CR	C	NR
Diazoles							
1,2-Diazolium-4-olates	**(288)**	CR	NR	NR	CR	C	O
1,2-Diazolium-4-aminides	**(290)**	CR	NR	NR	CR	C	NR
Thiazoles							
1,2-Thiazolium-4-olates	**(291)**	CR	S	NR	CR	C	O
1,2-Thiazolium-4-aminides	**(294)**	CR	S	NR	CR	C	NR
Dithioles							
1,2-Dithiolium-4-olates	**(295)**	CR	S	S	CR	C	O
1,2-Dithiolium-4-thiolates	**(302)**	CR	S	S	CR	C	S
Thiadiazoles							
1,2,5-Thiadiazolium-3-olates	**(304)**	N	S	NR	CR	C	O
Tetrazoles							
1,2,3,4-Tetrazolium-5-olates	**(307)**	N	NR	NR	N	C	O
1,2,3,4-Tetrazolium-5-aminides	**(310)**	N	NR	NR	N	C	NR
1,2,3,4-Tetrazolium-5-thiolates	**(311)**	N	NR	NR	N	C	S
1,2,3,4-Tetrazolium-5-methylides	**(320)**	N	NR	NR	N	C	CXY

[a] The groupings b and c each contribute 2 electrons to the π-electron system of the heterocycle; a, d, e, and f each contribute 1 electron.

A. *Dioxoles*

1. 1, 2, *Dioxolium-4-olates* **(283)**.



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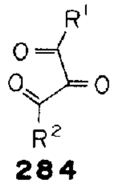
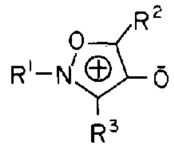


284

In principle, the 1, 2, 3-propane-triones (**284**) can exist in equilibrium with the meso-ionic valence tautomers (**283**). An X-ray study of the triketone (**284**; $R^1 = R^2 = p\cdot BrC_6H_4$) confirmed the absence of any valence tautomerism (**283**⇌**284**) and attempts to promote reactions of the meso-ionic species (**283**) in solutions of the triketone (**284**; $R^1 = R^2 = Ph$) were also unsuccessful.[373]

B. *Oxazoles*

1. 1, 2-*Oxazolium-4-olates* (**285**).



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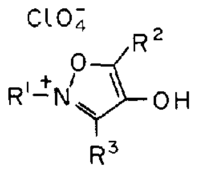

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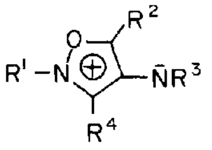


287

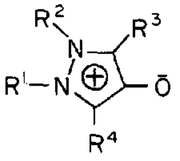
Meerwein methylation of 4-hydroxy-3, 5-diphenylisoxazole leads to the oxazolium perchlorate (**286**; $R^1 = Me$, $R^2 = R^3 = Ph$) which on treatment with methanolic alkali affords the yellow, unstable 1,2-oxazolium-4-olate (**285**; $R^1 = Me$, $R^2 = R^3 = Ph$) (84%), m.p. 76–78°.[374]

2. 1, 2-*Oxazolium-4-aminides* (**287**).

No new work has been reported on this system since the subject was last reviewed.[6]

C. *Diazoles*

1. 1, 2-*Diazolium-4-olates* (**288**).



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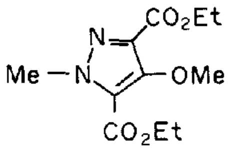
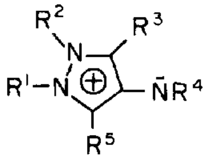


289

A large number of meso-ionic 1, 2-diazolium-4-olate derivatives (**288**; $R^1 = Me$, $R^2 = Me$, Ph, R^3 and $R^4 = Me$, Ph, CO_2Et) have been prepared by methylation (Me_2SO_4) of 4-hydroxy pyrazoles. The tetramethyl derivative is obtained by condensation of *N,N*-dimethyl hydrazine with 2-acetoxy-1,3-dimethylpropane-1,3-dione (Ac_2CHOAc). Compound (**288**; $R^1 = R^2 = Me$, $R^3 = R^4 = CO_2Et$) is unreactive towards acetylenes but slowly isomerised to the 4-methoxy pyrazole (**289**).[375]

2. 1, 2-*Diazolium-4-aminides* (**290**).

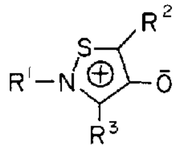


290

An X-ray analysis of the crystal structure of compound (**290**; $R^1 = R^2 = R^3 = R^5 = Me$, $R^4 = p$-$MeC_6H_4\cdot SO_2$) has been reported and the results are consistent with the meso-ionic formulation.[376]

D. *Thiazoles*

1. 1, 2-*Thiazolium-4-olates* (**291**).



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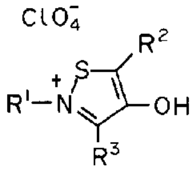

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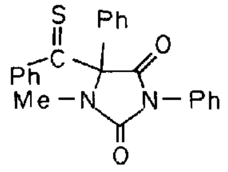
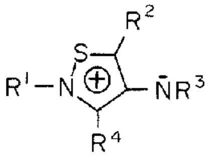


293

Two independent groups have recently achieved the synthesis of derivatives of this novel type B meso-ionic system.[121,377] Alkylation of 3, 5-diaryl-4-hydroxy isothiazoles gives the salts (**292**; $R^1 = Me$, $R^2 = R^3 = Ar$) which on treatment with base yield the red 1, 2-thiazolium-4-olates (**291**; $R^1 = Me$, $R^2 = R^3 = Ar$).[121,377] These compounds are methylated on the exocyclic oxygen atom by dimethyl sulphate.[377] With phenyl isocyanate in hot xylene the derivative (**291**; $R^1 = Me$, $R^2 = R^3 = Ph$) yields a blue compound which has been formulated as the hydantoin (**293**).[121]

The absorption spectra and dipole moments of 1, 2-thiazolium-4-olate derivatives (**291**) have been discussed.[378]

2. 1, 2-*Thiazolium-4-aminides* (**294**).

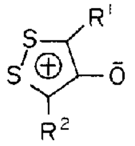


294

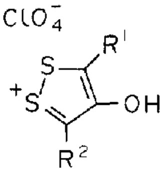
No new work on this meso-ionic system (**294**) has been reported since the subject was last reviewed.[6]

E. *Dithioles*

1. 1, 2-*Dithiolium-4-olates* (**295**).



295



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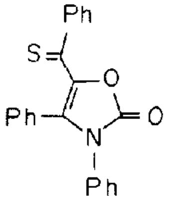


297

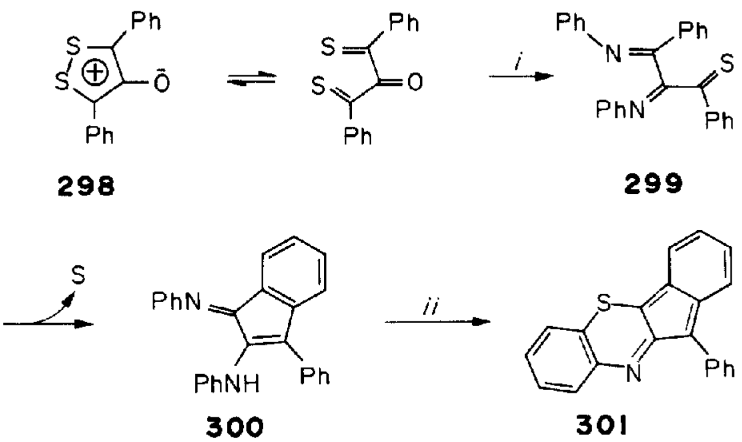
A new method of preparing derivatives of this meso-ionic system (**295**) involves treatment of propane-1, 3-dione esters ($(RCO)_2CHOAc$) with hydrogen disulphide or tetraphosphorus decasulphide followed by perchloric acid to give the salts (**296**) which are deprotonated by pyridine. This type of route has been used to prepare alkyl, thioalkyl and aryl derivatives (**295**; R^1 or $R^2 = $ Alkyl, S·Alkyl or Aryl).[379–382] Compound (**295**; $R^1 = Ph$, $R^2 = SMe$) is converted into the derivative (**295**; $R^1 = Ph$, $R^2 = p \cdot Me_2NC_6H_4$) by treatment with *N,N*-dimethylaniline.[382]

Several interesting transformations of the diphenyl derivative (**295**; $R^1 = R^2 = Ph$) have been reported. Reaction with phenyl isocyanate yields the 1, 3-oxazol-2-one (**297**) by a mechanism which presumably involves extrusion of sulphur.[121] Treatment with ammonia gives 3, 5-diphenyl-4-hydroxyisothiazole.[121,377] Reaction of 3, 5-diphenyl-1, 2-dithiolium-4-olate (**298**; $R^1 = R^2 = Ph$) with boiling aniline gives the blue benzothiazine (**301**)[121,383] and not 3, 4, 5-triphenylisothiazole as described by earlier workers.[384] A by-product in this reaction is the maroon indenylamine (**300**) which is probably formed by the sequence shown in Scheme 8.[121] In the presence of sulphur, boiling aniline converts compound (**300**) into the blue benzothiazine (**301**) suggesting that the indenylamine (**300**) is an intermediate in the transformation (**298**→**301**) (Scheme 8).[121,383]

Two X-ray investigations have confirmed the meso-ionic structure of compound (**295**; $R^1 = R^2 = Ph$).[373,378] Dipole moments and ^{13}C-NMR spectra have also been reported of 1, 2-dithiolium-4-olate derivatives (**295**).[378]

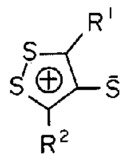
2. 1, 2-*Dithiolium-4-thiolates* (**302**).

Compound (**302**; $R^1 = CN$, $R^2 = NHCOPh$), the first example of this class of type B meso-ionic heterocycle, has been prepared from the dithiole derivatives (**303**). The highly functionalised nature of this meso-ionic molecule (**302**; $R^1 = CN$, $R^2 = NHCOPh$) leads to a number of interesting transformations including *S*-alkylation and oxidative dimerisation.[385]



Reagents: i, $PhNH_2$,; ii, $PhNH_2 + S$

Scheme 8.



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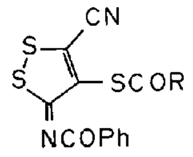
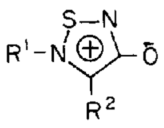


303

F. *Thiadiazoles*

1. 1, 2, 5-*Thiadiazolium*-3-*olates* (**304**).



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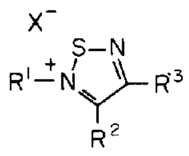

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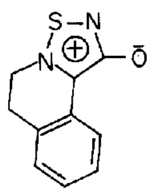


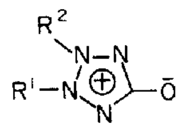
306

Treatment of α-amino amides ($R^1NH\text{-}CHR^2\text{-}CONH_2$; R^1 = alkyl, R^2 = aryl) with sulphur monochloride in DMF yields the 1, 2, 5-thiadiazolium chlorides (**305**; R^1 = alkyl, R^2 = aryl, $R^3 = OH$, $X = Cl$) which are readily deprotonated giving the meso-ionic derivatives (**304**). The tricyclic derivative (**306**) has been prepared similarly.[386]

Alkaline hydrolysis of compound (**304**; $R^1 = Me$, $R^2 = Ph$) yields an imino-amide ($MeN{=}CPh\cdot CONH_2$) and sodium borohydride reduction affords the amide ($MeNH\text{-}CHPh\cdot CONH_2$). Meerwein alkylation ($Et_3O^+BF_4^-$) of compound (**304**; $R^1 = Me$, $R^2 = Ph$) gives the salt (**305**; $R^1 = Me$, $R^2 = Ph$, $R^3 = OEt$, $X = BF_4$) which reacts with methylamine giving the salt (**305**; $R^1 = Me$, $R^2 = Ph$, $R^3 = NHMe$, $X = BF_4$).[386]

G. *Tetrazoles*

1. 1, 2, 3, 4-*Tetrazolium*-5-*olates* (**307**).



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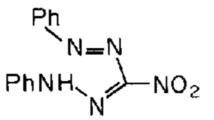

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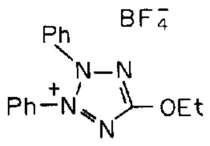


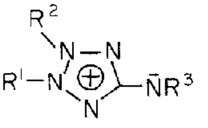
309

Oxidation of 3-nitro-1,5-diphenylformazan (**308**) by pentyl nitrite yields 2,3-diphenyl-1,2,3,4-

tetrazolium-5-olate (**307**; $R^1 = R^2 = Ph$) (79%). Meerwein alkylation ($Et_3O^+BF_4^-$) of this compound affords the 5-ethoxy tetrazolium salt (**309**): attempts to displace the ethoxy group by nucleophiles were unrewarding.[365] Pyrolysis of compound (**307**; $R^1 = R^2 = Ph$) at 150° results in isomerisation to the type A meso-ionic 1, 3-diphenyl-1, 2, 3, 4-tetrazolium-5-olate (**263**; $R^1 = R^2 = Ph$) (45%) (Section III M, 1).[141,358]

Two X-ray studies of the crystal structure of compound (**307**; $R^1 = R^2 = Ph$) have been reported and are consistent with the meso-ionic structure.[205,387]

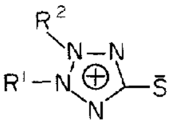
2. 1, 2, 3, 4-*Tetrazolium-5-aminides* (**310**).



310

No new work on this meso-ionic system has been reported since the subject was last reviewed.[6]

3. 1, 2, 3, 4-*Tetrazolium-5-thiolates* (**311**).



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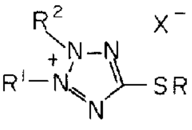

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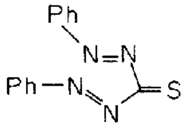
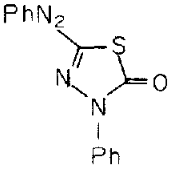


313

Dehydrodithizone (**311**; $R^1 = R^2 = Ph$) which is normally prepared by oxidation of dithizone ($PhN_2CSNHNHPh$)[1,388] has recently been prepared by reaction of diphenylthiocarbazide [$(PhNHNH)_2CS$] with diethoxydisulphide [$(EtO)_2S_2$].[389] Alkylation of dehydrodithizone (**311**; $R^1 = R^2 = Ph$) occurs on the exocyclic sulphur atom: treatment with chloroacetic acid yields the tetrazolium chloride (**312**; $R^1 = R^2 = Ph$, $R = CH_2CO_2H$, $X = Cl$)[388] and Meerwein ethylation gives the tetrafluoroborate (**312**; $R^1 = R^2 = Ph$, $R = Et$, $X = BF_4$).[365] Attempted displacement of the thioethoxy group in the latter salt yielded 3-ethylthio-1, 5-diphenylformazan (87%).[365] Thermolysis of dehydrodithizone (**311**; $R^1 = R^2 = Ph$) gives a low yield (16%) of the isomeric Type A 1, 2, 3, 4-tetrazolium-5-thiolate (**265**; $R^1 = R^2 = Ph$) (Section III M, 3).[141,358]

Many of the reactions of dehydrodithizone (**311**; $R^1 = R^2 = Ph$) can be interpreted in terms of participation of the acyclic valence tautomer (**313**)[6] (see Scheme 2). Treatment with iron pentacarbonyl [$Fe(CO)_5$] yields the 1, 3, 4-thiadiazolone (**314**).[141,390] Addition of β-piperidino styrene gives the adduct (**315**) and pyrrolidino cyclohexene affords the adduct (**316**).[391] With the electron rich 1-diethylamino-propyne the major product is the pyrazole (**317**).[391] Reaction with 2-(dialkylamino) indenes gives products with the general structure (**318**).[391,392]



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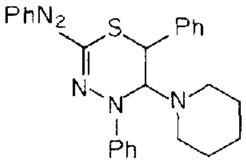

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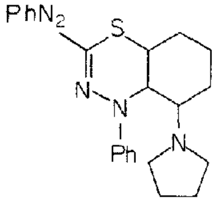

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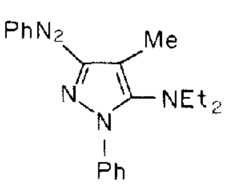

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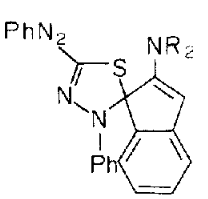

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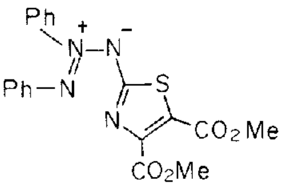
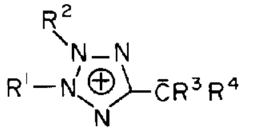


319

Addition of dimethyl acetylenedicarboxylate to dehydrodithizone (**311**; $R^1 = R^2 = Ph$) gives a product which has been shown by an X-ray analysis to have the dipolar structure (**319**):[393] reaction with tetraphenylcyclopentadienone gives a similar adduct.[394] Treatment of dehydrodithizone with benzyne yields 2-phenylazobenzothiazole.[393]

Other studies of 1, 2, 3, 4-tetrazolium-5-thiolates (**311**) include a description of their electronic absorption spectra[395] and their polarographic reduction.[396] Several Ni(II) and Cu(II) complexes of dehydrodithizone have been prepared.[397]

4. 1, 2, 3, 4-*Tetrazolium-5-methylides* (**320**).



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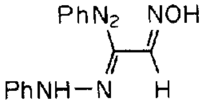

321

Mild oxidation of an authentic sample of the biformazan (**268**) (see also Section III M, 4) with tetrakis (4-methylphenyl)hydrazine [$(p \cdot Me \cdot C_6H_4)_4N_2$] yields the red-brown meso-ionic 1, 2, 3, 4-tetrazolium-5-methylide (**320**; $R^1 = R^2 = Ph$, $R^3 = R^4 = PhN_2$) (40%). Similarly, lead tetra-acetate oxidation of compound (**321**) gives the derivative (**320**; $R^1 = R^2 = Ph$, $R^3 = H$, $R^4 = NO$). These compounds are the first reported examples of Type B meso-ionic 1,2,3,4-tetrazolium-5-methylides (**320**).[398]

V. CONCLUSION

The number of papers published during the period 1976–1980 which describe the chemistry of meso-ionic systems is clear indication of the continuing interest in this class of heterocycles. In an earlier review Ollis and Ramsden have proposed[6] that the term meso-ionic be restricted to five membered heterocycles of types A and B (see Section II) and this is the definition which has been used to determine the scope of this review. We believe that the restriction of the term meso-ionic to these two classes of heterocycle is essential if the term is to retain its usefulness. This restriction on the use of the term has the clear advantage that meso-ionic compounds are precisely defined and their relationship to other heterocyclic molecules is readily understood.

The modified definition of the term meso-ionic has been welcomed by many chemists. However, some authors continue to describe other classes of dipolar species as meso-ionic. This can only lead to confusion. We strongly urge heterocyclic chemists to adopt the definition of meso-ionic which has been advocated by Ollis and Ramsden. A system of classifying and naming other classes of dipolar heterocyclic will be the subject of a future publication.[399]

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[1] E. Fischer and E. Besthorn, *Ann.* **212**, 316 (1882).
[2] W. Baker and W. D. Ollis, *Quart. Rev.* **11**, 15 (1957).
[3] J. C. Earl and A. W. Mackney, *J. Chem. Soc.* 899 (1935).
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